CONTRACEPTION

CHI Formulary Development Project

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Contents

Related Documents

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Abbreviations

ANSM	National Agency of Drug Safety
BMI	Body Mass Index
CADTH	Canadian Agency for Drugs and Technologies in Health
CDC	Centers for Disease Control and Prevention
CHC	Combined Hormonal Contraception
CHI	Council of Health Insurance
CIN	Cervical intraepithelial neoplasms
CNGOF	French National College of Obstetricians and Gynecologists
COC	Combined Oral Contraceptives
Cu-IUD	Copper-Bearing Intrauterine Device
CVA	Cerebrovascular Accident
CVD	Cardiovascular Disease
CVR	Contraceptive Vaginal Rings
DMPA	Depo-Medroxyprogesterone Acetate
DRSP	Drospirenone
EC	Emergency Contraception
ECP	Emergency Contraceptive Pills
EE	Ethinyl Estradiol
GnRH	Gonadotropin Releasing Hormone
GnRHa	Gonadotropin Releasing Hormone Analog
GoR	Grade of Recommendation
HAS	Haute Autorité de Santé
HFI	Hormone Free Interval
HIV	Human Immunodeficiency Virus
HNPCC	Hereditary Non-Polyposis Colon Cancer
HPV	Human Papillomavirus
HRT	Hormone Replacement Therapy
HSG	Hysterosalpingogram
HTA	Health Technology Assessment
IDF	Insurance Drug Formulary
IM	Intramuscular

INCa	Institut National de Cancer
IQWIG	Institute for Quality and Efficiency in Healthcare
IUD	Intrauterine Device
LARC	Long-Acting Reversible Contraceptive
LH	Luteinizing Hormone
LNG	Levonorgestrel
LNG-IUS	Levonorgestrel Intrauterine System
LoE	Level of Evidence
MBL	Menstrual blood loss
NICE	National Institute for Health and Care Excellence
NSAID	Nonsteroidal Anti-Inflammatory Drug
PBAC	Pharmaceutical Benefits Advisory Committee
PCOS	Polycystic Ovarian Syndrome
PID	Pelvic Inflammatory Disease
POC	Progestogen-Only Contraception
RA	Rheumatoid Arthritis
SC	Subcutaneous
SDM	Standard Days Method
SLE	Systemic Lupus Erythematosus
SoA	Strength of Agreement
SPRM	Selective Progesterone Receptor Modulator
STD	Sexually Transmitted Disease
STI	Sexually Transmitted Infection
TMRG	Tumeurs Malignes Rares Gynecologiques
U.S.SPR	United States Selected Practice Recommendations
UPA	Ulipristal Acetate
USMEC	United States Medical Eligibility Criteria
VRF	Vascular Risk Factor
VTE	Venous Thromboembolism

Executive Summary

Contraception refers to the deliberate and intentional use of methods, techniques, or devices to prevent pregnancy by inhibiting fertilization or implantation of a fertilized egg. It allows individuals or couples to control their reproductive choices and family planning by avoiding or spacing pregnancies according to their preferences and circumstances.

Contraceptive drugs can be classified into various categories based on their mode of action, administration route, and hormonal composition. Here is a classification of contraceptive drugs:

1. **Hormonal contraceptives**
    a. **Combined hormonal contraceptives (CHCs)**

Combined oral contraceptives (COCs): contain both estrogen and progestin.

Contraceptive patch: delivers estrogen and progestin through the skin.

Vaginal ring: releases estrogen and progestin when inserted into the vagina.

    b. **Progestin-only contraceptives (POCs)**

Progestin-only pills (Minipills): contain progestin only.

Progestin implants: small rods implanted under the skin, providing slow-release progestin.

Progestin injections (Depo-Provera): administered via injection every 12 weeks.

Progestin intrauterine device (IUD): releases progestin locally in the uterus.

2. **Non-Hormonal Contraceptives**
    a. **Barrier methods**

Male condoms: Placed over the penis to prevent sperm from reaching the cervix.

Female condoms: Inserted into the vagina to create a barrier.

Cervical caps: Placed over the cervix to block sperm.

Diaphragms: Covers the cervix and must be used with spermicide.

    b. **Intrauterine devices (IUDs)**

Copper IUD: Releases copper ions, which are toxic to sperm.

Progestin IUD: Releases progestin locally in the uterus.

    c. **Spermicides:** Chemical substances that immobilize or kill sperm.

3. **Emergency contraceptives**

These are used after unprotected intercourse to prevent pregnancy. They may contain progestin or a combination of hormones.

4. **Natural Methods**

These methods involve tracking a woman's natural fertility signs to determine when she is most and least fertile. Examples include the fertility awareness-based methods (FABMs) like the calendar method, cervical mucus method, and basal body temperature method.

5. **Permanent Contraception**

Irreversible methods to prevent pregnancy.

   a. **Tubal ligation (female sterilization):** blocking or sealing the fallopian tubes.

   b. **Vasectomy (Male Sterilization):** cutting or blocking the vas deferens, preventing the release of sperm during ejaculation.

The rapid expansion of the Saudi Arabian economy has led to significant sociodemographic shifts, creating a greater demand for birth spacing and the utilization of contraceptive methods. A recent investigation sought to assess the levels of knowledge, attitudes, and behaviors pertaining to contraception usage in the Makkah region of Saudi Arabia[1].

The findings indicated that participants possessed an awareness of and held positive attitudes towards family planning. However, their understanding of family planning and its implementation was found to be deficient. It is recommended that efforts be focused on heightening awareness and providing education to enhance both knowledge and practical application of family planning strategies. Saudi Arabia's overall fertility rate and birth rate substantially exceed those of Western countries. Nevertheless, the birth rate has notably decreased in recent times, dropping from 26.91 in 2000 to 17.09 in 2020.

The sociodemographic landscape of Saudi society is evolving rapidly, particularly in relation to women's employment and education. This transformation significantly influences attitudes and practices concerning fertility, leading to increased birth spacing and consequently, the greater adoption of contraceptive methods.

Within the Kingdom of Saudi Arabia, several contraception options are available, with oral contraceptives being the most prevalent, followed by intrauterine devices (IUDs). Interestingly, some studies have indicated that barrier contraceptives, such as condom usage, rank as the second most employed method, surpassing IUDs. Moreover, it is important to acknowledge that contraceptives serve purposes beyond family planning and the prevention of unintended pregnancies.

These applications include the management of menstrual disorders, reduction in the risk of ovarian and endometrial malignancies, symptomatic relief for polycystic ovarian syndrome (PCOS), and safeguarding against sexually transmitted diseases (STDs).

The prevalence of contraception varies widely across different regions of the world due to factors such as cultural, religious, socioeconomic, and healthcare-related influences. Here's a general overview of contraception prevalence in different regions:

- North America and Europe: Contraception use is generally widespread and widely accepted in these regions. A variety of methods are available and accessible, and there is typically a high awareness of family planning.
- Latin America and the Caribbean: Contraception prevalence varies across countries in this region. While some countries have high contraceptive use, others may have lower rates due to limited access to healthcare and cultural factors.
- Asia: Contraception use is diverse across Asian countries. Some countries have high contraceptive prevalence rates, while others may have lower rates due to cultural norms, limited access to resources, and varying levels of awareness.
- Africa: Contraception prevalence varies widely within different subregions of Africa. Factors such as limited access to healthcare, lack of education, and cultural factors can impact contraceptive use.
- Middle East: Contraception prevalence can vary significantly across countries in the Middle East due to cultural and religious influences. Some countries may have high usage rates of certain methods, while others may have lower rates.

It's important to note that contraception prevalence is not uniform within each region, and there are significant variations between countries and communities. Efforts to improve access to family planning services, education, and awareness play a crucial role in increasing contraception use and promoting reproductive health worldwide.

The management of contraception involves various aspects, including selecting appropriate contraceptive methods, providing education and counseling, ensuring proper usage, and addressing any concerns or side effects. Here are key points to consider in the management of contraception:

Patient counseling and education: Provide comprehensive information about available contraceptive methods, their effectiveness, benefits, risks, and potential side effects. Tailor counseling to the individual's medical history, lifestyle,

preferences, and family planning goals. Address any misconceptions or concerns the patient may have about contraception.

Method selection: Collaborate with the patient to choose a contraceptive method that aligns with their needs and preferences. Consider medical contraindications, allergies, and any pre-existing conditions that may impact method choice. Discuss short-term and long-term contraceptive options, including reversible and permanent methods.

Initiation and proper use: Provide clear instructions on how to use the chosen contraceptive method correctly. Demonstrate proper usage of barrier methods, such as condoms, if applicable. Ensure that the patient understands the importance of consistent and correct use to maximize effectiveness.

Follow-up and monitoring: Schedule follow-up appointments to assess the patient's experience with the chosen method and address any issues. Monitor for side effects, complications, or changes in health that may warrant a reevaluation of the chosen method.

Side effects and complications: Educate patients about common side effects and potential complications associated with their chosen method. Provide guidance on managing side effects and when to seek medical assistance.

Contraceptive adherence: Discuss strategies to improve adherence, such as setting reminders, tracking usage, and managing missed doses. Reinforce the importance of adherence for maintaining contraceptive effectiveness.

Emergency contraception: Educate patients about emergency contraception options and when they should be used. Provide information on accessing emergency contraception in a timely manner.

Switching or discontinuing methods: Address any concerns or reasons for wanting to switch or discontinue the current contraceptive method. Guide the patient through the process of transitioning to a new method or discontinuing use, ensuring that they remain protected from unintended pregnancies.

Long-term planning: Discuss future reproductive plans and provide information on fertility restoration after discontinuing certain methods.

Informed consent: Ensure that patients have a clear understanding of the benefits, risks, and alternatives associated with their chosen contraceptive method. Patient must be fully aware and educated about the planned contraceptive method, an informed consent should be obtained for invasive or irreversible methods.

Special populations: Tailor contraceptive management to the needs of specific populations, such as adolescents, postpartum women, women with medical conditions, and individuals with disabilities.

Collaboration and referrals: Collaborate with other healthcare providers, such as gynecologists and reproductive health specialists, as needed for complex cases or specialized care. Refer patients for additional support, counseling, or specialized services when appropriate.

Effective contraceptive management involves a patient-centered approach that takes into account individual preferences, medical considerations, and lifestyle factors. Open communication, education, and ongoing support are essential components of successful contraceptive management.

The management of contraception involves a multidisciplinary approach. Section 3 provides a full description of contraception options for the management of contraception on the global market. All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) reflecting specific drug class role in the management of contraception.

This report compiles all clinical and economic evidence related to contraception according to the relevant sources. The ultimate objective of issuing contraception guidelines by the Council of Health Insurance is to update the Insurance Drug Formulary (IDF) (CHI Drug Formulary) with **the best available clinical and economic evidence related to drug therapies, ensuring timely and safe access to contraception drugs in Saudi Arabia**. The focus of the review was on Saudi, North American, European, and international guidelines issued within the last five years in addition to recent systematic reviews and Meta-Analysis.

Main recommendations issued by different Health Technology Assessment (HTA) bodies on the use of the current medications in contraception were reviewed and summarized. These include the National Institute for Health and Care Excellence (NICE), the Canadian Agency for Drugs and Technologies in Health, Haute Autorité de Santé (HAS), the Institute for Quality and Efficiency in Healthcare (IQWIG), and the Pharmaceutical Benefits Advisory Committee (PBAC). Section 2.0 provides a full description of each pharmacological agent with final statements on the placement of contraceptive methods. All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) reflecting specific drug class role in the management of contraception.

Major recommendations for suggested contraception methods are summarized in the table below:

Table 1. Recommendations for SFDA Registered Drugs and Devices Used for Contraception

Class of Drug	Medication	Indication	Line of Therapy	Recommendation	Evidence
Combined Hormonal Contraception (CHC) tablet	Ethinylestradiol and Desogestrel	Contraception	2nd Line	A	1
	Ethinylestradiol and Levonorgestrel	Contraception	1st Line	A	1
Progesterone only pill	Levonorgestrel	Contraception Emergency Contraception	2nd Line 1st Line	A	1
	Desogestrel	Contraception	2nd Line 1st Line in the presence of a history of thrombosis	A	1
	Drospirenone	Contraception	2nd Line 1st Line in the presence of a history of thrombosis	A	1
Intra Uterine Device	Copper-Intrauterine Device (Cu-IUD)	Contraception Emergency Contraception	1st Line 1st Line	A	1
	LNG-IUD	Contraception	2nd Line	A	1
Implant	Etonogestrel	Contraception	2nd Line for women with contraindications or intolerance to CHC and IUD, or for women facing challenges with adherence to oral contraception	A	1

Injection	Medroxyprogesterone acetate (DMPA)	Contraception	2nd Line for women with contraindications or intolerance to CHC	A	1
Ring	Ethinylestradiol and Etonogestrel	Contraception	1st Line	A	1

Section 1.0 Summary of Reviewed Clinical Guidelines and Evidence

1.1 KSA Guidelines

1.1.1 Saudi Society of Family and Community Medicine

The Saudi Society of Family and Community Medicine issued clinical practice guidelines for the use of contraception[2]. The main recommendations are summarized below.

Table 2. Classification of Contraception

Classification of contraceptive methods	
Long-acting reversible contraception LARC	**Intrauterine Contraception (IUC)** Copper-Bearing Intrauterine Device (Cu-IUD) Levonorgestrel Intrauterine System (LNG-IUS)
	Progestogen-only Contraception (POC) Progestogen only implant Progestogen only injectable
Reversible contraception	**Progestogen only pill**
	Combined Hormonal Contraception (CHC) Combined oral contraception Combined transdermal patches Combined Vaginal rings
	Emergency Contraception (EC) COC

	Copper-Bearing IUD Oral EM Oral Progesterone-Only Ulipristal Acetate (UPA)
	Barrier Method Condom, diaphragm Coitus interrupts
Permanent	**Vasectomy for men** **Tubal Ligation for women**

The Saudi guidelines follows the United States Medical Eligibility Criteria (USMEC) for Contraceptive Use that includes recommendations for using specific contraceptive methods by women and men who have certain characteristics or medical conditions (table 3). These recommendations are intended to assist health care providers when they counsel women, men, and couples about contraceptive method choice.

Table 3. U.S. Medical Eligibility Criteria (USMEC) for Contraceptive Use

1	No restriction (method can be use)
2	Advantages generally outweigh theoretical or proven risks
3	Theoretical or proven risks usually outweigh the advantages
4	Unacceptable health risk (method not to be used)

Selecting an appropriate contraception method requires an all-encompassing and patient-centered strategy.

- Gather relevant medical history encompassing family, sexual, cervical smears, social aspects, medication usage, and prior contraceptive methods.
- Assess vital parameters like blood pressure, weight, and BMI.
- Rule out potential sexually transmitted infections (STIs) and perform a pregnancy test if applicable.
- Understand the patient's contraception preferences and priorities.
- Advocate for the use of barrier methods alongside the chosen option to enhance STI protection.
- Scrutinize for any contraindications using the United States Medical Eligibility Criteria (USMEC).

Following a thorough assessment of these variables, the medical practitioner can undertake the following actions:

1. Consider Long-Acting Reversible Contraceptives (LARCs) as the primary option.
2. Consider Combined Hormonal Contraception (CHC) under the following circumstances:
    - LARCs are not suitable.
    - Breastfeeding is not ongoing.
    - There are no contraindications involving estrogen (such as deep vein thrombosis, elevated BMI, hypertension, migraine with aura, smoking, cardiovascular disease, history of breast or cervical cancer).
    - The United States Medical Eligibility Criteria (USMEC) indicates a rating of 1-2.
3. Offer the progesterone-only pill (POC) in cases where CHC is deemed inappropriate.
4. Provide alternative choices if POC is not considered suitable.

Evaluating medical suitability for combined hormonal contraception (CHC)

USMEC Category 1 or single USMEC Category 2 rating

<u>First-line approach</u>:

1. Oral formulation: monophasic standard strength OR monophasic low strength if cardiovascular disease (CVD) risk factors are present.
2. Provide insight into:
    - Usage guidelines
    - Pros and cons
    - Potential adverse effects and cautions
    - Protocol for missed doses, adherence
    - Guidance for use during illness
    - Key warning signs

<u>Second-line alternatives</u>:

1. For elevated estrogen levels: opt for monophasic low strength formulations or combine monophasic low strength with 3rd generation progestogens.
2. For excessive progesterone: employ monophasic standard strength with 3rd generation progesterone.
3. Managing acne or hirsutism: recommend COC with androgenic-minimized progestogens like desogestrel, gestodene, or norgestimate.

4. Addressing cycle irregularities: adjust estrogen dosage, modify progesterone component.

Follow-Up Routine:

Initiate assessment after 3 months, followed by annual checkups

- Medical Suitability Reassessment
- User Satisfaction & Adherence
- Potential Drug Interactions
- Exploration of Alternative Contraceptive Methods
- Blood Pressure Monitoring

A. Intrauterine Contraception (IUC)

1. Copper-Bearing Intrauterine Device (Cu-IUD)

Illustrative Example:

Primary Choice (10-year authorization): Copper T380 A®

Secondary Options (5-year authorization): Copper T380®, 7 MED 380, Nova T380

Indication: Contraception

Optimal Insertion Timing:

Preferred to avoid heavy menstruation days. Ideally inserted after the conclusion of menstruation and prior to the calculated implantation timeframe. For post-delivery insertion, recommend 4-6 weeks postpartum.

Backup Contraception Requirements:

1. Initiation: No additional measures required.
2. Switching: No additional measures needed.
3. Replacement: No supplementary actions required.
4. Removal: If removal occurs after the third day of the menstrual cycle, alternative contraception should be utilized for at least 7 days post-removal if sexual intercourse takes place.

Evaluation and Monitoring Guidelines:

Initial gynecological assessment before insertion.

Follow-up visit 6-8 weeks post-insertion, and then annually.

Side Effects and Counseling Considerations:

1. Device-Related: Slightly elevated risk of ectopic pregnancy and pelvic infection (highest risk in the initial 20 days), potential for uterine injury, possible epileptic episodes upon insertion, risk of hemorrhage during insertion, and an extremely rare chance of uterine perforation (patients should be educated on thread inspection and immediate reporting of signs of perforation).
2. Menstrual Cycles: May result in menstrual irregularities, especially increased menstrual flow.

Contraindications:

USMEC Category 4: Deformed uterine cavity, Cervical cancer pending treatment (at initiation), Onset of endometrial cancer (at initiation), Gestational trophoblastic disease (Persistent elevation of ß-hCG levels or malignancy), Immediate aftermath of septic abortion, Ongoing pelvic inflammatory disease, Postpartum sepsis, Pregnancy, Ongoing purulent cervicitis or infections like chlamydia or gonorrhea (at initiation), Pelvic tuberculosis (at initiation).

USMEC Category 3: Gestational trophoblastic disease (Diminishing or undetectable ß-hCG levels), Human Immunodeficiency Virus (HIV) infection or undergoing Antiretroviral therapy (at initiation), Complex Solid Organ Transplantation, Severe thrombocytopenia (at initiation), Continuing pelvic tuberculosis, Unexplained vaginal bleeding.

2. Levonorgestrel Intrauterine System (LNG-IUS)

Illustrative Example: • Primary Selection (5-year approval): Mirena®

Indication: Contraception, management of menorrhagia (Mirena® favored), inclusion in Hormone Replacement Therapy (HRT), effectiveness for up to 4 years

Optimal Insertion Timing:

Within 7 days of menstruation onset OR

Anytime if reasonable certainty of non-pregnancy OR

Anytime for replacement OR

At least 4 weeks post-delivery

Application Guidelines:

1. Initiation: Required within 7 days; applicable if more than 7 days after menstrual cycle commencement.
2. Switching: Required within 7 days; applicable if more than 7 days after onset of menstruation.

3. Replacement: Ensured with 7 days of contraception prior to removal.
4. Removal: Followed by 7 days of contraception post-removal.

Evaluation and Monitoring:

Initial gynecological assessment before insertion.

Follow-up visit 6-8 weeks post-insertion, then annually.

Side Effects and Counseling Considerations:

1. Device-Related: Consistent with Cu-IUD
2. Menstrual Cycles: Early stages may entail irregular, prolonged, or infrequent menstrual bleeding for 3-6 months (which might continue in some individuals).
3. Progestogen-Related Effects: Typically resolve within months (encompassing breast changes, mood alterations, hirsutism, reduced libido, nervousness, ovarian cysts, weight variation). Uncommon occurrences include alopecia and edema.

Contraindications:

USMEC Category 4:

- Distorted uterine cavity
- Cervical cancer awaiting treatment (at initiation)
- Onset of endometrial cancer (at initiation)
- Gestational trophoblastic disease (Persistently elevated ß hCG levels or malignant disease)
- Immediate post-septic abortion
- Current pelvic inflammatory disease (at initiation)
- Puerperal sepsis
- Pregnancy
- Ongoing purulent cervicitis or infections like chlamydia or gonorrhea (at initiation)
- Pelvic tuberculosis (at initiation)

USMEC Category 3:

- Gestational trophoblastic disease (Decreasing or undetectable ß hCG levels)
- Human Immunodeficiency Virus (HIV) infection or undergoing Antiretroviral therapy (at initiation)

- Complex Solid Organ Transplantation
- Severe thrombocytopenia (at initiation)
- Continuing pelvic tuberculosis
- Unexplained vaginal bleeding

Additional USMEC Category 3 Criteria:

- Identical to Cu IUD, except for the following:
    - Current and historical ischemic heart disease (continuation)
    - Hepatocellular adenoma
    - Malignant liver tumors
    - Presence of positive or unknown antiphospholipid antibodies

B. Progesterone-only contraception (POC)

1. Subdermal implants

Illustrative Example: Etonogestrel (Implanon) (Valid for 3 years)

Indication: Long-term, reversible contraception

Side Effects:

- Common: Menstrual cycle irregularities, breast anomalies, hair loss, mood swings, hirsutism, vertigo, reduced libido, unease, ovarian cysts, weight fluctuations, fluid retention, mood changes, gas, sleep disruption.
- Uncommon: Embolism and thrombosis, vulvovaginal infections. Specific Adverse Effects: Implant migration, potential neurovascular damage.

2. Injection

Illustrative Example: (Medroxyprogesterone) 12 Weekly Subcutaneous (SC) or Deep Intramuscular (IM) Injection: Depo-Provera®, Sayana Press®

Indication: Extended and reversible contraception. Norethisterone injections can be employed for short-term contraception via IM route (8 weeks).

Side Effects:

- Common: Menstrual cycle irregularities, breast anomalies, hair loss, mood fluctuations, hirsutism, dizziness, reduced libido, unease, ovarian cysts, weight shifts, fluid retention, mood variations, gas, sleep disruption.
- Uncommon: Embolism and thrombosis, vulvovaginal infections.
- Specific Adverse Effects: Hypertension, vertigo, osteoporosis (monitoring not mandatory), lipodystrophy.

Missed Dose or Delayed Administration:

If the time span between doses exceeds 12 weeks and 5 days for IM administration or 13 weeks and 5 days for SC administration, confirm the absence of pregnancy and employ additional contraception for 7 days.

3. Progestin-only pill (POP)

Illustrative Example: Desogestrel 75mg (Cerazette®)

Indication: Contraception. Norethisterone (for endometriosis, halting bleeding in Dysfunctional Uterine Bleeding (DUB) and menorrhagia, alleviating dysmenorrhea, postponing menstruation)

Side Effects:

- Common: Menstrual cycle irregularities, breast anomalies, hair loss, mood changes, hirsutism, dizziness, reduced libido, unease, ovarian cysts, weight shifts, fluid retention, mood fluctuations, gas, sleep disruption.
- Uncommon: Embolism and thrombosis, vulvovaginal infections.
- Specific Adverse Effects: For Desogestrel: Intolerance to contact lenses, erythema nodosum.

Missed Dose or Delayed Administration:

Consume the missed pill promptly and take the next pill at the usual time. Employ supplementary contraception (condoms or abstain) for 2 days. If unprotected sexual intercourse occurred within 48 hours of resuming the POP, consider Emergency Contraception (EC).

Contraindications for All Progestin-Only Contraception (POC):

USMEC Category 4 for All POC:

- Ongoing breast cancer
- Acute porphyrias

USMEC Category 3 for All POC:

- Historical or non-evident breast cancer for a minimum of 5 years
- Migraine with aura (continuation)
- Severe cirrhosis
- Ongoing or historical Ischemic Heart Disease (continuation)
- Hepatocellular adenoma
- Malignant liver tumors
- Previous history of Cerebrovascular Accident (CVA) (continuation)

- Systemic Lupus Erythematosus (SLE) with Positive (or unknown) antiphospholipid antibodies

USMEC Category 3 for Injection (in addition to common contraindications):

- Concurrent Diabetes Mellitus with Nephropathy, Retinopathy, or Neuropathy, or ≥20 years' duration, or with vascular disease
- Hypertension (systolic ≥160 or diastolic ≥100) or with vascular disease
- Current or historical ischemic heart disease (initiation)
- Multiple risk factors for arterial cardiovascular disease, including age, smoking, diabetes, and hypertension
- Rheumatoid Arthritis (RA) with ongoing immunosuppressive therapy
- Historical Cerebrovascular Accident (initiation)
- Severe thrombocytopenia (initiation)
- Unexplained vaginal bleeding

USMEC Category 3 for POP (besides common contraindications):

- Historical bariatric surgery (Malabsorptive procedures)
- Specific antiretroviral therapy (Ritonavir-boosted protease inhibitors)
- Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)
- Certain antimicrobial therapy (Rifampicin or rifabutin)

C. Combined Hormonal Contraception (CHC)

Route

- Oral (COCs): 1st Line is oral admiration, other routes Not a cost-effective option, consider only if compliance issues with oral CHC and LARC unsuitable.
- Transdermal patches (CTP): apply on day 1, changed on day 8 and 15 then 7-day patch free period.
- Vaginal rings (CVR): 1 ring inserted on day 1 of cycle for 3 weeks, followed by 7-day ring free.

Preparations

- Monophasic: COCs containing a fixed amount of an estrogen & progestogen in each active tablet are termed ‘monophasic
- Multiphasic: COCs with varying amounts of the two hormones are termed ‘multiphasic’.

Preparation choice

- 1st line: Monophasic COCs containing ≤ 30 micrograms ethinylestradiol in combination with levonorgestrel or norethisterone (to minimize ca rdiovascular risk)
- Monophasic standard strength: Marvelon®, Microgynon®
- Monophasic low strength: Loestrin®
- Multiphasic: Logynon®, Synphase®, not available in KSA

Regimen

Traditionally: 21 days with a monthly withdrawal bleed during the 7-day hormone free interval (HFI)

Tailored CHC regimens can only be used with monophasic CHC containing (unlicensed use); Shortened HFI: 21 days of continuous use followed by a 4-day HFI;

Extended use (tricycling): 9 weeks of continuous use followed by a 4- or 7-day HFI; Flexible extended use: continuous use for 21 days or more followed by a 4 day

HFI when breakthrough bleeding occurs; Continuous use: continuous CHC use with no HFI.

Benefits of tailored regimens: less heavy or painful withdrawal bleeds, headaches, mood changes, and decreased risk of incorrect use

Indications

Menstrual symptoms, contraception

Side effects

- Estrogen related: Nausea, bloating, breast tenderness, vaginal discharge without infection, fluid retention.
- Progesterone related: (acne, headache, depression, breast symptoms, breakthrough bleeding, weight gain). Uncommon Alopecia; hypertension Rare Venous thromboembolism
- Breast cancer: small increase in the risk of having breast cancer diagnosed in women taking the COCs; this relative risk may be due to an earlier diagnosis. The most important factor for diagnosing breast cancer appears to be the age at which the contraceptive is stopped rather than the duration of use; any increase in the rate of diagnosis diminishes gradually during the 10 years after stopping and disappears by 10 years.
- Cervical cancer: Use of for 5 years or longer is associated with a small increased risk of cervical cancer; the risk diminishes after stopping and disappears by about 10 years.

Contraindications

USMEC4 Current & breast cancer, Acute porphyrias, Severe Cirrhosis, acute DVT, history of DVT with high risk for recurrence, major surgery with prolonged immobilization, migraine with aura or without if age ≥ 35, DM with (Nephropathy/retinopathy/neuropathy) or >20 years' duration) or with vascular disease, Hypertension (systolic ≥160 or diastolic ≥100) or with vascular disease, Hepatocellular adenoma, Malignant liver tumors, Peripartum cardiomyopathy, Postpartum: < 21 days, smoking Age ≥ 35, < 15 cigarettes/day, Solid organ transplantation: complicated, History of CVA, SLE with positive (or unknown) antiphospholipid antibodies, Thrombogenic mutations, complicated Valvular heart disease, acute or flare up of viral hepatitis.

USMEC 3 Breast cancer (past and no evidence of current disease for 5 years), breast feeding <1 month postpartum, history of DVT with low risk of recurrence, Gallbladder disease: current or medically treated, migraine without aura (continuation age < 35) (initiation age ≥ 35), hyperlipidemia, history of cholestasis post COC use, Hypertension: adequately controlled or systolic 140-159 or diastolic 90-99, inflammatory Bowel disease, postpartum 21-41 days with risk factors for VTE, smoking Age ≥ 35, < 15 cigarettes/day, Anticonvulsants: (phenytoin, carbamazepine, barbiturates, primidone, topiramate, coxcarbazepine, Lamotrigine Antimicrobial: rifampicin or rifabutin

Surgery

Discontinue COCs at least 4 weeks prior to major elective surgery, surgery to the legs or pelvis, or that involves prolonged immobilization of a lower limb. An alternative contraception should be used to prevent unintentional pregnancy, and CHC may be recommenced 2 weeks after full remobilization.

Healthcare benefits

Reduced risk of ovarian, endometrial, and colorectal cancer, Predictable bleeding patterns, Reduced dysmenorrhea and menorrhagia, Management of symptoms of PCOS, endometriosis and premenstrual syndrome, Improvement of acne, reduced menopausal symptoms, Maintaining bone mineral density in peri-menopausal females under the age of 50 years.

Efficacy

User-dependent; if used perfectly (i.e., correctly and consistently) failure rate is less than 1%

- Certain factors such as the weight, malabsorption (COC only), and drug interactions may contribute to contraceptive failure

Starting, switching & back up contraception requirements

Start in the first 5 days **OR** anytime if reasonably certain woman is not pregnant starting on day 6 of cycle or later, additional precautions (barrier methods) necessary during first 7 days.

Changing to COC containing different progestogen: If previous contraceptive used correctly start the first active tablet of new brand immediately.

Changing from progestogen-only tablet: If previous contraceptive used correctly, or pregnancy can reasonably be excluded, start new brand immediately, additional precautions (barrier methods) necessary for first 7 days.

After childbirth (not breast-feeding): 3 weeks in the absence of additional risk factors for thromboembolism, or 6 weeks after childbirth in the presence of additional risk factors for thromboembolism additional precautions (barrier methods) necessary for first 7 days.

After abortion, miscarriage, ectopic pregnancy, or gestational trophoblastic disease: additional contraceptive precautions (barrier methods) required for 7 days if started after day 5 following treatment.

Acne: If side effect for current COC switch to COC with progestogen that has minimal androgenic effect; desogestrel, gestodene, or norgestimate (Marvelon®)

- If severe acne unresponsive to topical therapy and oral antibiotics: **Co-Cyprindiol2000/35** tabs (not licensed solely for contraception). Higher VTE risk: Discontinue 3-4 cycles after acne has resolved. Continuation of treatment with co-cyprindiol should be under a specialist. Higher risk of meningioma.

Tables 4, 5, and 6 detail recommendations for missed dosing of oral contraceptives, contraception in special situations, and options for emergency contraception.

Table 4. Missed Pill Sick Day Rule (Retrieved from the Saudi Society of Family and Community Medicine Contraception Clinical Practice Guidelines)

Missed pill Sick day rule	If **ONE pill** has been missed (48 – 72 hours since last pill in current packet or 24- 48 hours late starting first pill in new pack)	IF **TWO** or **MORE** pills have been missed (>72 since last pill in current packet or >48 hours late starting first pill in new packet)
	Continuing contraceptive cover •The missed pill should be taken as soon as it is remembered •The remaining pills should be continued at the usual time	**Continuing contraceptive cover** •The most recent pill missed should be taken as soon as possible. – if vomiting or diarrhea, take the next pill as soon as tolerated •The remaining pills should be continued at the usual time. •Condoms should be used or sex avoided until seven consecutive active pills have been taken. This advice may be over-cautious in the second and third weeks, but the advice is a back-up in the event that further pills are missed.
	Minimising the risk of pregnancy EC is not usually required but may need to be considered if pills have been missed earlier in the packet or in the last week of the previous packet	**Minimising the risk of pregnancy** •*If pills are missed in the 1st week (Pills 1-7):* EC should be considered if unprotected sex occurred in the pill-free interval or in the first week of pill taking •*If pills are missed in the second week (pills 8-14):* No indication for EC if pills in the preceding 7 days have been taken consistently and correctly, provided the pills thereafter are taken correctly and additional contraceptive precautions used •*If pills are missed in the third week (pills 15-21):* **OMIT THE PILL-FREE INTERVAL** by finishing the pills in the current pack (or discarding any placebo tablets) and starting a new pack the next day

Table 5. Contraception in Special Situations

Condition	Options	Remarks
Age	POP, progesterone implants and LNG-IUD are safer options in older women with high CVD risk	Healthy, non-smoking women without specific risk factors for cardiovascular disease can continue use till age of 50-55
Postpartum	POP can be use immediately after delivery USMEC 1 COC can be used 4-6 weeks after delivery	IUDs can be placed at any time postpartum, although there may be an increased risk of expulsion if placed less than 4 weeks from delivery.
Breast feeding	POC	Exclusively breast-feeding mom, with amenorrhea, meet criteria of LAM method of contraception
Trophoblastic disease	Any	Trophoblastic disease treated with suction curettage and falling or undetectable HCG – Any hormonal method of contraception is considered appropriate
Obesity	POP and LNG-IUD is considered safer option in women with obesity and older than 35 yrs CHC is rated as USMEC 2 for women with obesity	Surgery compromising the absorption of oral medication like Roux-en-Y gastric bypass or biliopancreatic diversion – should not use oral contraception USMEC3
Migraine	No restriction in use of progesterone only methods in patient with migraine with or without aura USMEC1	CHC can be used in women with migraine without aura and no other risk factor for stroke USMEC2
Diabetes	POP, LNG-IUD and subdermal implants are suitable options	Uncomplicated Insulin and non-insulin dependent diabetics-hormonal methods of contraception are USMEC2 DMPA is also USMEC 3 in such

		patient as of increase lipoprotein profile
Hypertension	BP below 140/90- any contraceptive method can be used	Women on antihypertensive medication progesterone only or non-hormonal methods are recommended DMPA is also USMEC 3 in such patient as of increase lipoprotein profile
Mood disorders	Women with depressive disorders can use all methods of hormonal contraception	CHC does not modify the metabolism and effectiveness of SSRI and SNRI
Drug interaction	Women taking Rifampin and liver enzyme inducing antiepileptic and antiretroviral medication that interfere with contraceptive efficacy can use DMPA and LNG-IUD	COC and POP are not recommended because of increased contraceptive failure (USMEC 3) All other broad-spectrum antibiotics, antifungal and antiparasitic do not interfere with OC efficacy
Epilepsy	Avoid oral routes with certain anticonvulsants	Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)

Table 6. Emergency Contraception

Method	Dosage	Timing of Use After UPSI
Combined oral contraceptive	100 mcg of ethinyl estradiol plus 0.5 mg of levonorgestrel; two doses taken 12 hours apart 4 pills stat and 4 pills 12 h later	5 days
Levonorgestrel, split dose	0.75 mg; two doses taken at the same time or 12 hours apart	3 days
Levonorgestrel, single dose	1.5 mg, single dose	3 days
Ulipristal (Ella)	30 mg, single dose	5 days
Cu-IUD	Single device, can be left for long term contraception	5 days

Approaching the menopausal transition:

Considerations for contraceptive selection - options without limitations

- Barrier methods
- Copper intrauterine devices (IUDs)
- Levonorgestrel-releasing intrauterine system (IUS)
- Progesterone-only pill and implant
- Progesterone-only injections usable until the age of 50
- Age alone doesn't contraindicate combined hormonal contraception, but factors like smoking and migraine history need evaluation. A pill containing 20 mcg ethinylestradiol could be a reasonable initial choice if appropriate.

Choice influenced by non-contraceptive benefits:

- Vasomotor symptoms (hot flushes): Combined hormonal contraception might alleviate symptoms.
- Osteoporosis: Combined hormonal contraception could enhance bone mineral density, whereas depot medroxyprogesterone acetate may reduce BMD.
- Menstrual discomfort, bleeding irregularities: Combined hormonal contraception might mitigate symptoms. Progestogen-only methods could lessen pain.
- Heavy menstrual bleeding: The LNG IUS decreases bleeding and could lead to amenorrhea.

Important advice: hormone replacement therapy is not a contraceptive method.

Cessation of contraception

For those utilizing a non-hormonal contraception approach:

- ❖ Maintain usage until:
    - 1 year of amenorrhea after the age of 50, or
    - 2 years of amenorrhea prior to turning 50
- ❖ If menstruation persists beyond 55 years, recommend contraceptive use until 1 year of amenorrhea is attained.

For those using hormonal contraception:

- ❖ If a woman desires to discontinue contraception before the age of 50:

- Advise transitioning to a non-hormonal method and waiting for 2 years of amenorrhea (3 years if transferring from progestogen-only injections).

❖ Regarding combined hormonal contraception and progestogen-only injections:

- Continue until reaching 50 years of age, then switch to a non-hormonal method OR select from the following options: POP, Progestogen-only implant, or LNG IUS.
- Follow the guidelines for the chosen method.

❖ For POP, Progestogen-only implant, or LNG IUS:

- Maintain usage until age 55.
- If amenorrhea is not achieved by age 55, persist until 1 year of amenorrhea is reached.
- If amenorrheic and aged over 50, arrange for confirmation of menopause (two FSH readings taken six weeks apart, both yielding results above 30), and continue contraception for an additional year.

1.2 North American Guidelines

1.2.1 Center for Disease Control and Prevention (CDC) U.S. Selected Practice Recommendations (U.S. SPR) for Contraceptive Use (2016)

Unplanned pregnancy rates continue to persist at elevated levels within the United States, with roughly 45% of all pregnancies categorized as unintended. This proportion escalates among adolescents and young women, individuals from racial or ethnic minority backgrounds, as well as those with limited educational and financial resources. The occurrence of unintended pregnancies introduces an augmented likelihood of unfavorable outcomes for both maternal health and infant well-being. Notably, in the year 2010 alone, these pregnancies led to government healthcare expenses totaling $21 billion.

Approximately half of these unintended pregnancies materialize among women who were not employing contraception at the time of conception, while the remaining half are experienced by women who found themselves pregnant despite reported utilization of contraceptive methods. To mitigate the occurrence of unintended pregnancies, strategies must be deployed to assist women who are vulnerable to such situations, along with their partners, in selecting suitable contraceptive approaches. Moreover, comprehensive support is crucial in ensuring

the proper and consistent use of chosen methods, thereby effectively averting unplanned pregnancies.

According to WHO, to provide contraceptive options to clients in a manner that upholds and honors their fundamental human rights necessitates empowering clients to autonomously arrive at informed decisions. Regrettably, Women's choices are frequently undermined or restricted due to overt or underlying socio-economic and cultural factors. Viewed from a woman's perspective, the decisions she makes are contextual, shaped by the unique circumstances and prevailing societal and cultural influences. These choices manifest as intricate, influenced by a multitude of factors, and are susceptible to modification over time.

Engaging in the process of selecting contraceptive methods typically entails navigating trade-offs between the advantages and disadvantages associated with various options. These considerations fluctuate in alignment with individual situations, perceptions, and interpretations.

Essential elements to contemplate when opting for a specific contraceptive approach encompass the individual characteristics of potential users, the baseline risk of associated conditions, the profile of adverse effects linked to diverse products, financial implications, product availability, and the inclinations of the patient.

The main recommendations published by the U.S. SPR for contraceptive use are detailed below[3].

1.2.1.1 Summary of Changes from the 2013 U.S. SPR/ Updated Recommendations

Revised guidelines have been issued pertaining to the optimal timing for the initiation of routine contraception following the utilization of ulipristal acetate (UPA) emergency contraceptive pills:

It is recommended to counsel the individual to commence or recommence hormonal contraception no earlier than 5 days after employing UPA. Additionally, offer or prescribe the regular contraceptive method as required.

For methods that necessitate a healthcare provider visit, like depo-medroxyprogesterone acetate (DMPA), implants, and intrauterine devices (IUDs), deliberation can be given to initiating the method at the time of UPA use. However, the potential reduction in UPA's efficacy due to the regular contraceptive method must be balanced against the consequences of refraining from commencing a routine hormonal contraceptive approach.

During the 7 days subsequent to initiating or resuming standard contraception, or until the commencement of her subsequent menstruation—whichever transpires first—the woman should either abstain from sexual intercourse or use barrier contraception.

The immediate commencement of any nonhormonal contraceptive method is feasible following the utilization of UPA.

In the event of the absence of withdrawal bleeding within 3 weeks, it is advisable to recommend a pregnancy test to the woman.

1.2.1.2 New Recommendations

Updated guidelines have been introduced regarding the administration of medications to facilitate the process of inserting intrauterine devices (IUDs):

The routine utilization of misoprostol before IUD insertion is not recommended. However, there could be specific situations where misoprostol might provide benefits (e.g., for women who experienced a recent unsuccessful insertion attempt).

Implementing a paracervical block with lidocaine could potentially alleviate patient discomfort during the insertion of an IUD.

The WHO-conceived classification framework, later adopted by the Centers for Disease Control and Prevention CDC, serves to classify the relevance of different examinations or tests before commencing contraceptive methods:

Category A: These tests and evaluations are imperative and obligatory under all circumstances to ensure the secure and proficient application of the chosen contraceptive approach.

Category B: While these tests and evaluations significantly enhance the safety and effectiveness of usage, their execution can be evaluated within the larger scope of public health provisions, service delivery settings, or both. The decision to forego a particular examination or test should be weighed against the advantages of extending access to the contraceptive method.

Category C: These tests and evaluations do not notably contribute to enhancing the safety and efficacy of the selected contraceptive method.

1.2.1.3 Contraceptive Method Choice

The selection of the most suitable contraceptive method necessitates the careful consideration of numerous factors unique to each individual woman, man, or couple. Among these factors are aspects such as safety, efficacy, accessibility (encompassing availability and affordability), and personal acceptability. Although most contraceptive methods are generally safe for most women, the U.S. Medical Eligibility Criteria for Contraceptive Use (U.S. MEC) furnishes specific recommendations regarding the safety of particular methods for women with specific attributes or medical conditions. For a comprehensive overview, the

classification of medical eligibility criteria for contraceptive utilization (table 7) is provided.

Table 7. Categories of U.S. Medical Eligibility Criteria (MEC) for Contraceptive Use

U.S. MEC	Definition
1	A condition for which there is no restriction for the use of the contraceptive method.
2	A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
3	A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
4	A condition that represents an unacceptable health risk if the contraceptive method is used.

Maintaining the principle of informed voluntary choice concerning contraceptive methods is of utmost importance. In cases where applicable, contraceptive counseling plays a significant role in fostering the effective utilization of contraception.

The efficacy of contraceptive methods is contingent upon both the inherent effectiveness of the method itself and the consistency and accuracy of its application (figure 1). The extent of consistent and accurate usage can significantly vary based on factors like age, income, pregnancy prevention preferences, and cultural influences.

Intrauterine devices (IUDs) and implants fall under the category of long-acting reversible contraception (LARC). These methods boast high effectiveness due to their independence from regular user compliance. It is incumbent upon healthcare providers to furnish comprehensive counseling to all women, ensuring they are fully informed about the breadth of contraceptive options available and their respective levels of effectiveness, provided they are medically eligible. This enables them to make well-informed decisions regarding the most suitable method for their unique circumstances.

When deliberating upon a contraceptive method, the concept of dual protection against both human immunodeficiency virus (HIV) and other sexually transmitted diseases (STDs) should also be factored in. While hormonal contraceptives and intrauterine devices (IUDs) exhibit high efficacy in preventing pregnancies, they do not furnish any defense against STDs, including HIV. To effectively diminish the risk of HIV infection and other STDs such as chlamydial infection, gonococcal infection, and trichomoniasis, consistent and accurate utilization of male latex condoms is paramount.

Although the available evidence is limited, employing female condoms may offer a degree of protection against both the contraction and transmission of STDs. Irrespective of their chosen contraceptive method, all patients ought to receive counseling regarding condom usage and the potential exposure to STDs, encompassing HIV infection.

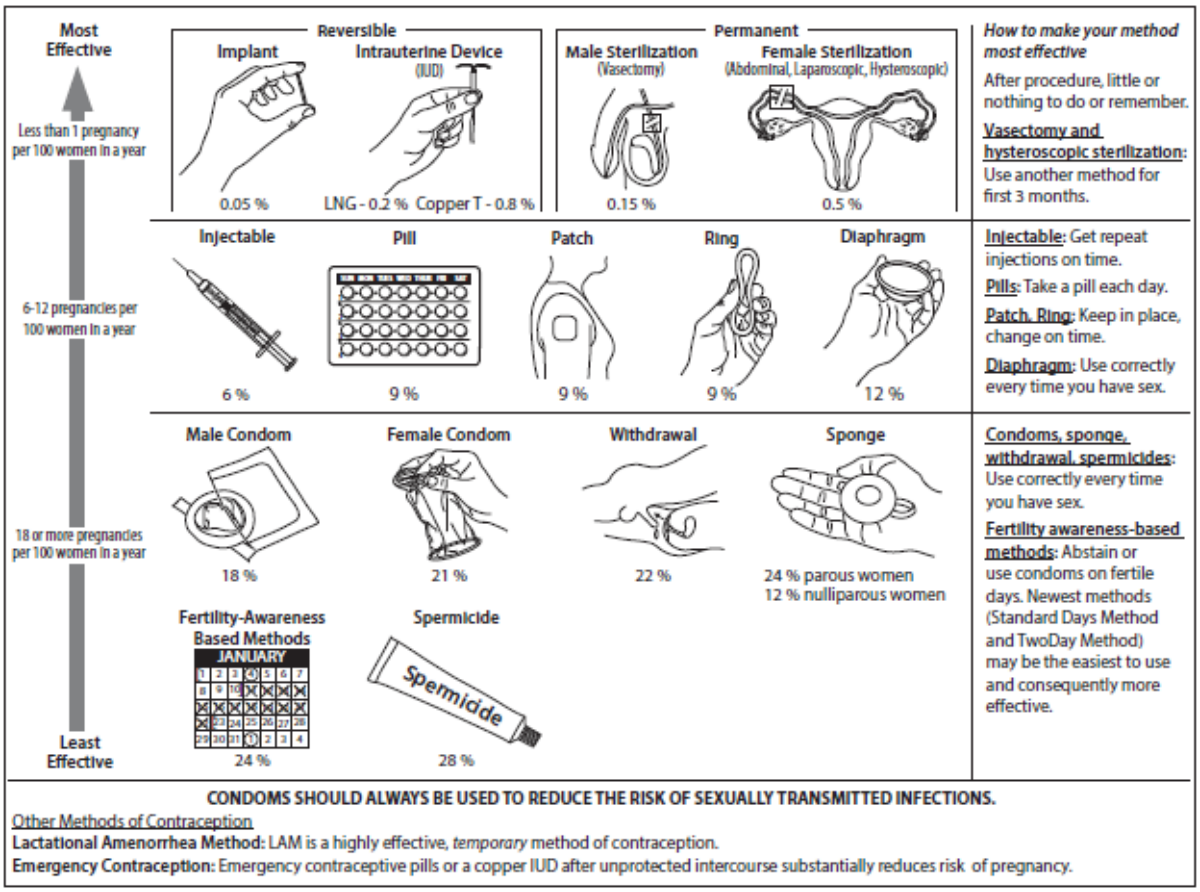


Figure 1. *Effectiveness of Family Planning Methods. Retrieved from Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recommendations and Reports. 2021;65(4):1-66. doi:10.15585/MMWR.RR6504A1.*

How to be reasonably certain that a woman is not pregnant

Typically, an in-depth medical history yields the most precise evaluation of pregnancy risk for a woman initiating a contraceptive method. The following recommendation outlines a set of criteria for assessing pregnancy risk. It's worth noting that these criteria exhibit a remarkably high level of accuracy, specifically a negative predictive value ranging between 99% to 100%. This means they are exceptionally reliable in excluding pregnancy among non-pregnant women. Consequently, the CDC suggests that healthcare providers employ these criteria to determine a woman's pregnancy status before initiating contraceptive measures (table 8).

Table 8. How to Be Reasonably Certain That a Woman Is Not Pregnant

A health care provider can be reasonably certain that a woman is not pregnant if she has no symptoms or signs of pregnancy and meets any one of the following criteria:
is ≤7 days after the start of normal menses
has not had sexual intercourse since the start of last normal menses
has been correctly and consistently using a reliable method of contraception
is ≤ 7 days after spontaneous or induced abortion
is within 4 weeks postpartum
is fully or nearly fully breastfeeding (exclusively breastfeeding or the vast majority [≥ 85%] of feeds are breastfeeds), amenorrheic, and <6 months postpartum

Healthcare providers can consider including a urine pregnancy test as part of their assessment. It's important for them to be mindful of the test's limitations, particularly in terms of its accuracy concerning the timing of the last sexual encounter and recent events like childbirth, miscarriage, or abortion. Conducting routine pregnancy tests for all women is not a mandatory practice.

However, if a woman has engaged in unprotected sexual intercourse recently (within the last 5 days) and does not desire pregnancy, it may be prudent to discuss the option of emergency contraception. This can include either a Copper Intrauterine Device (Cu-IUD) or Emergency Contraceptive Pills (ECPs).

1.2.1.4 Intrauterine Contraception

In the United States, there are four available intrauterine devices (IUDs), encompassing the copper-containing IUD and three variants releasing levonorgestrel (with total levonorgestrel content of either 13.5 mg or 52 mg).

The rate of unintended pregnancy during the initial year of IUD use stands at less than 1 in 100 women (typical use). IUDs possess the qualities of being long-acting, reversible, and are applicable across all age groups, including adolescents, as well as parous and nulliparous women.

Importantly, IUDs do not provide protection against sexually transmitted diseases (STDs); to mitigate the risk of STDs, including HIV, consistent and accurate application of male latex condoms is essential.

A. Initiation of Copper Intrauterine Devices (Cu-IUDs)

Timing:

The Cu-IUD can be introduced at any point in time, provided reasonable certainty of non-pregnancy exists (table 8).

Additionally, the Cu-IUD can be inserted within 5 days following the initial instance of unprotected sexual intercourse, serving as an emergency contraceptive. If the day of ovulation can be estimated, insertion can occur beyond 5 days post-intercourse, so long as it remains within 5 days after ovulation.

Necessity for Backup Contraception:

No supplementary contraceptive measures are required following Cu-IUD placement.

Special Considerations

1. Amenorrhea (Excluding Postpartum):

Timing: Introduction of the Cu-IUD is feasible at any juncture if reasonable assurance of non-pregnancy exists (table 8).

Additional contraceptive protection is unnecessary.

2. Postpartum (Including After Cesarean Delivery):

Timing: Cu-IUD insertion can take place at any point postpartum, including immediate postpartum (U.S. MEC 1 or 2) (table 7), contingent upon reasonable certainty of non-pregnancy (table 8). However, insertion is not advised for women with postpartum sepsis (e.g., chorioamnionitis or endometritis) (U.S. MEC 4).

No supplementary contraceptive measures are required.

3. Postabortion (Spontaneous or Induced):

Timing: Cu-IUD insertion can occur within the initial 7 days, including immediately postabortion (U.S. MEC 1 for first-trimester abortion and U.S. MEC 2 for second-trimester abortion). However, immediate insertion following a septic abortion is cautioned against (U.S. MEC 4).

Additional contraceptive protection is unnecessary.

4. Transitioning from Another Contraceptive Method:

Timing: Immediate Cu-IUD insertion is permissible if a reasonable certainty of non-pregnancy is established (Box 2). Awaiting the subsequent menstrual cycle is unnecessary.

No supplementary contraceptive measures are required.

Insights and Summary of Evidence:

In instances where the healthcare provider cannot ascertain with reasonable certainty that the woman is not pregnant, an alternative contraceptive method should be provided to her. This substitute method should be used until the healthcare provider can establish reasonable certainty of non-pregnancy and subsequently proceed with the insertion of the Cu-IUD.

Based on a comprehensive systematic review, a collection of eight studies was identified. These studies indicated that the timing of Cu-IUD insertion relative to the menstrual cycle for non-postpartum women had minimal impact on both long-term outcomes (such as rates of continuation, removal, expulsion, or pregnancy) and short-term outcomes (including pain and bleeding during insertion, as well as immediate expulsion).

B. Initiation of Levonorgestrel Intrauterine Devices (LNG-IUDs)

Timing for LNG-IUD Insertion:

- The LNG-IUD can be introduced at any time, given there is reasonable certainty that the woman is not pregnant (table 8).

Necessity for Backup Contraception:

- If the LNG-IUD is inserted within the initial 7 days of the commencement of menstrual bleeding, no additional contraceptive measures are required.
- However, if the LNG-IUD is inserted more than 7 days after the onset of menstrual bleeding, the woman should either abstain from sexual intercourse or employ supplementary contraceptive protection for the subsequent 7 days.

Special Considerations

1. Amenorrhea (Excluding Postpartum):

- Timing: The LNG-IUD can be inserted at any point if reasonable certainty of non-pregnancy is established (table 8).
- Need for backup contraception: The woman should either abstain from sexual intercourse or employ additional contraceptive protection for the following 7 days.

2. Postpartum (Including After Cesarean Delivery):

- Timing: The LNG-IUD can be inserted at any juncture, even immediately postpartum (U.S. MEC 1 or 2), contingent upon reasonable certainty of non-pregnancy (table 8). However, caution should be exercised, and the LNG-IUD should not be inserted in cases involving postpartum sepsis (e.g., chorioamnionitis or endometritis) (U.S. MEC 4).

- Need for backup contraception: If the woman is within 6 months postpartum, amenorrheic, and fully or almost entirely breastfeeding (including exclusive breastfeeding or the vast majority [≥ 85%] of feeds being breastfeeds), then additional contraceptive protection is not required.
- No additional contraceptive protection is deemed necessary under the following circumstances:

  A woman who is within 6 months postpartum, amenorrheic, and fully or almost entirely breastfeeding (including exclusive breastfeeding or the vast majority [≥ 85%] of feeds being breastfeeds).
- However, in other situations:

  A woman who is ≥21 days postpartum and has not experienced the return of her menstrual cycle should either abstain from sexual intercourse or utilize additional contraceptive protection for the subsequent 7 days.

  If her menstrual cycles have resumed, and it has been over 7 days since menstrual bleeding began, she should similarly abstain from sexual intercourse or employ supplementary contraceptive protection for the following 7 days.

3. Postabortion (Spontaneous or Induced):

- Timing: The LNG-IUD can be introduced within the initial 7 days, even immediately postabortion (U.S. MEC 1) for first-trimester abortion and U.S. MEC 2 for second-trimester abortion. However, it's crucial to note that immediate insertion following a septic abortion is not recommended (U.S. MEC 4).
- Need for backup contraception: Unless the IUD is placed during a surgical abortion, the woman should either abstain from sexual intercourse or utilize additional contraceptive protection for the following 7 days.

4. Switching from Another Contraceptive Method:

- Timing: The LNG-IUD can be inserted promptly if there is reasonable certainty that the woman is not pregnant (table 8). Waiting for her next menstrual cycle is unnecessary.
- Need for backup contraception: If it has been more than 7 days since menstrual bleeding began, the woman should either abstain from sexual intercourse or use supplementary contraceptive protection for the ensuing 7 days.
- Transitioning from a Cu-IUD: If a woman has engaged in sexual intercourse since the commencement of her current menstrual cycle and more than 5 days have passed since the onset of menstrual bleeding, theoretically, residual

sperm may remain in the genital tract, which could potentially lead to fertilization if ovulation occurs. In this scenario, a healthcare provider may contemplate offering ECPs at the time of LNG-IUD insertion.

Comments:

In cases where healthcare providers harbor uncertainty regarding whether a woman might be pregnant, it is advisable to provide her with an alternative contraceptive method for use until reasonable certainty of non-pregnancy is established, allowing for the subsequent insertion of the LNG-IUD.

If a woman requires additional contraceptive protection when transitioning to an LNG-IUD from another contraceptive method, it may be considered to continue her previous method for 7 days following LNG-IUD insertion. Notably, there is no direct evidence available concerning the effects of LNG-IUD insertion on different days of the menstrual cycle on short- or long-term outcomes.

C. Examinations and Tests Needed Before Initiation of a Cu-IUD or an LNG-IUD

Before IUD insertion, both a bimanual examination and cervical inspection are essential. It might be valuable to document a baseline weight and measure Body Mass Index (BMI) to facilitate ongoing monitoring of IUD users (Table 4). Additionally, if a woman has not undergone screening for sexually transmitted diseases (STDs) as per the recommended STD screening guidelines, this screening can be conducted at the time of IUD insertion.

In cases involving women with known medical conditions or other unique circumstances, there could be a necessity for supplementary examinations or tests to ascertain their suitability for a specific contraceptive method. The U.S. Medical Eligibility Criteria (MEC) can be a valuable resource in such scenarios.

Table 9. Classification of Examinations and Tests Needed Before IUD Insertion. Retrieved from Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recommendations and Reports. 2021;65(4):1-66. doi:10.15585/MMWR.RR6504A1.

Examination or test	Class*	
	Copper-containing IUD	Levonorgestrel-releasing IUD
Examination		
Blood pressure	C	C
Weight (BMI) (weight [kg] / height [m]^2)	—†	—†
Clinical breast examination	C	C
Bimanual examination and cervical inspection	A	A
Laboratory test		
Glucose	C	C
Lipids	C	C
Liver enzymes	C	C
Hemoglobin	C	C
Thrombogenic mutations	C	C
Cervical cytology (Papanicolaou smear)	C	C
STD screening with laboratory tests	—§	—§
HIV screening with laboratory tests	C	C

Abbreviations: BMI = body mass index; HIV = human immunodeficiency virus; IUD = intrauterine device; STD = sexually transmitted disease; U.S. MEC = *U.S. Medical Eligibility Criteria for Contraceptive Use.*

* **Class A:** essential and mandatory in all circumstances for safe and effective use of the contraceptive method. **Class B:** contributes substantially to safe and effective use, but implementation may be considered within the public health and/or service context; the risk of not performing an examination or test should be balanced against the benefits of making the contraceptive method available. **Class C:** does not contribute substantially to safe and effective use of the contraceptive method.

† Weight (BMI) measurement is not needed to determine medical eligibility for any methods of contraception because all methods can be used (U.S. MEC 1) or generally can be used (U.S. MEC 2) among obese women (Box 1). However, measuring weight and calculating BMI at baseline might be helpful for monitoring any changes and counseling women who might be concerned about weight change perceived to be associated with their contraceptive method.

§ Most women do not require additional STD screening at the time of IUD insertion. If a woman with risk factors for STDs has not been screened for gonorrhea and chlamydia according to CDC's *STD Treatment Guidelines* (http://www.cdc.gov/std/treatment), screening can be performed at the time of IUD insertion, and insertion should not be delayed. Women with current purulent cervicitis or chlamydial infection or gonococcal infection should not undergo IUD insertion (U.S. MEC 4).

Comments:

Weight (BMI): Obese women can confidently employ IUDs, as they fall under the category of U.S. Medical Eligibility Criteria 1. Consequently, there is no imperative requirement to screen for obesity when initiating IUD usage. Nevertheless, obtaining initial weight measurements and calculating Body Mass Index (BMI) using the formula (weight [kg] / height [m2]) could prove beneficial. This practice aids in the ongoing monitoring of potential changes in weight and offers a platform for counseling women who may have concerns about perceived weight changes related to their chosen contraceptive method.

Bimanual Examination and Cervical Inspection: Before the insertion of an IUD, it is imperative to perform a bimanual examination and cervical inspection. These procedures serve the purpose of evaluating uterine size and position, while also detecting any abnormalities in the cervix or uterus that could potentially indicate infection or other factors that might hinder the smooth insertion of the IUD.

Screening for Sexually Transmitted Diseases (STDs): Women should undergo routine screening for chlamydial infection and gonorrhea in accordance with national screening guidelines. Detailed information regarding eligibility, timing, and frequency of screening, as well as specific guidelines for individuals with risk factors,

can be found in the CDC's Sexually Transmitted Diseases Treatment Guidelines (http://www.cdc.gov/std/treatment).

In situations where STD screening guidelines have been adhered to, most women do not necessitate additional STD screening at the time of IUD insertion. This should not lead to any delays in the insertion process. However, for women with risk factors for STDs who have not undergone screening for gonorrhea and chlamydia as per the CDC's STD treatment guidelines, screening can be conducted concurrently with IUD insertion, without causing any delays.

It is important to note that women who currently exhibit purulent cervicitis, chlamydial infection, or gonococcal infection should not undergo IUD insertion (U.S. MEC 4).

Overall, the risk of Pelvic Inflammatory Disease PID among women with risk factors for STDs is low. While women with STDs at the time of IUD insertion do face a slightly elevated risk of PID, it is crucial to emphasize that the overall PID rate among all IUD users remains low.

Hemoglobin Levels: For women considering the use of the LNG-IUD, it's essential to understand that individuals with iron-deficiency anemia can confidently employ this contraceptive method (U.S. MEC 1). Consequently, there is no necessity to conduct screening for anemia as part of the safe initiation process for the LNG-IUD.

Similarly, women with iron-deficiency anemia can generally use Cu-IUDs (U.S. MEC 2). Prior measurement of hemoglobin levels before initiating Cu-IUDs is typically not required. This is due to the minimal fluctuations observed in hemoglobin levels among women with and without anemia who use Cu-IUDs.

Lipids: There is typically no requirement for screening for dyslipidemias as part of the safe initiation process for Cu-IUD or LNG-IUD. This is primarily due to the infrequent occurrence of undiagnosed diseases in women of reproductive age and the low probability of observing clinically significant alterations in lipid profiles as a result of hormonal contraceptive use.

Research findings have produced mixed results concerning the impact of hormonal contraceptive methods on lipid levels, both in healthy women and in women with pre-existing lipid abnormalities. Furthermore, the clinical significance of these observed changes remains uncertain.

Liver enzymes: Screening for liver disease is typically not required for the safe initiation of the Cu-IUD. This is because women with liver disease can generally use the Cu-IUD without safety concerns (U.S. MEC 1). However, when it comes to the LNG-IUD, the situation differs slightly. While women with specific liver diseases should generally avoid using the LNG-IUD (U.S. MEC 3), there is no need for routine screening for liver disease before initiating the LNG-IUD. This is primarily due to the

low prevalence of these specific liver conditions and the high probability that women with liver disease would have already received a diagnosis.

It is worth noting that because estrogen and progestins are metabolized in the liver, concerns might theoretically arise regarding the use of hormonal contraceptives among women with liver disease. However, available evidence suggests that the use of hormonal contraceptives, specifically combined oral contraceptives (COCs) and progestin-only pills (POPs), does not impact disease progression or severity in women with conditions such as hepatitis, cirrhosis, or benign focal nodular hyperplasia. It should be noted that evidence in this area is limited, and no specific evidence exists regarding the LNG-IUD.

Clinical breast examination: Screening for breast disease is generally not required for the safe initiation of the Cu-IUD. This is because women with breast disease can typically use the Cu-IUD without safety concerns (U.S. MEC 1). However, when it comes to the LNG-IUD, the situation differs slightly. Women with current breast cancer should not use the LNG-IUD (U.S. MEC 4).

Nevertheless, there is no need for routine screening, such as a clinical breast examination, in asymptomatic women before inserting an IUD. This is primarily due to the low prevalence of breast cancer among women of reproductive age.

Cervical Cytology: Screening asymptomatic women with cervical cytology before IUD insertion is typically not necessary. This is because there are several factors that make routine screening unnecessary. Although women with cervical cancer should not undergo IUD insertion (U.S. MEC 4), the high rates of cervical screening, the low incidence of cervical cancer in the United States, and the likelihood that a woman with cervical cancer would have already been diagnosed make pre-IUD screening redundant.

HIV Screening: Routine HIV screening is typically not required before IUD insertion. This is because women with HIV infection can generally use IUDs without safety concerns. Specifically, they are classified as either eligible with no restrictions (U.S. MEC 1) or generally eligible (U.S. MEC 2) for IUD use. As of now, there is no evidence to suggest that routine HIV screening before IUD insertion provides significant benefits.

Other screening: Screening for other conditions such as hypertension, diabetes, or thrombogenic mutations is typically not required before the safe initiation of IUDs. This is because women with these conditions can generally use IUDs without significant safety concerns. They are categorized as either eligible with no restrictions (U.S. MEC 1) or generally eligible (U.S. MEC 2) for IUD use.

D. Provision of Medications to Ease IUD Insertion

Routine use of misoprostol before IUD insertion is not recommended. However, it might be considered in specific situations, such as when women have experienced a recent failed insertion.

The administration of a paracervical block with lidocaine is a potential strategy to alleviate patient discomfort during the IUD insertion procedure.

E. Provision of Prophylactic Antibiotics at the Time of IUD Insertion

Prophylactic antibiotics are generally not recommended for Cu-IUD or LNG-IUD insertion.

F. Routine Follow-Up After IUD Insertion

These recommendations pertain to the necessity of regular follow-up visits to ensure the safe and effective ongoing use of contraception in healthy women. It's important to note that these recommendations are general in nature and may require customization for different users and circumstances. Certain populations, such as adolescents, individuals with specific medical conditions or characteristics, and those with multiple medical conditions, may benefit from more frequent follow-up appointments.

Here are the key points for health care providers regarding routine follow-up visits:

- Women should be informed that they can return at any time if they experience side effects, encounter any issues with their current contraceptive method, or when it's time for the removal or replacement of their contraceptive device. Routine follow-up visits are not mandatory.
- During other routine visits, health care providers attending to IUD users should:
    - Assess the woman's satisfaction with her chosen contraceptive method and inquire about any concerns related to its use.
    - Evaluate any changes in the woman's health status, including modifications in medication usage that may impact the continued safe and effective use of the IUD, taking into account the guidance provided by the U.S. MEC (including category 3 and 4 conditions and characteristics).
    - Consider performing an examination to confirm the presence of the IUD strings.

- Weigh the potential impact of changes in weight and provide counseling to women who express concerns about weight fluctuations they associate with their contraceptive method.

G. Bleeding Irregularities with Cu-IUD Use

Before inserting a Cu-IUD, it is essential to provide counseling regarding potential alterations in bleeding patterns that may occur during Cu-IUD use. It's common for women to experience unscheduled spotting or light bleeding, as well as episodes of heavy or prolonged bleeding during the initial 3 to 6 months of Cu-IUD use. Importantly, these changes are generally not harmful and tend to decrease as the woman continues to use the Cu-IUD.

Should clinical indications arise, healthcare providers should consider the possibility of an underlying gynecological issue. This may include factors such as Cu-IUD displacement, a sexually transmitted disease (STD), pregnancy, or new pathologic uterine conditions like polyps or fibroids. This consideration becomes especially pertinent for women who have been using the Cu-IUD for several months or longer and develop new instances of heavy or prolonged bleeding. If an underlying gynecological issue is identified, appropriate treatment or referral for further care should be provided.

In cases where no underlying gynecological problem is discovered, and the woman expresses a desire for treatment, healthcare providers can consider the following treatment option during days of bleeding:

- Short-term use of nonsteroidal anti-inflammatory drugs (NSAIDs) for a duration of 5 to 7 days.

Should the bleeding persist, and the woman deems it unacceptable, it is advisable to counsel her on alternative contraceptive methods. Additionally, healthcare providers should offer another contraceptive method if the woman desires to switch.

H. Bleeding Irregularities (Including Amenorrhea) with LNG-IUD Use

Before inserting an LNG-IUD, it is crucial to offer counseling regarding the possible alterations in bleeding patterns that may arise during LNG-IUD usage. It should be noted that unscheduled spotting or light bleeding is anticipated during the initial 3 to 6 months of LNG-IUD use. Importantly, this kind of bleeding is typically not harmful and tends to decrease as the woman continues to use the LNG-IUD.

As time progresses, bleeding patterns generally improve with LNG-IUD use. Many women eventually experience only light menstrual bleeding or even amenorrhea (the absence of menstruation). It is uncommon for women using an LNG-IUD to

experience heavy or prolonged bleeding, whether it's unscheduled or occurs during their regular menstrual cycles.

Irregular Bleeding (Including Spotting, Light Bleeding, or Heavy/Prolonged Bleeding):

- If there are clinical indications, it's important to consider potential underlying gynecological issues like displacement of the LNG-IUD, STD, pregnancy, or newly developed uterine conditions such as polyps or fibroids. If any such gynecological issue is identified, it should be treated, or the woman should be referred for appropriate care.
- In cases where persistent bleeding is deemed unacceptable by the woman, counseling should be provided regarding alternative contraceptive methods. If desired, another contraceptive method should be offered.

Amenorrhea:

- Amenorrhea typically doesn't necessitate medical intervention. Reassurance should be provided.
- In instances where a woman experiences a sudden change from her regular bleeding pattern to amenorrhea, pregnancy should be considered and ruled out if clinically relevant.
- If amenorrhea continues and the woman finds it undesirable, counseling about alternative contraceptive methods should be offered, and another method should be provided if desired.

I. Management of the IUD when a Cu-IUD or an LNG-IUD User Is Found to Have PID

- Treat PID according to the guidelines outlined in the CDC Sexually Transmitted Diseases Treatment Guidelines.
- Provide comprehensive management for STDs, including counseling on condom use.
- Immediate removal of the IUD is not necessary if the woman requires ongoing contraception.
- Reevaluate the woman's condition within 48–72 hours. If there is no clinical improvement, continue with antibiotics and consider IUD removal.
- If the woman wishes to discontinue IUD use, it's advisable to remove the IUD after initiating antibiotic treatment to reduce the potential risk of bacterial spread during removal.

- In case of IUD removal, consider the appropriateness of emergency contraceptive pills (ECPs). Offer counseling on alternative contraceptive methods and provide another method if desired.

J. Management of the IUD when a Cu-IUD or an LNG-IUD User is Found to Be Pregnant

Evaluate for possible ectopic pregnancy.

Inform the woman that leaving the IUD in place increases her risk of spontaneous abortion, including potentially life-threatening septic abortion, and preterm delivery. Removal of the IUD can reduce these risks but might not lower them to the baseline level of a pregnancy without an IUD.

If she does not wish to continue the pregnancy, provide counseling on available options.

If she intends to continue the pregnancy, advise her to seek prompt medical attention in case of heavy bleeding, cramping, pain, abnormal vaginal discharge, or fever.

IUD strings are visible or can be safely retrieved from the cervical canal:

- It's advisable to remove the IUD as soon as possible.

  If she chooses to have it removed, gently pull on the strings to extract it.

  Instruct the woman to return promptly if she experiences heavy bleeding, cramping, pain, abnormal vaginal discharge, or fever.
- If she opts to retain the IUD, advise her to seek prompt medical care if she encounters heavy bleeding, cramping, pain, abnormal vaginal discharge, or fever.
- If ultrasonography is available, consider performing or referring for an ultrasound examination to determine the IUD's location.

IUD strings are not visible and cannot be safely retrieved:

- If the IUD cannot be located, it might have been expelled or perforated the uterine wall.
- If ultrasonography is not feasible or the ultrasound indicates the IUD is inside the uterus, counsel the woman to seek prompt medical care if she experiences heavy bleeding, cramping, pain, abnormal vaginal discharge, or fever.

1.2.1.5 Implants

The etonogestrel implant, consisting of a single rod containing 68 mg of etonogestrel, is accessible in the United States. It boasts a low pregnancy rate, with fewer than 1 out of 100 women experiencing pregnancy during the first year of typical use. This implant offers long-lasting contraceptive protection, is reversible, and is suitable for women across all age groups, including adolescents. Importantly, it does not provide protection against STDs, highlighting the need for consistent and proper use of male latex condoms to reduce the risk of STD transmission, including HIV.

A. Initiation of Implants

Timing

- The implant can be inserted at any time if there is a reasonable certainty that the woman is not pregnant (table 8).

Need for back-up contraception

- If the implant is inserted within the first 5 days since the beginning of menstrual bleeding, no additional contraceptive protection is required.
- If the implant is inserted more than 5 days after the onset of menstrual bleeding, the woman should either abstain from sexual intercourse or use additional contraceptive protection for the following 7 days.

Special Considerations

Amenorrhea (Not Postpartum):

- Timing: The implant can be inserted at any time if there is a reasonable certainty that the woman is not pregnant (table 8).
- Need for back-up contraception: The woman should abstain from sexual intercourse or use additional contraceptive protection for the next 7 days.

Postpartum (Breastfeeding):

- Timing: The implant can be inserted at any time (U.S. MEC 2 if <1 month postpartum and U.S. MEC 1 if ≥1 month postpartum) if there is reasonable certainty that the woman is not pregnant (table 8).
- Need for back-up contraception: If the woman is <6 months postpartum, amenorrheic, and fully or nearly fully breastfeeding (exclusively breastfeeding or the vast majority [≥85%] of feeds are breastfeeds), no additional contraceptive protection is needed. Otherwise, a woman who is ≥21 days postpartum and has not experienced a return of her menstrual cycle needs to either abstain from sexual intercourse or use additional contraceptive

protection for the next 7 days. If her menstrual cycles have returned and it has been >5 days since menstrual bleeding started, she needs to either abstain from sexual intercourse or use additional contraceptive protection for the next 7 days.

Postpartum (Not Breastfeeding):

- Timing: The implant can be inserted at any time, including immediately postpartum (U.S. MEC 1), if there is reasonable certainty that the woman is not pregnant (table 8).
- Need for back-up contraception: If a woman is <21 days postpartum, no additional contraceptive protection is required. A woman who is ≥21 days postpartum and has not experienced a return of her menstrual cycle needs to either abstain from sexual intercourse or use additional contraceptive protection for the next 7 days. If her menstrual cycles have returned and it has been >5 days since menstrual bleeding started, she needs to abstain from sexual intercourse or use additional contraceptive protection for the next 7 days.

Postabortion (Spontaneous or Induced):

- Timing: The implant can be inserted within the first 7 days, including immediately after the abortion (U.S. MEC 1).
- Need for back-up contraception: The woman needs to abstain from sexual intercourse or use additional contraceptive protection for the next 7 days unless the implant is placed at the time of a surgical abortion.

Switching from Another Contraceptive Method:

- Timing: The implant can be inserted immediately if there is reasonable certainty that the woman is not pregnant (Box 2). Waiting for her next menstrual cycle is unnecessary.
- Need for back-up contraception: If it has been >5 days since menstrual bleeding started, the woman needs to either abstain from sexual intercourse or use additional contraceptive protection for the next 7 days after insertion.
- Switching from an IUD: If the woman has had sexual intercourse since the start of her current menstrual cycle and it has been >5 days since menstrual bleeding started, theoretically, residual sperm might be in the genital tract, which could lead to fertilization if ovulation occurs. A health care provider may consider any of the following options:
    - Advise the woman to retain the IUD for at least 7 days after the implant is inserted and return for IUD removal.

- Advise the woman to abstain from sexual intercourse or use barrier contraception for 7 days before removing the IUD and switching to the new method.
- If the woman cannot return for IUD removal and has not abstained from sexual intercourse or used barrier contraception for 7 days, advise the woman to use ECPs (with the exception of UPA) at the time of IUD removal.

B. Examinations and Tests Needed Before Implant Insertion

Among healthy women, no examinations or tests are required before starting an implant, though having baseline weight and BMI measurements may be beneficial for monitoring implant users over time (table 10). Women with known medical conditions or special circumstances might necessitate additional examinations or tests to determine their suitability for a specific contraceptive method. U.S. MEC guidelines could be valuable in such cases.

Comments:

- **Weight (BMI):** Obese women can safely use implants (U.S. MEC 1), so screening for obesity is unnecessary for the safe initiation of implants. However, measuring weight and calculating BMI at the outset could assist in tracking changes and addressing concerns about weight fluctuations that may be associated with their chosen contraceptive method.
- **Bimanual examination and cervical inspection:** A pelvic examination is not required before starting implants because it wouldn't aid in identifying conditions that would make implant use unsafe. Women with current breast cancer should not use implants (U.S. MEC 4), and women with certain liver diseases generally should not use them (U.S. MEC 3). However, these conditions are unlikely to be detected through a pelvic examination.
- **Lipids**: Screening for dyslipidemias isn't necessary when initiating implants due to the low prevalence of undiagnosed disease among women of reproductive age and the low likelihood of clinically significant changes resulting from hormonal contraceptive use.
- **Liver enzymes**: Although women with specific liver diseases should generally avoid using implants (U.S. MEC 3), screening for liver disease before implant initiation isn't necessary due to the low prevalence of these conditions and the high probability that women with liver disease would have already received a diagnosis. Although estrogen and progestins are metabolized in the liver, concerns about hormonal contraceptive use among women with liver disease are theoretical. Specifically, there is no evidence to suggest that hormonal

contraceptives, including COCs and POPs, affect the progression or severity of diseases like hepatitis, cirrhosis, or benign focal nodular hyperplasia.

Table 10. Classification of Examinations and Tests Needed Before Implant Insertion. Retrieved from Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recommendations and Reports. 2021;65(4):1-66. doi:10.15585/MMWR.RR6504A1.

Examination or test	Class*
Examination	
Blood pressure	C
Weight (BMI) (weight [kg] / height [m]^2)	—†
Clinical breast examination	C
Bimanual examination and cervical inspection	C
Laboratory test	
Glucose	C
Lipids	C
Liver enzymes	C
Hemoglobin	C
Thrombogenic mutations	C
Cervical cytology (Papanicolaou smear)	C
STD screening with laboratory tests	C
HIV screening with laboratory tests	C

Abbreviations: BMI = body mass index; HIV = human immunodeficiency virus; STD = sexually transmitted disease; U.S. MEC = *U.S. Medical Eligibility Criteria for Contraceptive Use*.

* **Class A:** essential and mandatory in all circumstances for safe and effective use of the contraceptive method. **Class B:** contributes substantially to safe and effective use, but implementation may be considered within the public health and/or service context; the risk of not performing an examination or test should be balanced against the benefits of making the contraceptive method available. **Class C:** does not contribute substantially to safe and effective use of the contraceptive method.

† Weight (BMI) measurement is not needed to determine medical eligibility for any methods of contraception because all methods can be used (U.S. MEC 1) or generally can be used (U.S. MEC 2) among obese women (Box 1). However, measuring weight and calculating BMI at baseline might be helpful for monitoring any changes and counseling women who might be concerned about weight change perceived to be associated with their contraceptive method.

- **Clinical breast examination:** Although women with current breast cancer should not use implants (U.S. MEC 4), screening asymptomatic women with a clinical breast examination before initiation of implants is not necessary because of the low prevalence of breast cancer among women of reproductive age (15–49 years).
- **Other Screening**: Women with hypertension, diabetes, anemia, thrombogenic mutations, cervical intraepithelial neoplasia, cervical cancer, STDs, or HIV infection can either use implants without restriction (U.S. MEC 1) or can generally use them (U.S. MEC 2). Consequently, there's no need for screening these conditions before safely initiating implants.

C. Routine Follow-Up After Implant Insertion

These recommendations address the necessity for routine follow-up to ensure the safe and effective continued use of contraception, specifically for healthy women. It's important to note that these recommendations are general and may vary depending on individual circumstances. Certain populations, such as adolescents, individuals with specific medical conditions or characteristics, and those with multiple medical conditions, might benefit from more frequent follow-up visits.

- Women should be advised to return for a consultation at any time to discuss any side effects or issues related to their contraceptive method. If they wish to change their method or when it's time to remove or replace the contraceptive device, they should also return. There is no requirement for routine follow-up visits.
- During other routine visits, healthcare providers attending to implant users should perform the following actions:
    - Evaluate the woman's satisfaction with her chosen contraceptive method and address any concerns she may have about its use.
    - Assess any changes in her health status, including alterations in medications, which might impact the appropriateness of the implant for her safe and effective continued use based on U.S. MEC guidelines, particularly in the context of category 3 and 4 conditions and characteristics.
    - Consider evaluating weight changes and provide counseling to women who have concerns about weight changes they perceive to be associated with their contraceptive method.

Bleeding Irregularities (Including Amenorrhea) During Implant Use:

- Prior to implant insertion, it's crucial to provide counseling about potential changes in bleeding patterns that can occur during implant use. These patterns may include unscheduled spotting or light bleeding, and some women may experience amenorrhea. These bleeding changes are generally not harmful and may or may not diminish with continued implant use. Heavy or prolonged bleeding, whether unscheduled or menstrual, is rare during implant use.

Irregular Bleeding (Spotting, Light Bleeding, or Heavy or Prolonged Bleeding):

- If clinically warranted, healthcare providers should consider the possibility of an underlying gynecological issue, such as interactions with other medications, STD, pregnancy, or new pathologic uterine conditions (e.g.,

polyps or fibroids). If an underlying gynecological problem is identified, it should be treated, or the patient should be referred for care.

- If no underlying gynecological issue is found and the woman desires treatment, various options can be considered for treatment during days of bleeding, including short-term use of NSAIDs (5-7 days) or hormonal treatment (if medically eligible) with low-dose COCs or estrogen for short-term use (10-20 days).
- If irregular bleeding persists, and the woman deems it unacceptable, healthcare providers should offer counseling on alternative contraceptive methods and provide another method if desired.

Amenorrhea:

- Amenorrhea does not necessitate any medical treatment. Reassurance should be provided.
- If a woman's regular bleeding pattern abruptly changes to amenorrhea, the possibility of pregnancy should be considered if clinically indicated.
- If amenorrhea persists, and the woman finds it unacceptable, healthcare providers should counsel her on alternative contraceptive methods and offer another method if desired.

1.2.1.6 Injectables

Progestin-only injectable contraceptives are available in the United States, with two formulations differing only in their routes of administration:

- DMPA, 150 mg intramuscularly
- DMPA, 104 mg subcutaneously

In typical use, approximately 6 out of 100 women will become pregnant in the first year of using DMPA.

DMPA is a reversible method and is suitable for women of all ages, including adolescents. It's important to note that DMPA does not offer protection against STDs. Consistent and correct use of male latex condoms is recommended to reduce the risk of STDs, including HIV.

A. Initiation of Injectables

Timing

- The initial DMPA injection can be administered at any time, provided there is reasonable certainty that the woman is not pregnant (table 8).

Need for back-up contraception

- If DMPA is initiated within the first 7 days since the onset of menstrual bleeding, no additional contraceptive protection is necessary.
- If DMPA is initiated more than 7 days after the start of menstrual bleeding, the woman should either abstain from sexual intercourse or use additional contraceptive protection for the following 7 days.

Special considerations

Amenorrhea (Not Postpartum):

- Regarding timing, the first DMPA injection can be administered at any time if there is reasonable certainty that the woman is not pregnant (table 8).
- In terms of the need for back-up contraception, the woman should either abstain from sexual intercourse or use additional contraceptive protection for the next 7 days.

Postpartum (Breastfeeding):

- Timing: The initial DMPA injection can be administered at any time, including immediately postpartum. The timing varies based on the woman's postpartum status, specifically, whether she is less than 1 month postpartum (U.S. MEC 2) or 1 month or more postpartum (U.S. MEC 1). However, this is contingent upon reasonable certainty that the woman is not pregnant (table 8).
- Need for Back-Up Contraception:
    - If the woman is less than 6 months postpartum, amenorrheic, and fully or nearly fully breastfeeding (including exclusively breastfeeding or the vast majority [≥ 85%] of feeds being breastfeeds), no additional contraceptive protection is required.
    - Conversely, a woman who is 21 days or more postpartum, has not experienced a return of her menstrual cycle, and her menstrual cycles have not resumed for more than 7 days after the onset of menstrual bleeding, should either abstain from sexual intercourse or use additional contraceptive protection for the next 7 days. This precaution applies even if her menstrual cycles have returned, and it has been more than 7 days since the start of menstrual bleeding.

Postpartum (Not Breastfeeding):

- Timing: The initial DMPA injection can be administered at any time, even immediately postpartum (U.S. MEC 1), provided there is reasonable certainty that the woman is not pregnant (table 8).

- Need for Back-Up Contraception:
    - If a woman is less than 21 days postpartum, there is no requirement for additional contraceptive protection.
    - However, a woman who is 21 days or more postpartum and has not experienced the return of her menstrual cycle must either abstain from sexual intercourse or use extra contraceptive protection for the subsequent 7 days. This rule also applies if her menstrual cycles have resumed, and it has been more than 7 days since the onset of menstrual bleeding.

Postabortion (Spontaneous or Induced):

- Timing: The initial DMPA injection can be administered within the first 7 days, including immediately after the abortion (U.S. MEC 1).
- Need for Back-Up Contraception: The woman must either abstain from sexual intercourse or use additional contraceptive protection for the subsequent 7 days, unless the injection is given during a surgical abortion.

Switching from Another Contraceptive Method:

- Timing: The initial DMPA injection can be administered immediately if it is reasonably certain that the woman is not pregnant (Box 2). Waiting for her next menstrual cycle is unnecessary.
- Need for Back-Up Contraception: If it has been more than 7 days since menstrual bleeding began, the woman must either abstain from sexual intercourse or use additional contraceptive protection for the next 7 days.
- Switching from an IUD: If the woman has engaged in sexual intercourse since the start of her current menstrual cycle, and it has been over 5 days since menstrual bleeding began, theoretically, residual sperm might be present in the genital tract, which could lead to fertilization if ovulation occurs. In such cases, a health care provider may consider the following options:
    - Advise the woman to retain the IUD for at least 7 days after the injection and then return for IUD removal.
    - Recommend that the woman abstain from sexual intercourse or use barrier contraception for 7 days before removing the IUD and transitioning to the new method.
    - If the woman cannot return for IUD removal and has not abstained from sexual intercourse or used barrier contraception for 7 days, advise the woman to use emergency contraceptive pills (excluding UPA) at the time of IUD removal.

B. Examinations and Tests Needed Before Initiation of an Injectable

No medical examinations or tests are required for healthy women before starting DMPA, although measuring weight and BMI at the outset could be beneficial for tracking DMPA users over time (table 11).

Women with established medical conditions or unique circumstances might necessitate additional evaluations or assessments before they are deemed suitable candidates for a specific contraceptive method. U.S. MEC could be valuable in guiding decisions in such situations.

Table 11. Classification of Examinations and Tests Needed Before Depo-Medroxyprogesterone Acetate (DPMA) Initiation. Retrieved from Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recommendations and Reports. 2021;65(4):1-66. doi:10.15585/MMWR.RR6504A1.

Examination or test	Class*
Examination	
Blood pressure	C
Weight (BMI) (weight [kg]/height [m]^2)	—†
Clinical breast examination	C
Bimanual examination and cervical inspection	C
Laboratory test	
Glucose	C
Lipids	C
Liver enzymes	C
Hemoglobin	C
Thrombogenic mutations	C
Cervical cytology (Papanicolaou smear)	C
STD screening with laboratory tests	C
HIV screening with laboratory tests	C

Abbreviations: BMI = body mass index; HIV = human immunodeficiency virus; STD = sexually transmitted disease; U.S. MEC = *U.S. Medical Eligibility Criteria for Contraceptive Use.*

* **Class A:** essential and mandatory in all circumstances for safe and effective use of the contraceptive method. **Class B:** contributes substantially to safe and effective use, but implementation may be considered within the public health and/or service context; the risk of not performing an examination or test should be balanced against the benefits of making the contraceptive method available. **Class C:** does not contribute substantially to safe and effective use of the contraceptive method.

† Weight (BMI) measurement is not needed to determine medical eligibility for any methods of contraception because all methods can be used (U.S. MEC 1) or generally can be used (U.S. MEC 2) among obese women (Box 1). However, measuring weight and calculating BMI at baseline might be helpful for monitoring any changes and counseling women who might be concerned about weight change perceived to be associated with their contraceptive method.

Comments:

Weight (BMI): Obese women can safely use DMPA (U.S. MEC 1) or generally use it (U.S. MEC 2). Consequently, screening for obesity is not essential before starting DMPA. However, measuring weight and calculating BMI at the beginning might be beneficial for monitoring any alterations and providing guidance to women who may be worried about weight changes they associate with their chosen contraceptive method.

Bimanual examination and cervical inspection: A pelvic examination is not required before starting DMPA because it doesn't aid in the detection of conditions that would make DMPA unsafe. While it's important to note that women with current breast cancer should avoid using DMPA (U.S. MEC 4), and women with severe hypertension, heart disease, vascular disease, or specific liver diseases generally should not use DMPA (U.S. MEC 3), it's worth emphasizing that these conditions are not typically detectable through a pelvic examination.

Blood Pressure: Testing for hypertension prior to starting DMPA is not deemed necessary. This is because most cases of severe hypertension are typically diagnosed already, and the prevalence of undiagnosed severe hypertension is low. In general, women with hypertension can use DMPA (U.S. MEC 2), except for those with severe hypertension or vascular disease, who should generally avoid DMPA (U.S. MEC 3)

Glucose: Conducting diabetes screening before starting DMPA is generally considered unnecessary. This is because the prevalence of undiagnosed diabetes is low, and women with complicated diabetes would likely have already received a diagnosis. While women with complicated diabetes should typically avoid using DMPA (U.S. MEC 3), routine screening for diabetes is not warranted.

Lipids: Routine screening for dyslipidemias is generally unnecessary before initiating injectable contraception. This is because there is a low prevalence of undiagnosed dyslipidemias in women of reproductive age, and the probability of experiencing clinically significant lipid profile changes due to hormonal contraceptives is minimal.

Liver enzymes: There's typically no need for pre-screening for liver disease before starting DMPA as the prevalence of such conditions is low among women, and it's highly likely that those with liver disease would have already been diagnosed.

Clinical Breast Examination: Conducting a clinical breast examination for asymptomatic women before initiating DMPA is generally not required due to the low occurrence of breast cancer in women of reproductive age.

Other screening: Screening for conditions such as anemia, thrombogenic mutations, cervical intraepithelial neoplasia, cervical cancer, HIV infection, or other STDs is generally not needed before initiating DMPA, as women with these conditions can usually use DMPA safely (U.S. MEC 1 or 2) according to the guidelines.

C. Routine Follow-Up After Injectable Initiation

These recommendations provide guidance on when routine follow-up visits are advisable to ensure the safe and effective use of contraception in healthy women. It's important to note that these recommendations are general in nature and may vary depending on individual users and situations. Certain populations, such as adolescents, individuals with specific medical conditions or characteristics, and

those with multiple medical conditions, may benefit from more frequent follow-up visits.

Here is a summary of the key points:

- Women should be informed that they can return at any time to discuss any side effects or concerns, to explore the possibility of changing their contraceptive method, and when it's time for reinjection, if applicable. No routine follow-up visit is mandatory.
- During other routine visits, healthcare providers attending to injectable contraceptive users should perform the following actions:
    - Evaluate the woman's satisfaction with her chosen contraceptive method and inquire about any concerns related to its use.
    - Assess any changes in the woman's health status, including alterations in medications, that could affect the appropriateness of continued use of the injectable contraceptive. This evaluation should be based on U.S. MEC guidelines, especially in cases involving category 3 and 4 conditions and characteristics.
    - Consider monitoring weight changes and provide counseling to women who express concerns about weight fluctuations they associate with their contraceptive method.

D. Timing of Repeat Injections

Reinjection Interval

Administer repeat DMPA injections every 3 months (approximately 13 weeks).

Special Considerations

- **Early Injection**

The repeat DMPA injection can be administered earlier than scheduled when necessary.

- **Late Injection**
    - The repeat DMPA injection can be administered up to 2 weeks late (approximately 15 weeks from the last injection) without the need for additional contraceptive protection.
    - If a woman is more than 2 weeks late (beyond approximately 15 weeks from the last injection) for a repeat DMPA injection, she can receive the injection if there is reasonable certainty that she is not pregnant (Box 2). During the following 7 days, she must either abstain from sexual intercourse or use additional contraceptive protection. If appropriate,

she may also consider the use of emergency contraception, excluding ulipristal acetate (UPA).

E. Bleeding Irregularities (Including Amenorrhea) During Injectable Use

Before starting DMPA, offer counseling regarding possible alterations in bleeding patterns while using DMPA. It's important to note that amenorrhea, as well as unexpected episodes of spotting or light bleeding, are frequently observed with DMPA use, and there's a possibility of experiencing heavy or extended bleeding. These variations in bleeding patterns are typically not associated with harm and may potentially diminish with continued DMPA use.

Unscheduled Spotting or Light Bleeding

- If clinically necessary, explore potential underlying gynecological issues, such as interactions with other medications, STD, pregnancy, or new pathological uterine conditions (e.g., polyps or fibroids). If such an issue is identified, either provide treatment or make a referral for further care.
- In cases where no underlying gynecological issue is identified and the woman seeks treatment, consider the following treatment option during days of bleeding: NSAIDs for short-term treatment (5–7 days).
- If unscheduled spotting or light bleeding persists, and the woman deems it unacceptable, provide counseling on alternative contraceptive methods, and offer another method if she desires a change.

Heavy or Prolonged Bleeding

- If clinically necessary, explore potential underlying gynecological issues, such as interactions with other medications, STD, pregnancy, or new pathological uterine conditions (like fibroids or polyps). If such an issue is identified, either provide treatment or make a referral for further care.
- In cases where no underlying gynecological issue is identified and the woman seeks treatment, consider the following treatment options during days of heavy or prolonged bleeding:
    - NSAIDs for short-term treatment (5–7 days).
    - Hormonal treatment (if medically eligible) with low-dose COCs or estrogen for short-term treatment (10–20 days).
- If heavy or prolonged bleeding persists and the woman deems it unacceptable, provide counseling on alternative contraceptive methods, and offer another method if she desires a change.

Amenorrhea

- Amenorrhea does not necessitate medical intervention. Reassure the individual.
    - If a woman's usual menstrual cycle abruptly transitions to amenorrhea, consider pregnancy testing if clinically warranted.
- If amenorrhea persists and the woman is dissatisfied with it, provide counseling on alternative contraceptive options, and offer a different method if she desires one.

1.2.1.7 Combined Hormonal Contraceptives

Combined hormonal contraceptives encompass formulations that include both estrogen and progestin. These include:

- **Combined Oral Contraceptives** (COCs) in various formulations.
- **Transdermal contraceptive patch**: releases 150 µg of norelgestromin and 20 µg ethinyl estradiol daily.
- **Vaginal contraceptive ring**: releases 120 µg etonogestrel and 15 µg ethinyl estradiol daily.

With typical use, approximately 9 out of 100 women experience pregnancy in the first year of using combined hormonal contraceptives. These methods are reversible and suitable for women of all ages.

Typically, combined hormonal contraceptives are used for 21–24 consecutive days, followed by 4–7 hormone-free days, during which either no contraception or placebo pills are used. In some cases, these methods are used for extended periods with infrequent or no hormone-free days.

It's important to note that combined hormonal contraceptives do not protect against STDs. To reduce the risk of STDs, including HIV, consistent and correct use of male latex condoms is recommended.

A. Initiation of Combined Hormonal Contraceptives

Commencing the use of combined hormonal contraceptives is permissible at any point, provided there is a high level of confidence that the woman is not pregnant, as delineated in table 8.

In terms of the necessity for added contraceptive safeguards:

If combined hormonal contraceptives are commenced within the initial 5 days of the menstrual bleeding onset, there is no need for supplementary contraceptive precautions.

Nevertheless, if their commencement occurs more than 5 days after the commencement of menstrual bleeding, the woman should either refrain from sexual intercourse or employ additional contraceptive protection for the ensuing 7 days.

Special Considerations:

Amenorrhea (Not Postpartum): These contraceptives can be initiated at any time if there is reasonable certainty that the woman is not pregnant (table 8).

When using them, women should either abstain from sexual intercourse or use supplementary contraceptive protection for the following 7 days.

Postpartum (Breastfeeding): The initiation of combined hormonal contraceptives is contingent upon adherence to medical eligibility guidelines and the reasonable assurance that the woman is not pregnant, as specified in table 8.

In the case of postpartum women who are breastfeeding, it is advisable to steer clear of combined hormonal contraceptives during the initial 3 weeks following delivery (as per U.S. MEC 4). This precautionary approach is rooted in concerns about an elevated risk of venous thromboembolism. Furthermore, in the fourth week after childbirth, their use is generally discouraged (U.S. MEC 3) due to potential impacts on breastfeeding performance.

For postpartum breastfeeding women who possess additional risk factors for venous thromboembolism, the utilization of combined hormonal contraceptives is generally not recommended from 4 to 6 weeks post-delivery (U.S. MEC 3).

- Need for supplementary contraception: If the woman is within the first 6 months postpartum, not experiencing menstruation, and is fully or almost entirely reliant on breastfeeding (exclusive or at least 85% of feeds are breastfeeds), there is no requirement for additional contraceptive protection. However, a woman who is at least 21 days postpartum and hasn't had her menstrual cycle return needs to either abstain from sexual intercourse or employ additional contraceptive protection for the subsequent 7 days. If her menstrual cycles have resumed, and it has been more than 5 days since menstrual bleeding began, she should either abstain from sexual intercourse or use supplementary contraceptive protection for the next 7 days.

Postpartum (Not Breastfeeding)

- Timing: the commencement of combined hormonal contraceptives is contingent upon the woman meeting the necessary medical criteria and ensuring there's a reasonable assurance of her not being pregnant, as delineated in table 8.
- Postpartum women are advised to refrain from using combined hormonal contraceptives during the initial 3 weeks following childbirth (per U.S. MEC 4)

due to concerns regarding an increased risk of venous thromboembolism. For postpartum women who have additional risk factors for venous thromboembolism, the use of combined hormonal contraceptives should generally be avoided between 3 and 6 weeks after delivery (per U.S. MEC 3).

- Requirement for supplementary contraception: If a woman is within 21 days postpartum, there is no requirement for extra contraceptive protection. However, if a woman is at least 21 days postpartum and has not yet experienced a return of her menstrual cycles, she should either abstain from sexual intercourse or employ supplementary contraceptive protection for the subsequent 7 days. If her menstrual cycles have resumed, and it has been more than 5 days since the onset of menstrual bleeding, she should either abstain from sexual intercourse or use supplementary contraceptive protection for the following 7 days.

Postabortion (Spontaneous or Induced)

- Timing: Combined hormonal contraceptives can be initiated within the initial 7 days following a first or second-trimester abortion, which includes immediate postabortion (U.S. MEC 1).
- Requirement for supplementary contraception: Unless combined hormonal contraceptives are initiated at the moment of a surgical abortion, the woman must either abstain from sexual intercourse or employ additional contraceptive protection for the ensuing 7 days.

Switching from Another Contraceptive Method

- Timing: combined hormonal contraceptives can be promptly initiated if there is reasonable certainty that the woman is not pregnant (table 8), eliminating the need to await her next menstrual cycle.
- Need for supplementary contraception: When it has been more than 5 days since the onset of menstrual bleeding, she must choose between abstaining from sexual intercourse or employing additional contraceptive protection for the subsequent 7 days.
- Switching from an IUD: if the woman has engaged in sexual intercourse since the beginning of her current menstrual cycle and it has been more than 5 days since menstrual bleeding commenced, there exists a theoretical possibility of lingering sperm in the genital tract that could potentially lead to fertilization should ovulation occur. A healthcare provider might consider these options:
    - It is advisable to instruct the woman to keep the IUD in place for a minimum of 7 days after commencing combined hormonal contraceptives and then schedule a return visit for IUD removal.

- Furthermore, counsel the woman to either refrain from sexual intercourse or employ barrier contraception for 7 days before removing the IUD and making the transition to the new contraceptive method.
- In cases where the woman is unable to return for IUD removal and has not practiced abstinence from sexual intercourse or used barrier contraception for 7 days, it is recommended to consider the use of Emergency Contraceptive Pills (ECPs) at the time of IUD removal. Combined hormonal contraceptives can be initiated immediately after using ECPs, except for UPA, for which the commencement of combined hormonal contraceptives should be delayed by no less than 5 days following its use.

B. Examinations and Test Needed Before Initiation of Combined Hormonal Contraceptives

For healthy women, there is limited necessity for medical examinations or tests prior to beginning combined hormonal contraceptives (table 12). It is advisable to check blood pressure before starting these contraceptives. Additionally, obtaining baseline measurements for weight and BMI can be beneficial for monitoring women using combined hormonal contraceptives over time. Nevertheless, women with established medical conditions or unique circumstances may require further evaluations or tests to determine their suitability for a specific contraceptive method, with the guidance of U.S. MEC potentially playing a role in such assessments.

Table 12. Classification of Examinations and Tests Needed Before Combined Hormonal Contraceptive Initiation. Retrieved from Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recommendations and Reports. 2021;65(4):1-66. doi:10.15585/MMWR.RR6504A1.

Examination or test	Class*
Examination	
Blood pressure	A†
Weight (BMI) (weight [kg]/height [m]^2)	—§
Clinical breast examination	C
Bimanual examination and cervical inspection	C
Laboratory test	
Glucose	C
Lipids	C
Liver enzymes	C
Hemoglobin	C
Thrombogenic mutations	C
Cervical cytology (Papanicolaou smear)	C
STD screening with laboratory tests	C
HIV screening with laboratory tests	C

Abbreviations: BMI = body mass index; HIV = human immunodeficiency virus; STD = sexually transmitted disease; U.S. MEC = *U.S. Medical Eligibility Criteria for Contraceptive Use.*

* **Class A:** essential and mandatory in all circumstances for safe and effective use of the contraceptive method. **Class B:** contributes substantially to safe and effective use, but implementation may be considered within the public health and/or service context; the risk of not performing an examination or test should be balanced against the benefits of making the contraceptive method available. **Class C:** does not contribute substantially to safe and effective use of the contraceptive method.

† In instances in which blood pressure cannot be measured by a provider, blood pressure measured in other settings can be reported by the woman to her provider.

§ Weight (BMI) measurement is not needed to determine medical eligibility for any methods of contraception because all methods can be used (U.S. MEC 1) or generally can be used (U.S. MEC 2) among obese women (Box 1). However, measuring weight and calculating BMI at baseline might be helpful for monitoring any changes and counseling women who might be concerned about weight change perceived to be associated with their contraceptive method.

Comments:

Blood Pressure: Prior to initiating CHCs, it is imperative to conduct a blood pressure assessment. Women with more pronounced hypertension, indicated by a systolic pressure of ≥160 mmHg or diastolic pressure of ≥100 mm Hg, or those with a history of vascular disease, are advised to abstain from the use of combined hormonal contraceptives, as per U.S. MEC 4.

Similarly, women exhibiting less severe hypertension, with systolic pressure falling within the range of 140–159 mm Hg or diastolic pressure between 90–99 mm Hg, or those who have effectively managed their hypertension, should generally refrain from using CHCs, in accordance with U.S. MEC 3.

Weight (BMI): In most cases, obese women can use CHCs U.S. MEC 2. Therefore, there is usually no requirement to screen for obesity before starting these contraceptives. However, it may be beneficial to measure weight and calculate BMI at the outset to facilitate ongoing monitoring and provide guidance to women who may have concerns about potential weight changes related to their chosen contraceptive method.

Bimanual examination and cervical inspection: A pelvic examination is typically not required before starting CHCs because it does not assist in identifying conditions that would make these contraceptives unsafe. Women with specific medical conditions like current breast cancer, severe hypertension or vascular disease, heart disease, migraine headaches with aura, certain liver diseases, as well as women aged ≥35 years who smoke ≥15 cigarettes per day, should not use (U.S. MEC 4) or are generally discouraged from using (U.S. MEC 3) CHCs. However, it's important to note that these conditions are not typically detectable through a pelvic examination.

Glucose: Screening for diabetes prior to starting hormonal contraceptives is generally not required, as the prevalence of undiagnosed diabetes among women of reproductive age is low, and it's highly probable that women with complicated diabetes would have already received a diagnosis. It's important to note that while women with complicated diabetes should not use (U.S. MEC 4) or are generally discouraged from using (U.S. MEC 3) combined hormonal contraceptives, this recommendation is based on the severity of the condition.

Lipids: Screening for dyslipidemias is typically unnecessary before starting combined hormonal contraceptives. This is due to the low prevalence of undiagnosed dyslipidemia in women of reproductive age and the minimal likelihood of experiencing clinically significant changes in lipid profiles as a result of using hormonal contraceptives.

Liver enzymes: Screening for liver diseases is generally unnecessary before starting combined hormonal contraceptives. This is primarily because these conditions have a low prevalence among women of reproductive age, and it's highly likely that women with liver diseases would have already received a diagnosis.

Thrombogenic mutations: Screening for thrombogenic mutations in women before starting combined hormonal contraceptives is generally not recommended due to the low prevalence of these conditions and the high cost of screening. It's important to note that women with thrombogenic mutations should avoid using combined hormonal contraceptives due to the increased risk of venous thromboembolism.

Clinical breast examination: Conducting a clinical breast examination in asymptomatic women before starting combined hormonal contraceptives is generally not necessarily due to the low prevalence of breast cancer among women of reproductive age. It's important to note that women with current breast cancer should avoid using combined hormonal contraceptives.

Other screening: Screening for conditions such as anemia, cervical intraepithelial neoplasia, cervical cancer, HIV infection, or other STDs is generally not necessary before initiating combined hormonal contraceptives since women with these conditions can use them safely under U.S. MEC 1 or 2 recommendations.

C. Number of Pill Packs that Should Be Provided at Initial and Return Visits

During the initial and follow-up visits, offer or prescribe a supply of COCs for up to one year, typically including 13 sets of 28-day pill packs, tailored to the woman's preferences and intended use.

Access to COCs should be convenient, ensuring that women can acquire them in the quantity and timing that suits their needs. It's important to note that providing more pill packs, up to a total of 13 cycles, tends to increase the likelihood of continuation. Conversely, limiting the distribution or prescription of pill packs can lead to unplanned discontinuation of the method, elevating the risk of pregnancy.

D. Routine Follow-Up After Combined Hormonal Contraceptive Initiation

These guidelines provide recommendations for when routine follow-up is advisable to ensure the safe and effective use of contraception in healthy women. It's important to note that these recommendations are general and may need adjustment based on individual circumstances. Some specific groups that may require more frequent follow-up visits include adolescents, individuals with particular medical conditions or characteristics, and those with multiple medical conditions.

- Women should be informed that they can return at any time for discussions regarding side effects, concerns, or if they wish to change their chosen contraceptive method. In such cases, there is no mandatory routine follow-up visit.
- During other routine visits, healthcare providers attending to users of COCs should:
    - Evaluate the woman's satisfaction with her contraceptive method and inquire about any concerns related to its use.
    - Examine any changes in her health status, including medication use, that might affect the appropriateness of continued use of combined hormonal contraceptives, considering U.S. MEC recommendations, especially for conditions falling under categories 3 and 4.
    - Monitor blood pressure.
    - Optionally, assess weight changes and provide counseling to address any concerns about perceived weight changes associated with the chosen contraceptive method.

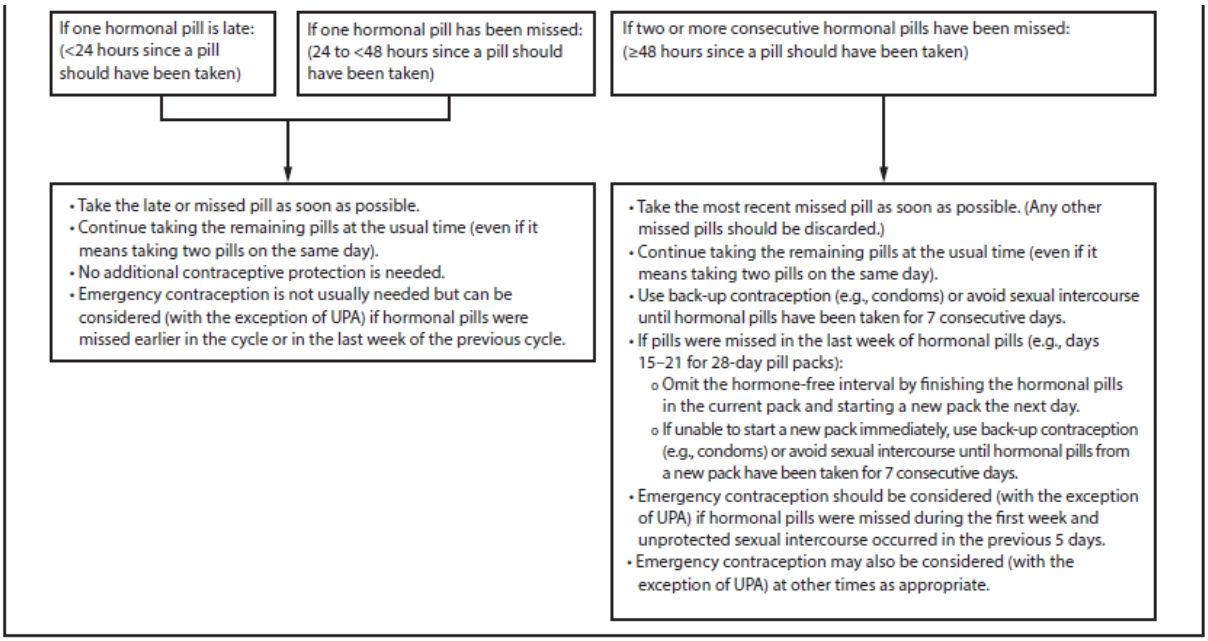
E. Late or Missed Doses and Side Effects from Combined Hormonal Contraceptive Use

The following recommendations pertain to the timing of contraceptive doses. A dose is considered late if it's taken within less than 24 hours after the scheduled time, while it's considered missed if it's taken 24 hours or more after the scheduled time.

To illustrate, if a COC pill should be taken on Monday at 9:00 a.m. but is taken at 11:00 a.m., it's considered late. However, by Tuesday at 11:00 a.m., the pill from Monday at 9:00 a.m. is considered missed, and the Tuesday 9:00 a.m. pill is considered late. It's important to note that these recommendations specifically address late or missed hormonally active pills and not placebo pills.

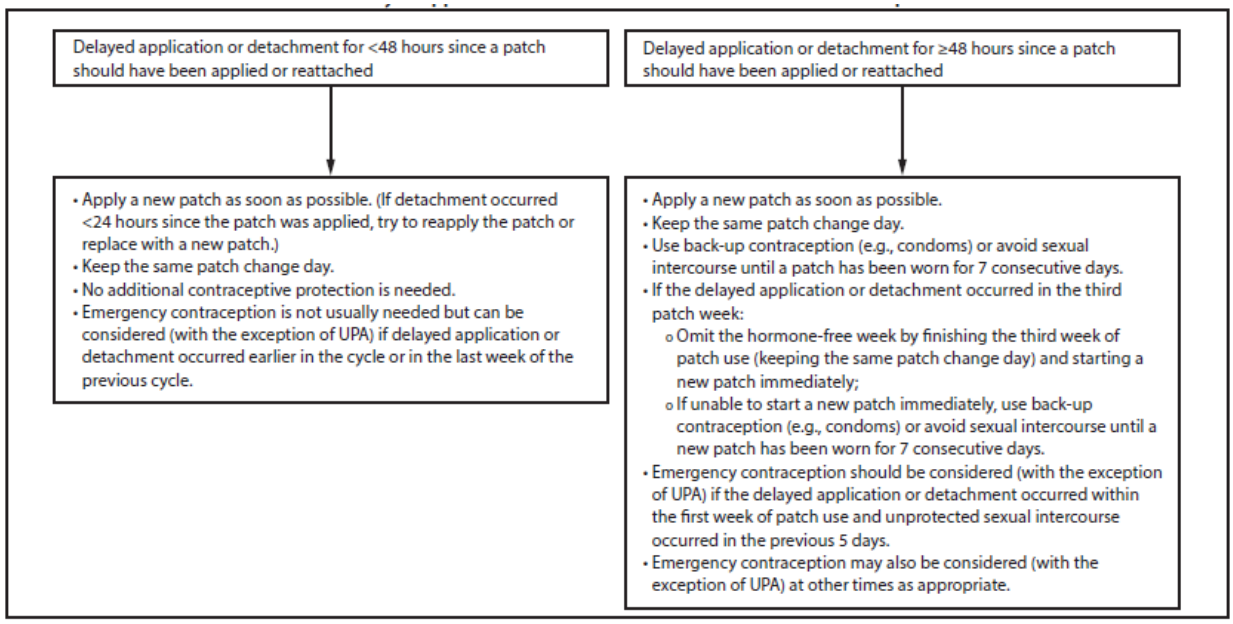
The guidance covers late or missed pills (figure 2), the contraceptive patch (figure 3), and the vaginal ring (figure 4).

Inconsistent or incorrect usage of combined hormonal contraceptives is a significant factor contributing to contraceptive failure. Missing combined hormonal contraceptives during the hormone-free interval, in particular, is considered a high-risk situation as it can lead to unreliable prevention of ovulation. The recommendations aim to strike a balance between providing practical guidance and adhering to the scientific precision of these methods. Women who frequently miss their combined oral contraceptives (COCs), make usage errors with the combined hormonal patch, or encounter problems with the combined vaginal ring should consider alternative contraceptive methods that are less reliant on user adherence to ensure effectiveness. Examples of such methods include intrauterine devices (IUDs), implants, or injectables.



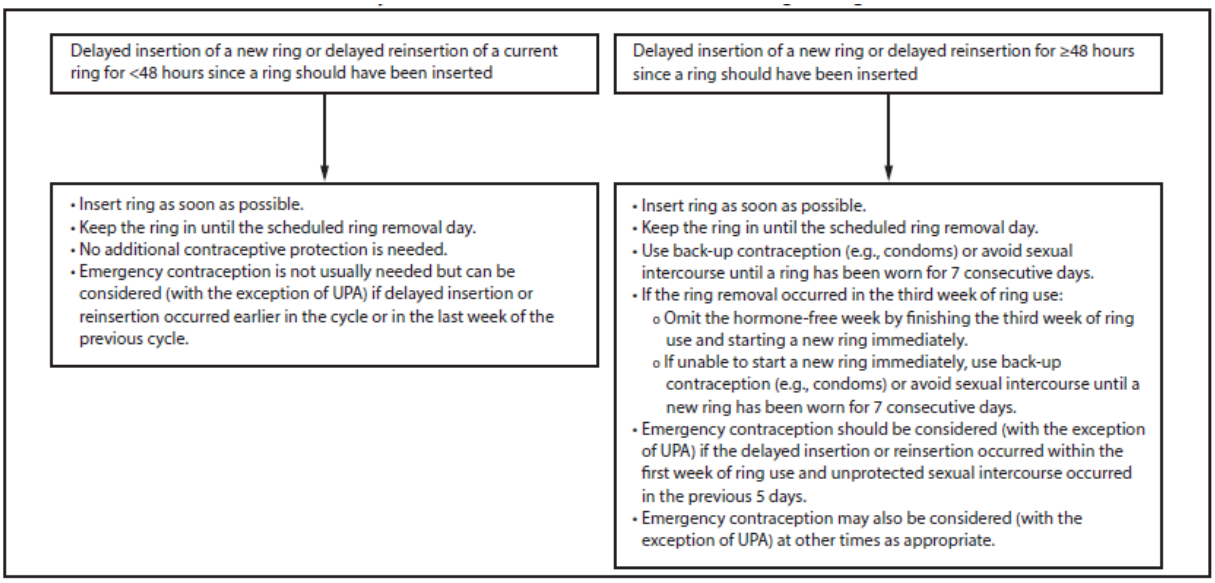
Abbreviation: UPA = ulipristal acetate.

Figure 2. *Recommended Actions After Late or Missed Combined Oral Contraceptives. Retrieved from Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recommendations and Reports. 2021;65(4):1-66. doi:10.15585/MMWR.RR6504A1.*



Abbreviation: UPA = ulipristal acetate.
* If detachment takes place but the woman is unsure when the detachment occurred, consider the patch to have been detached for ≥48 hours since a patch should have been applied or reattached.

Figure 3. *Recommended Actions After Delayed Application or Detachment* with Combined Hormonal Patch. Retrieved from Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recommendations and Reports. 2021;65(4):1-66. doi:10.15585/MMWR.RR6504A1.*



Abbreviation: UPA = ulipristal acetate.
* If removal takes place but the woman is unsure of how long the ring has been removed, consider the ring to have been removed for ≥48 hours since a ring should have been inserted or reinserted.

Figure 4. *Recommended Actions After Delayed Insertion or Reinsertion* with Combined Vaginal Ring. Retrieved from Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recommendations and Reports. 2021;65(4):1-66. doi:10.15585/MMWR.RR6504A1.*

F. Vomiting or Severe Diarrhea While Using COCs

Women who encounter vomiting or severe diarrhea while using combined oral contraceptives (COCs) should follow specific steps outlined in figure 5. However, it's important to note that these recommendations are based on those for missed COCs due to the absence of conclusive evidence regarding the impact of vomiting or severe diarrhea on COC contraceptive effectiveness. There is a lack of data concerning the effects of vomiting or diarrhea on various measures of contraceptive effectiveness, such as pregnancy rates, follicular development, hormone levels, or cervical mucus quality.

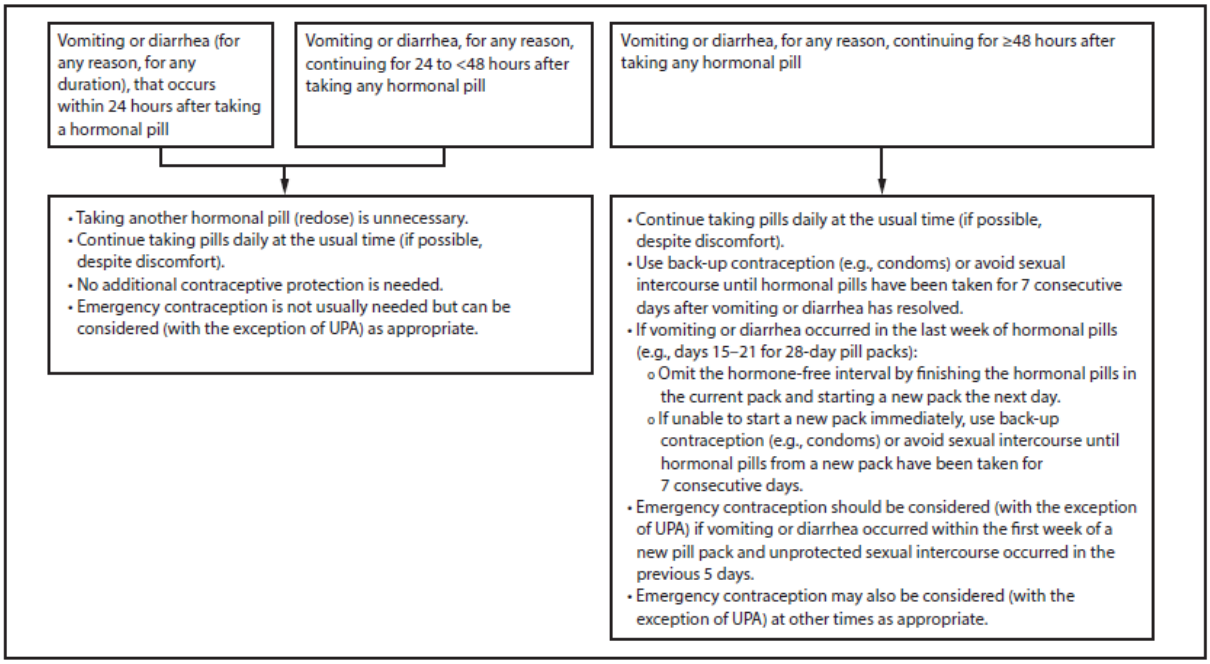


Figure 5. *Recommended Actions After Vomiting or Diarrhea While Using Combined Oral Contraceptives. Retrieved from Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recommendations and Reports. 2021;65(4):1-66. doi:10.15585/MMWR.RR6504A1.*

G. Unscheduled Bleeding with Extended or Continuous Use of Combined Hormonal Contraceptives

Before starting CHCs, it's essential to provide counseling regarding potential changes in bleeding patterns, especially when CHCs are used continuously or with extended cycles (defined as a planned hormone-free interval after at least two consecutive cycles). Here are the key recommendations:

1. **Unscheduled Spotting or Bleeding**: It's common to experience unscheduled spotting or bleeding during the first 3 to 6 months of using extended or continuous CHCs. This is generally not harmful and tends to decrease with continued use of CHCs.
2. **Clinical Evaluation**: If necessary, consider evaluating for underlying gynecological issues. These may include inconsistent CHC use, interactions with other medications, smoking, STD, pregnancy, or newly developed uterine conditions like polyps or fibroids. If such an issue is identified, provide appropriate treatment, or refer the woman for care.
3. **Treatment Options**: If no underlying gynecological problem is found and the woman desires treatment for unscheduled bleeding, consider the following option:

- Advise the woman to discontinue CHC use, leading to a hormone-free interval for 3 to 4 consecutive days. However, it's crucial to note that a hormone-free interval is not recommended during the first 21 days of continuous or extended CHC use. Additionally, having more than one hormone-free interval per month is discouraged as it might reduce contraceptive effectiveness.

4. **Alternative Contraceptive Methods**: If unscheduled spotting or bleeding persists and the woman finds it unacceptable, offer counseling on alternative contraceptive methods, and provide another method if desired.

1.2.1.8 Progestin-Only Pills

POPs exclusively contain a progestin hormone and do not include estrogen. They are readily accessible in the United States. With typical use, around 9 out of 100 women become pregnant during the first year of using POPs. POPs are a reversible contraceptive option suitable for women of all age groups. However, it's important to note that POPs do not provide protection against STDs. To reduce the risk of STD transmission, it is advisable to use male latex condoms consistently and correctly alongside POPs.

A. Initiation of POPs

Timing:

- POPs can be initiated at any time if it is reasonably certain that the woman is not pregnant (table 8).

Need for Back-Up Contraception:

- If POPs are commenced within the first 5 days of menstrual bleeding, no additional contraceptive protection is necessary.
- If POPs are started more than 5 days after the onset of menstrual bleeding, the woman should either abstain from sexual intercourse or use extra contraceptive protection for the subsequent 2 days.

Special Considerations:

Amenorrhea (Not Postpartum)

- Timing: POPs can be introduced at any time when there is reasonable certainty that the woman is not pregnant (table 8).
- Need for back-up contraception: The woman should abstain from sexual intercourse or use additional contraceptive protection for the following 2 days.

Postpartum (Breastfeeding)

- Timing: Progestin-only pills (POPs) can be commenced without specific timing constraints, including immediately following childbirth (U.S. MEC 2 if <1 month postpartum; U.S. MEC 1 if ≥1 month postpartum), provided there is reasonable certainty that the woman is not pregnant, as explained in table 8.
- Need for supplementary contraception: If the woman is within the first 6 months postpartum, is experiencing amenorrhea, and is fully or almost exclusively breastfeeding (where at least ≥85% of feeds are from breastfeeding), there is no requirement for additional contraceptive protection. Alternatively, if a woman is ≥21 days postpartum and has not yet resumed menstruation, she should choose between abstaining from sexual intercourse or using extra contraceptive protection for the subsequent 2 days. On the other hand, if her menstrual cycles have returned and it has been more than 5 days since the onset of menstrual bleeding, she must opt to abstain from sexual intercourse or employ additional contraceptive protection for the following 2 days.

Postpartum (Not Breastfeeding)

- Timing: The initiation of progestin-only pills (POPs) can occur at any moment, including immediately following childbirth (U.S. MEC 1), provided there is a reasonable certainty that the woman is not pregnant, as outlined in table 8.
- Need for supplementary contraception: For women who are < 21 days postpartum, there is no need for additional contraceptive protection. Women who are ≥ 21 days postpartum and have not yet resumed their menstrual cycles should opt for either sexual abstinence or the use of additional contraceptive protection for the subsequent 2 days. In the case where her menstrual cycles have returned and it has been more than 5 days since the onset of menstrual bleeding, she should also choose between sexual abstinence or the use of supplementary contraceptive protection for the ensuing 2 days.

Postabortion (Spontaneous or Induced)

- Timing: The commencement of progestin-only pills (POPs) can take place within the initial 7 days, which includes immediate use following an abortion (U.S. MEC 1).
- Need for supplementary contraception: Unless POPs are initiated at the time of a surgical abortion, the woman is advised to practice sexual abstinence or employ additional contraceptive protection for the following 2 days.

Switching from Another Contraceptive Method

- Timing: The initiation of progestin-only pills (POPs) can occur immediately, provided there is reasonable certainty that the woman is not pregnant (table 8). There is no need to wait for her next menstrual cycle.
- Need for supplementary contraception: If more than 5 days have passed since the onset of menstrual bleeding, the woman should opt for either sexual abstinence or the use of additional contraceptive protection for the ensuing 2 days.
- Transitioning from an IUD: If the woman has engaged in sexual intercourse since the commencement of her current menstrual cycle and it has been over 5 days since the onset of menstrual bleeding, there is a theoretical possibility of lingering sperm in the genital tract, which, if ovulation takes place, could potentially lead to fertilization. A healthcare provider may consider any of the following options:
- Recommend that the woman retain the IUD for a minimum of 2 days after initiating POPs and then schedule a return visit for IUD removal.
- Suggest to the woman to either abstain from sexual intercourse or use barrier contraception for 7 days before removing the IUD and transitioning to the new contraceptive method.
- In cases where the woman cannot return for IUD removal and has not practiced sexual abstinence or used barrier contraception for 7 days, advise her to consider the use of ECPs at the time of IUD removal. POPs can be immediately initiated following the use of ECPs, except for UPA. In situations where there is uncertainty about a potential pregnancy, it is generally advisable to initiate POPs, as the benefits are likely to outweigh any potential risks. Therefore, the initiation of POPs should be contemplated at any time, with a follow-up pregnancy test recommended within 2–4 weeks.

Unlike COCs, POPs hinder ovulation in approximately 50% of menstrual cycles, with variations in effectiveness observed from one individual to another. After taking POPs, peak serum steroid levels are attained roughly two hours post-administration, followed by swift distribution and elimination. Consequently, serum steroid levels tend to revert to nearly their baseline levels within 24 hours after the ingestion of POPs.

Due to its rapid elimination from the body, the key to the effectiveness of POPs lies in taking them at roughly the same time every day. It's worth emphasizing that maintaining approximately 48 hours of continuous POP use is essential to establish the contraceptive impact on cervical mucus.

In cases where a woman requires supplementary contraceptive protection while transitioning to POPs from another contraceptive method, it might be prudent to continue her previous method for an additional 2 days following the initiation of POPs. However, when switching from UPA, the commencement of POPs should not occur until at least 5 days after its use.

B. Examinations and Tests Needed Before Initiation of POPs

In healthy women, there is generally no requirement for medical examinations or tests before starting POPs. However, it might be beneficial to measure baseline weight and BMI for the purpose of monitoring POP users over time (table 13).

Women with known medical conditions or specific health considerations may necessitate additional medical evaluations or tests to determine their suitability for a particular contraception method. In such cases, the U.S. Medical Eligibility Criteria (MEC) can provide valuable guidance.

Table 13. Classification of Examinations and Tests Needed Before Progestin-Only Pill Initiation. Retrieved from Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recommendations and Reports. 2021;65(4):1-66. doi:10.15585/MMWR.RR6504A1.

Examination or test	Class*
Examination	
Blood pressure	C
Weight (BMI) (weight [kg]/height [m]^2)	—†
Clinical breast examination	C
Bimanual examination and cervical inspection	C
Laboratory test	
Glucose	C
Lipids	C
Liver enzymes	C
Hemoglobin	C
Thrombogenic mutations	C
Cervical cytology (Papanicolaou smear)	C
STD screening with laboratory tests	C
HIV screening with laboratory tests	C

Abbreviations: BMI = body mass index; HIV = human immunodeficiency virus; STD = sexually transmitted disease; U.S. MEC = *U.S. Medical Eligibility Criteria for Contraceptive Use.*

* **Class A:** essential and mandatory in all circumstances for safe and effective use of the contraceptive method. **Class B:** contributes substantially to safe and effective use, but implementation may be considered within the public health and/or service context; the risk of not performing an examination or test should be balanced against the benefits of making the contraceptive method available. **Class C:** does not contribute substantially to safe and effective use of the contraceptive method.

† Weight (BMI) measurement is not needed to determine medical eligibility for any methods of contraception because all methods can be used (U.S. MEC 1) or generally can be used (U.S. MEC 2) among obese women (Box 1). However, measuring weight and calculating BMI at baseline might be helpful for monitoring any changes and counseling women who might be concerned about weight change perceived to be associated with their contraceptive method.

Comments:

Body weight: Regarding weight and Body Mass Index (BMI), there is no requirement to screen for obesity before starting POPs since obese women can generally use POPs safely (U.S. MEC 1). However, it might be useful to measure weight and calculate BMI at the beginning to monitor for any changes and to counsel women who may have concerns about weight fluctuations related to their chosen contraceptive method.

In terms of clinical examinations, there is no need for a pelvic examination before initiating POPs because it does not aid in detecting conditions that would make POPs unsafe. Pelvic examination does not provide information relevant to the use of POPs. It's important to note that women with current breast cancer should not use POPs (U.S. MEC 4), and women with specific liver diseases should generally avoid POPs (U.S. MEC 3). However, pelvic examinations are not suitable for detecting these conditions. Screening for these health conditions would require other appropriate diagnostic methods.

Lipids: There is no need for screening for dyslipidemias before starting POPs as it is not essential for the safe initiation of these contraceptives. This is primarily because dyslipidemias are relatively rare among women of reproductive age, and the

chances of experiencing clinically significant changes in lipid levels due to hormonal contraceptives are low. Therefore, routine screening for dyslipidemias before starting POPs is not considered necessary.

Liver enzymes: Screening for liver disease before initiating POPs is not deemed necessary, even though women with certain liver diseases are generally advised against using POPs (U.S. MEC 3). This recommendation is grounded in the relatively low prevalence of these liver conditions among women of reproductive age and the high probability that women with liver disease would have already received a diagnosis for their condition. Consequently, routine screening for liver disease is not considered essential before starting POPs.

Clinical Breast Examination: Before initiating POPs, there is no requirement for conducting a clinical breast examination for asymptomatic women. This recommendation is based on the relatively low prevalence of breast cancer among women of reproductive age. Even though women with current breast cancer are advised against using POPs (U.S. MEC 4), routine clinical breast examination for screening purposes is not considered necessary.

Other screening: Women with conditions such as hypertension, diabetes, anemia, thrombogenic mutations, cervical intraepithelial neoplasia, cervical cancer, STDs, or HIV infection can safely use POPs according to U.S. Medical Eligibility Criteria ratings of 1 or 2. Hence, there is no requirement for screening for these conditions as a prerequisite for the safe initiation of POPs.

C. Number of Pill Packs that Should Be Provided at Initial and Return Visits

- During the initial and follow-up appointments, offer or prescribe a supply of POPs sufficient for up to one year, which typically includes 13 packs of 28-day pills, tailored to the woman's preferences and expected usage.

  Ensure that women can easily access the quantity of POPs they require, precisely when they need them.
- Increasing the number of pill packs supplied up to a total of 13 cycles tends to boost continuation rates. Limiting the quantity of pill packs provided or prescribed can lead to unintended method discontinuation and a higher risk of pregnancy.

D. Routine Follow-Up After POP Initiation

These recommendations outline when routine follow-up is advisable to ensure the safe and effective ongoing use of contraception for healthy women. It's important to note that these recommendations are general and may vary for different individuals and situations. Certain populations, such as adolescents and individuals with specific

medical conditions or characteristics, may benefit from more frequent follow-up visits.

Here are the key points for healthcare providers when managing POP users during routine visits:

- Advise women that they can return at any time to discuss side effects, concerns, or if they wish to switch their contraceptive method. No mandatory routine follow-up visit is necessary.
- During other routine visits, healthcare providers should:
    - Evaluate the woman's satisfaction with her chosen contraceptive method and inquire about any concerns related to its use.
    - Assess any changes in her health status, including modifications in medications, that might impact the suitability of POPs for safe and effective continued use, considering factors outlined in the U.S. MEC (e.g., category 3 and 4 conditions and characteristics).
    - Consider monitoring weight changes and offer counseling to women who express concerns about weight changes they perceive to be associated with their contraceptive method.

E. Missed POPs

A dose is classified as missed when it has exceeded the scheduled time by more than 3 hours. In the event of a missed dose, promptly take one pill.

- Maintain the daily pill regimen, ingesting one pill daily at the same time each day, even if it necessitates taking two pills on the same day.
- Utilize supplementary contraceptive methods, such as condoms, or opt for sexual abstinence until you have consistently taken the pills correctly and on time for two consecutive days.
- Contemplate the use of emergency contraception (excluding UPA) if unprotected sexual intercourse has occurred.

F. Vomiting or Diarrhea (for any Reason or Duration) that Occurs Within 3 Hours After Taking a Pill

- In the event of vomiting or diarrhea, take another pill as soon as possible, even if it causes discomfort.
- Maintain your daily pill routine, taking one pill each day at the same time, as originally scheduled.

- Employ supplementary contraceptive methods, like condoms, or choose sexual abstinence until two days after vomiting or diarrhea have subsided.
- If unprotected sexual intercourse has taken place, contemplate the use of emergency contraception (excluding UPA).

G. Standard Days Method

The Standard Days Method (SDM) relies on fertility awareness, requiring users to abstain from unprotected sexual intercourse between days 8 and 19 of the menstrual cycle. With perfect (i.e., accurate and consistent) use, approximately 5 out of 100 women become pregnant within the first year of using SDM. The effectiveness of SDM with typical use is unavailable but is expected to be lower than with perfect use. SDM is a reversible method suitable for women of all ages. It does not offer protection against STDs; to reduce the risk of STDs, including HIV, it is crucial to use male latex condoms consistently and correctly.

H. Use of SDM Among Women with Various Durations of the Menstrual Cycle

Menstrual Cycles of 26–32 Days

- The woman is eligible to use the method.
- If she desires additional protection, offer a barrier method of contraception during days 8 to 19.
- If she engages in unprotected sexual intercourse during days 8 to 19, consider recommending emergency contraception if appropriate.

Two or More Cycles of <26 or >32 Days Within Any 1 Year of SDM Use

- Counsel the woman that SDM might not be suitable for her due to an increased risk of pregnancy.
- Assist her in exploring alternative contraceptive methods.

Pregnancy risk rises when the menstrual cycle deviates from the 26–32-day range, even if unprotected sexual intercourse is avoided during days 8–19.

1.2.1.9 Emergency Contraception

Emergency contraception encompasses methods utilized by women following sexual intercourse to prevent pregnancy. These methods differ in their effectiveness based on the specific method and when it is administered. Four options are accessible in the United States, including the Cu-IUD and three forms of ECPs.

Types of Emergency Contraception

Intrauterine Device

- Cu-IUD

ECPs

1. UPA in a single dose (30 mg)
2. Levonorgestrel in a single dose (1.5 mg) or as a split dose (1 dose of 0.75 mg of levonorgestrel followed by a second dose of 0.75 mg of levonorgestrel 12 hours later)
3. Combined estrogen and progestin in 2 doses (Yuzpe regimen: 1 dose of 100 µg of ethinyl estradiol plus 0.50 mg of levonorgestrel followed by a second dose of 100 µg of ethinyl estradiol plus 0.50 mg of levonorgestrel 12 hours later)

Initiation of Emergency Contraception

Timing

1. Cu-IUD

The Cu-IUD can be inserted within 5 days of the first act of unprotected sexual intercourse as an emergency contraceptive.

In addition, when the day of ovulation can be estimated, the Cu-IUD can be inserted beyond 5 days after sexual intercourse, as long as insertion does not occur > 5 days after ovulation.

2. ECPs

ECPs should be taken as soon as possible within 5 days of unprotected sexual intercourse.

Cu-IUDs are extremely effective as a means of emergency contraception and can subsequently be maintained for ongoing contraception. UPA and levonorgestrel ECPs exhibit comparable effectiveness when administered within 3 days following unprotected sexual intercourse. Nevertheless, UPA has demonstrated superior efficacy when taken between 3 to 5 days after unprotected sexual intercourse compared to the levonorgestrel variant.

Advance Provision of ECPs

A preemptive provision of ECPs can be made to ensure their availability for timely use following unprotected sexual intercourse.

Initiation of Regular Contraception After ECPs

UPA

Advise the woman to initiate or recommence hormonal contraception no earlier than 5 days following UPA use and provide or prescribe her regular contraceptive method as required. In cases where the regular contraceptive method necessitates a healthcare provider's visit, like DMPA, implants, and IUDs, starting the method concurrently with UPA use might be contemplated. However, it's essential to consider the potential impact of the regular contraceptive method on UPA's effectiveness versus the risk of not initiating a regular hormonal contraceptive method.

The woman should either abstain from sexual intercourse or employ barrier contraception for the subsequent 7 days after beginning or resuming regular contraception or until her next menstrual cycle, whichever occurs first.

Following the use of UPA, any nonhormonal contraceptive method can be promptly initiated.

Furthermore, advise the woman to undergo a pregnancy test if she does not experience a withdrawal bleed within 3 weeks.

Levonorgestrel and Combined Estrogen and Progestin ECPs

- Following the use of levonorgestrel or combined estrogen and progestin ECPs, the woman can promptly initiate any regular contraceptive method.
- She should abstain from sexual intercourse or employ barrier contraception for 7 days.
- It is advisable to undergo a pregnancy test if she does not experience a withdrawal bleed within 3 weeks.

The decision to resume or begin regular hormonal contraception after using ECPs involves a careful assessment of the risk of pregnancy if ECPs fail and the risks associated with unintended pregnancy if the initiation of contraception is postponed until the next menstrual cycle.

Health care providers may offer or prescribe contraceptive pills, patches, or rings for women to start no sooner than 5 days after taking UPA.

When considering methods like DMPA, implants, and IUDs that require a healthcare provider's visit, it may be an option to commence these methods concurrently with the use of UPA. However, this decision should consider the balance between the potential impact of the regular contraceptive method on UPA's effectiveness and the risk associated with delaying the initiation of a regular hormonal contraceptive method.

Prevention and Management of Nausea and Vomiting with ECP Use

Nausea and Vomiting

- Levonorgestrel and UPA ECPs cause less nausea and vomiting than combined estrogen and progestin ECPs.
- Routine use of antiemetics before taking ECPs is not recommended. Pretreatment with antiemetics may be considered depending on availability and clinical judgment.

Vomiting Within 3 Hours of Taking ECPs

- Another dose of ECP should be taken as soon as possible.

Use of an antiemetic should be considered.

Nausea or vomiting is not universally experienced by women taking ECPs, and predicting which women will have these symptoms can be challenging. While it is not recommended to routinely use antiemetics before taking ECPs, they can be effective for some women and may be offered when appropriate. Healthcare providers should make the decision to offer antiemetics to women taking ECPs based on the following considerations:

Women taking combined estrogen and progestin ECPs are more likely to experience nausea and vomiting compared to those using levonorgestrel or UPA ECPs.

There is evidence suggesting that antiemetics can reduce the occurrence of nausea and vomiting in women taking combined estrogen and progestin ECPs.

It's important to note that women who take antiemetics might experience other side effects associated with these medications.

1.2.1.10 Female Sterilization

Laparoscopic, abdominal, and hysteroscopic procedures for female sterilization are available in the United States. Some of these methods can be performed in an outpatient or office setting. The risk of pregnancy in the first year after female sterilization is less than 1 out of 100 women.

However, it's essential to counsel all women considering sterilization about its permanency and inform them about the availability of highly effective, long-acting, reversible contraception methods. Female sterilization does not provide protection against STDs. To reduce the risk of STDs, including HIV, consistent and correct use of male latex condoms is recommended.

When Hysteroscopic Sterilization is Reliable for Contraception

- To ensure the effectiveness of hysteroscopic sterilization as a contraceptive method, a hysterosalpingogram (HSG) should be conducted three months

after the sterilization procedure to verify that both fallopian tubes are completely blocked.

- It's important to inform the woman that she should refrain from sexual intercourse or use additional contraception until bilateral tubal occlusion is confirmed.

When Laparoscopic and Abdominal Approaches are Reliable for Contraception

- A woman can rely on sterilization for contraception immediately after laparoscopic and abdominal approaches.

No additional contraceptive protection is needed.

Confirmation through a hysterosalpingogram (HSG) is essential to verify bilateral tubal occlusion after hysteroscopic sterilization. In the United States, the hysteroscopic sterilization system involves placing inserts bilaterally into the fallopian tubes, which necessitates a waiting period of three months for sufficient fibrosis and scarring to ensure complete bilateral tubal occlusion.

Following hysteroscopic sterilization, it is advisable for the woman to use an effective contraception method while awaiting confirmation consistently and correctly. If there are concerns about adherence to another contraceptive method, the woman and her healthcare provider can discuss the option of a DMPA injection at the time of sterilization to ensure adequate contraception for the three-month waiting period.

It's worth noting that unlike laparoscopic and abdominal sterilizations, there is limited research on the risk of pregnancy beyond seven years of follow-up among women who have undergone hysteroscopic sterilization. Extensive studies have been conducted on pregnancies occurring after at least ten years of follow-up among women who have had laparoscopic and abdominal sterilizations. These methods are highly effective, but pregnancies can still occur many years after the procedure, with a higher risk among younger women.

1.2.1.11 Male Sterilization

Male sterilization, known as vasectomy, is among the limited contraceptive options available to men. This procedure can be conducted in an outpatient or office setting. The risk of pregnancy for a woman whose male partner has undergone sterilization is less than 1 out of 100 within the first year.

Since vasectomy is designed to be an irreversible contraceptive method, it is essential to provide appropriate counseling to men about the permanent nature of sterilization and inform them about the availability of highly effective, long-acting, reversible contraception options for women.

It is important to emphasize that male sterilization does not provide protection against STDs. To reduce the risk of STDs, including HIV, it is necessary to use male latex condoms consistently and correctly.

When Vasectomy is Reliable for Contraception

After a vasectomy, it is recommended to conduct a semen analysis within a period of 8 to 16 weeks. This analysis is crucial to verify the success of the vasectomy procedure.

Men should be informed that they must either use supplementary contraceptive protection or abstain from sexual intercourse until they receive confirmation of the vasectomy's success through a post vasectomy semen analysis.

Other Post-Procedure Recommendations

- The man should refrain from ejaculation for approximately 1 week after the vasectomy to allow for healing of surgical sites and, after certain methods of vasectomy, occlusion of the vas.

1.2.1.12 When Women Can Stop Using Contraceptives

The need for contraceptive protection persists for women over the age of 44 if they wish to prevent pregnancy. This recommendation is based on the fact that **the exact age at which a woman is no longer at risk of pregnancy is uncertain**. While it is rare, spontaneous pregnancies can occur among women aged over 44. Leading medical organizations like the American College of Obstetricians and Gynecologists and the North American Menopause Society suggest that women continue using contraception until they reach menopause or reach the age of 50 to 55. The average age of menopause in North America is around 51, although it can vary from 40 to 60.

There is no definitive laboratory test available to confirm the point at which a woman loses her fertility. Assessing follicle-stimulating hormone levels to determine fertility cessation may not yield accurate results.

Healthcare providers should weigh the risks associated with becoming pregnant at an advanced age and the risks of continuing contraception until menopause. Pregnancies in older women carry higher risks of maternal complications such as hemorrhage, venous thromboembolism, and maternal death, as well as fetal complications like miscarriage, stillbirth, and congenital abnormalities. Additionally, the risks linked to the ongoing use of contraception, such as acute cardiovascular events (e.g., venous thromboembolism, heart attack, or stroke) or breast cancer, should be considered.

According to the U.S. Medical Eligibility Criteria (U.S. MEC), women aged over 45 can safely use progestin-only pills (POPs), implants, the levonorgestrel-releasing intrauterine device (LNG-IUD), or the copper intrauterine device (Cu-IUD) (U.S. MEC1).

Women aged over 45 generally can use combined hormonal contraceptives and depot medroxyprogesterone acetate (DMPA) (U.S. MEC 2). However, women in this age group may have chronic conditions or other risk factors that could make the use of hormonal contraceptive methods unsafe. In such cases, the U.S. MEC can provide guidance on the safe use of contraceptives for these individuals.

For most women, the initiation of contraceptive methods can occur at any time, with minimal or no need for examinations or tests. Routine follow-up typically involves assessing the woman's satisfaction with her chosen contraceptive method, addressing any concerns related to its use, and evaluating any changes in her health status or medications that could affect her eligibility for continued use of the method.

Since irregular bleeding patterns are a common reason for discontinuing contraception, guidelines are provided to manage such irregularities with various contraceptive methods. Additionally, instructions regarding missed pills and dosing errors for the contraceptive patch and ring are streamlined to simplify their use.

Emergency contraception, including emergency use of the copper intrauterine device (Cu-IUD), is highlighted as important options for women. Recommendations are provided for using these methods, as well as for resuming regular contraception after employing emergency contraception.

Male and female sterilization are highly effective options for individuals and couples who have completed their childbearing. However, individuals undergoing vasectomy or hysteroscopic sterilization procedures should use additional contraceptive protection until the success of the procedure can be confirmed.

1.3 European Guidelines

1.3.1 French National College of Gynecologists and Obstetricians (CNGOF) Clinical Practice Guidelines for Contraception (2019)

The French College of Obstetrics and Gynecology (CNGOF) has released its first comprehensive recommendations for clinical practices in contraception in 2019[4]. Specific practical recommendations are provided for the management of contraception prescription, patient information concerning effectiveness, risks, and benefits of the different methods, patient follow-up, intrauterine contraception, emergency contraception, local and natural methods, contraception in teenagers, in women after 40, for women at high thromboembolism or cardiovascular risk, and for those at of primary cancer or relapse.

A. Pharmacology and drugs interactions with contraceptives

The risk of drug interactions with hormonal contraceptives must be anticipated since they have the potential to result in unplanned pregnancies, especially when certain contraceptive methods, such as implants, may not always be perceived as hormonal.

In France, healthcare providers must utilize the National Agency of Drug Safety's (ANSM) official thesaurus when assessing the risk of drug interactions with contraceptive medications.

Most commonly, drug interactions impact CHCs, which consist of both estrogen and progestin. These interactions typically diminish the effectiveness of CHCs due to the induction of hepatic enzymes. Consequently, it is imperative to consider the possibility that drug interactions could compromise the effectiveness of all hormonal contraceptives, whether administered orally, transdermally (via patches), subcutaneously (implants), vaginally (using a ring), or through injections.

Clinicians should remain mindful of the potential reduction in contraceptive effectiveness due to drug interactions, especially for women using CHCs, regardless of the administration method. This awareness should extend to the prescription of any new medication, even if it's for a short duration, and healthcare providers should ensure that women are informed about the risks associated with medication interactions. This risk becomes more pronounced as the contraceptive dose decreases.

When prescribing enzyme-inducing drugs like Saint John's Wort, certain antiepileptic agents, antituberculosis agents, and other medications to women using hormonal contraception, an additional mechanical contraceptive method (such as a barrier method) should be used during the entire short-term treatment period and throughout the subsequent cycle. If the treatment duration is extended, a non-hormonal contraceptive method should be considered. In cases where an enzyme-inducing drug has been taken in the preceding months, it is advisable to use non-hormonal emergency contraception (copper IUD) if possible. If that is not an option, doubling the dose of levonorgestrel is recommended.

Women who use oral contraception should be educated on how to manage severe vomiting or diarrhea, irrespective of the cause (medication-related or not), following the guidelines of the ANSM, and pharmacological data (HAS).

For medications containing coal, it is advisable to take them at least two hours apart, if feasible, from the administration of an oral contraceptive.

When a woman using a CHC with a high dose of ethinyl estradiol (EE) is prescribed medications like etoricoxib, atorvastatin, azole antifungal agents, or boceprevir, healthcare providers should consider the increased risk of elevated EE concentrations.

Starting a CHC during the dose-adjustment period for lamotrigine is not recommended. Any changes (initiation, modification, or discontinuation) in hormonal contraception necessitate concurrent adjustments to the lamotrigine dosage, in consultation with a neurologist.

Saint John's Wort, a potentially effective antidepressant, should be avoided as it significantly reduces CHC estrogen concentrations and is contraindicated in conjunction with hormonal contraception. Conversely, large quantities of grapefruit juice can have the opposite effect, increasing estrogen concentrations.

Combining a copper IUD with non-steroidal anti-inflammatory drugs (NSAIDs) has not been shown to diminish its contraceptive effectiveness.

Using a copper IUD for contraception is not considered contraindicated when undergoing either chronic or occasional NSAID treatment. There is insufficient data available to draw any definitive conclusions regarding the use of glucocorticoids in conjunction with a long-term copper IUD.

In situations where emergency contraception is needed for a woman who is either already using hormonal contraception or plans to use it following emergency contraception, levonorgestrel is the preferred choice over ulipristal.

If there is a plan to initiate or resume hormonal contraception after using ulipristal acetate for emergency contraception, it is recommended to use additional mechanical contraception for the 12 days following the ulipristal intake.

B. Consultation for contraception

A structured consultation empowers women to modify their contraceptive choice and reduces the occurrence of unintended pregnancies when compared to conventional, non-individualized consultations. The key topics to address during this consultation include **effectiveness, risks, expenses, duration of activity, and practical considerations**. Effective interpersonal communication seems to lead to a higher rate of ongoing contraception use and greater satisfaction with the chosen contraception at the two-year mark.

It is strongly advised that consultations related to contraception and family planning be both structured (providing comprehensive information and involving the patient in decision-making) and evidence-based to conclude with a customized prescription. In fact, **personalizing contraceptive guidance** is encouraged.

The potential adverse effects of the chosen contraceptive method should be thoroughly explained to the woman, as these explanations have been shown to enhance the likelihood of continued contraceptive use.

Decision support, such as through audiovisual presentations, has demonstrated its utility when there are multiple therapeutic options available. During consultations,

categorizing contraceptives by their level of effectiveness helps women better understand the differences in effectiveness, more so than presenting statistics about pregnancy rates.

C. Emergency contraception (EC)

In France, there are two methods of emergency contraception in use:

1. Hormonal methods (emergency oral contraceptives), which involve either **levonorgestrel (LNG)** or **ulipristal,**
2. Mechanical method, which involves the postcoital insertion of a copper IUD.

It's important to note that hormonal emergency contraception is not entirely foolproof, and its effectiveness decreases as the time between unprotected intercourse and taking the emergency contraception increases. Women should be informed that emergency contraception is not 100% effective.

If menstruation is delayed following the use of emergency contraception, a pregnancy test is recommended.

LNG is a progestin that should be used within 72 hours after unprotected intercourse or contraceptive method failure. Its effectiveness increases the closer it is taken to the time of unprotected intercourse and when taken as early as possible before ovulation. LNG is more likely to result in early menstruation.

Ulipristal delays follicle rupture by 5 days when administered just before the LH surge and is more effective in delaying ovulation compared to LNG when given in the late follicular phase. Its adverse effect profile is similar to that of LNG, and it's more likely to cause delayed periods.

Ulipristal should not be used for emergency contraception in women using long-term hormonal contraception.

The copper IUD is the most effective form of emergency contraception. It can be used up to 5 days (120 hours) after unprotected sexual intercourse or in cases where the contraceptive method used has failed. Furthermore, the copper IUD offers the advantage of providing long-term contraception after insertion. It is considered a first-line treatment, and its use is encouraged. However, data on the use of the LNG-IUD for emergency contraception are currently insufficient to recommend it.

Regarding the impact of obesity, a body mass index (BMI) greater than 25 reduces the effectiveness of LNG as emergency contraception. For obese women with a BMI over 30, the risk of emergency contraception failure is multiplied by 4.4 for LNG and by 2.6 for ulipristal. Therefore, a copper IUD or ulipristal is recommended for emergency contraception in women with a BMI exceeding 30.

D. Intrauterine contraception

Intrauterine contraception can be offered to adolescents and women who have not given birth (nulliparas). This is because it boasts excellent effectiveness, high continuation rates, and a low risk of complications, which are no greater than those observed in other age groups or among women who have already experienced childbirth.

The available data do not indicate a higher risk of infection for women living with HIV before reaching the AIDS stage. The use of intrauterine contraception does not increase the risk of either virus progression or transmission to a partner. Consequently, the IUD is not contraindicated for women living with HIV before the AIDS stage.

Several studies involving women with heart disease have not found any contraindication to intrauterine contraception. In cases of severe heart disease, the benefit-risk balance of IUD placement appears to favor it over pregnancy. However, antibiotic prophylaxis is necessary for preventing the risk of infectious endocarditis in women with severe valve disease.

Before placing an IUD, it is formally recommended to perform only a digital cervical examination, along with a bimanual examination and cervical inspection. The standard cervical cancer screening regimen should not be altered for IUD users.

Routine screening for STDs is not recommended before IUD placement. However, practitioners should screen for STDs, particularly Chlamydia trachomatis and Neisseria gonorrhea, when STD risk factors are present, such as age under 25 years, being in a relationship for less than three months, having multiple partners in the last year, a history of STD, or engaging in unprotected intercourse. Ideally, this screening should be conducted on the day the IUD is prescribed (using vaginal and endocervical samples or self-samples), but it can also be performed on the day of IUD placement without delaying the procedure, provided the woman is asymptomatic.

An IUD can be inserted at any point during the menstrual cycle as long as it is certain that pregnancy is not underway. There is no need for antibiotic prophylaxis or routine premedication for IUD placement.

It is advisable to trim the strings to a length of 2-3 cm from their projection outside the external os immediately after insertion. They can be shortened at a subsequent visit if discomfort, particularly during sexual intercourse, is experienced.

After IUD insertion, women should be informed about the symptoms that should prompt them to consult their healthcare provider. A follow-up visit can be recommended in the weeks following IUD placement, and women should be informed of the date when the IUD should be removed.

Systematic ultrasound verification is not recommended if the woman is asymptomatic, the IUD insertion was uncomplicated, and the strings are visible and of the expected length upon examination.

Uterine perforation is a rare complication of intrauterine contraception. Although it often occurs during placement, it may be diagnosed at a later time. Risk factors include ongoing breastfeeding, placement within 6 months of delivery, operator inexperience, and extreme uterine positions (ante- or retro-versions). If there is any suspicion of perforation, pelvic ultrasound scans and plain abdominal radiography should be performed to locate the IUD. In the event that the IUD has migrated into the abdomen, the laparoscopic approach is preferred for removal.

Expulsion most commonly occurs during the first year following placement. Risk factors for expulsion include age below 20 years, menorrhagia, dysmenorrhea, myomas, adenomyosis, a history of expulsion, and a large transverse diameter of the endometrial cavity. During the follow-up visit in the weeks after IUD placement and then annually, it is essential to verify the presence of the threads during gynecologic examinations.

The copper IUD is associated with an increase in menstrual flow, while the 52-mg LNG-IUD can lead to a reduction in menstrual flow or even amenorrhea. Women should be informed about potential modifications in menstrual flow before IUD placement.

Regardless of the type of IUD used, persistent vaginal bleeding or pelvic pain should prompt additional evaluation to identify potential complications.

Intrauterine contraception is not a risk factor for ectopic pregnancy. However, if a pregnancy occurs despite the presence of the IUD, it is appropriate to rule out an ectopic pregnancy. A history of ectopic pregnancy is not a contraindication to IUD placement.

The presence of a viable and desired intrauterine pregnancy is considered a more significant complication when an IUD is present. If the threads are accessible, the IUD should be removed.

Functional ovarian cysts are relatively common during the use of a 52-mg LNG-IUD, but they typically resolve on their own. In asymptomatic patients, there is no need to remove the device. Having a history of functional cysts is not a contraindication for LNG-IUD placement.

In the case of Actinomyces-like organisms being detected on a PAP smear in an asymptomatic woman, this finding should not prompt additional investigation, early removal of the IUD, or antibiotic treatment.

Intrauterine contraception does not appear to be a risk factor for upper genital tract infections, except during the early period (3 weeks to 4 months) after insertion.

Therefore, it is not recommended to immediately remove the IUD after diagnosing a sexually transmitted infection or upper genital tract infection. If the prescribed treatment does not yield a favorable outcome within 48–72 hours, the possibility of removing the device should be discussed. Having a history of sexually transmitted infections or upper genital tract infections does not constitute a contraindication to IUD placement, as long as it occurs at a reasonable interval from the episode.

E. Contraceptives for women with venous and arterial risk

a. Venous thromboembolic risk

It is now firmly established that the use of CHCs increases the risk of venous thromboembolism (VTE) by a factor of 3–6 when compared to non-users. This risk is most pronounced during the first year of CHC use. The overall increase in risk depends on the hormonal composition of the combination, including the type of estrogen (ethinyl estradiol or 17 beta estradiol), the ethinyl estradiol dosage, and the specific progestin used.

CHCs containing third-generation progestins (gestodene or desogestrel), drospirenone, or cyproterone acetate are associated with a higher risk of VTE than those containing levonorgestrel, while those containing norgestimate have a VTE risk similar to that of levonorgestrel-containing contraceptives. The VTE risk for non-oral CHC administration routes is likely equivalent to that of oral CHCs containing third-generation progestins.

Family histories of VTE, especially those involving first-degree relatives (parents and siblings) or a high number of relatives, regardless of the degree of relationship, along with known thrombophilia, are significant risk factors for VTE. These risks are particularly relevant when the history of VTE occurred in a context involving hormone-related factors such as estrogen-progestin treatment or pregnancy.

Progestin-only contraceptives, whether taken orally, as implants, or via LNG-IUDs, do not appear to be associated with an increased risk of VTE, unlike progestin-only contraception administered via intramuscular (IM) medroxyprogesterone acetate (RR 2.6, 95% CI 1.8–3.8). Therefore, it is advisable for physicians to assess all vascular risk factors for VTE, including family history, through history-taking and clinical examination before prescribing combined hormonal contraception.

In the absence of a family history of vascular disease, there is no recommendation for a thrombophilia work-up before prescribing CHCs. However, a first-degree family history of VTE (from either the paternal or maternal side) with an onset before the age of 50 is considered a contraindication to the use of CHCs.

CHCs, regardless of the type or route of administration, are contraindicated for women with confirmed congenital thrombophilia.

For women without contraindications, **the first-line CHC prescribed should contain either levonorgestrel or norgestimate.** Progestin-only contraceptives are recommended for women at high risk of VTE who desire hormonal contraception. Injectable depot medroxyprogesterone acetate (DMPA) contraception should not be prescribed for women at high risk of VTE.

In the event of a deep vein thrombosis or pulmonary embolism, CHC use should be discontinued unless there is no risk of pregnancy during the current cycle. DMPA should not be renewed. There is insufficient data available to make a recommendation regarding the continuation of progestin-only contraception during the acute phase of a venous thromboembolism.

b. Arterial disease risk and hormonal contraceptives

Numerous epidemiological studies have examined the link between oral CHC use and the risk of myocardial infarction (MI). These studies found a pooled risk associated with CHC use, regardless of its specific components, of 1.7 (95% CI 1.2–2.3).

A recent Cochrane review that included 24 epidemiological studies, indicated that only combined oral contraception containing at least 50 mcg of ethinyl estradiol (EE) is associated with the risk of arterial events (MI or ischemic stroke)

This meta-analysis did not find any differences in risk between the generations of oral CHC.

In summary, there is no significant difference in the risk of arterial thrombosis between the generations of oral CHCs currently used in France. Data regarding non-oral routes of administration, such as the ring or patch, are insufficient to draw valid conclusions. No epidemiological study has assessed the arterial risk of contraceptives containing estradiol.

There is a dose-dependent synergistic effect of smoking (more than 15 cigarettes/day) in CHC users in relation to the risk of MI and likely ischemic stroke.

Oral CHC is contraindicated in women at a high risk of arterial disease. Among smokers, individual risk should be assessed based on associated cardiovascular risk factors (table 14).

No significant increase in the risk of MI or ischemic stroke has been reported in the literature in connection with the use of progestin-only contraception, whether oral (minipill) or in the form of an implant or LNG-IUD. In conclusion, progestin-only contraceptives, regardless of their type, do not appear to be associated with arterial risk (ischemic stroke or MI). The data regarding DMPA are limited.

Unlike other forms of progestin-only contraception, DMPA, administered via quarterly injection, should not be prescribed to women with at least two cardiovascular risk factors or a history of arterial ischemic events.

When an arterial event (MI or ischemic stroke) occurs, CHC use should be discontinued, unless there is no risk of pregnancy during the current cycle.

Non-hormonal contraception should be the preferred first-line treatment.

Table 14. Arterial or Venous Vascular Risk Factors (VRFs) and Use of Combined Hormonal (Estrogen-Progestin) Contraception (CHC). Retrieved from Chabbert-Buffet N, Marret H, Agostini A, et al. Clinical practice guidelines for contraception by the French National College of Gynecologists and Obstetricians (CNGOF). J Gynecol Obstet Hum Reprod. 2019;48(7):441-454. doi:10.1016/j.jogoh.2019.04.009.

Risk factors	Use of CHC
Age > 35 years	Possible, if no other VRFs
Overweight – obesity	Possible, if no other VRFs
Smokes > 15 cig/day	Possible, if no other VRFs
1 st degree family history of MI or stroke before the age of 55 years (men) or 65 years (women)	Contraindication
Hypertension	Contraindication
Dyslipidemia	Contraindication
Uncontrolled	Possible, if no other VRFs
Controlled	Relative contraindication, if dyslipidemia began with CHC
Insulin-dependent (Type I) diabetes	Contraindication if diabetes > 20 years or if vascular complications
Type 2 diabetes	Possible, if no other VRFs but in second line (1 st choice: progestin-only contraception or copper IUD).
Migraine with aura	Contraindication
Migraine simple	Possible if no other VRFs

Venous risk factors	Use of CHC
Age > 35 years	Possible, if no other VRFs
Overweight – obesity	Possible, if no other VRFs
Laboratory-diagnosed thrombophilia	Contraindication
1 st degree family history of VTD (venous thromboembolic disease) before the age of 50 years	Contraindication

c. Migraine and contraceptives

The European consensus group conducted an assessment of the absolute risk of ischemic stroke among women aged 20–44 years. They found that migraines with aura were associated with a stroke incidence of 5.9/100,000, compared to 4.0/100,000 for migraines without aura, and 2.5/100,000 for women without migraines. The use of CHC significantly increased these risks, particularly for women with migraines. For women with migraines, the respective stroke incidence increased to 36.9, while for those with migraines without aura, it increased to 25.4/100,000, and for women without migraines, it increased to 6.3/100,000.

These risks were even higher among women who had other risk factors, especially smoking.

Therefore, before prescribing CHC, healthcare providers should inquire about the patient's migraine history and distinguish between migraines with aura and those without.

It is strongly recommended that **CHC not be prescribed to women who have migraines with aura or to those who have migraines without aura and have another vascular risk factor.**

For women with migraines with aura, non-hormonal contraception or progestin-only hormonal contraception should be recommended.

F. Contraception and cancer

f. Contraception and cancer risk

Overall, the use of contraception has not been associated with an increase in cancer incidence or mortality for all types of cancer.

However, the ongoing use of CHC has been linked to a moderate increase in the risk of breast cancer. This elevated risk tends to decrease after discontinuation of CHC use. A similar moderate increase in breast cancer risk has also been reported with progestin-only contraceptives, including the LNG-IUD, although there is conflicting data regarding this association. Limited data are available regarding the risk associated with DMPA and progestin implants, making it challenging to draw definitive conclusions.

There has been an increased risk of invasive cervical cancer reported in users of oral contraception, particularly with prolonged use, but this effect appears to diminish after discontinuation. Analyzing this risk is complicated by the fact that Human papillomavirus (HPV) exposure and oral contraception use are not independent factors.

On the positive side, CHC has been linked to a reduced risk of endometrial cancer, ovarian cancer, malignant blood diseases, and colorectal cancer, and these reductions in risk persist even after discontinuation. LNG-IUD has also been associated with a reduced risk of endometrial and ovarian cancer.

There has been no observed increase in the overall risk of melanoma, hepatocellular carcinoma, thyroid cancer, bronchial cancer in nonsmokers, or central nervous system tumors.

While cancer risk information is an important part of the discussion with women who do not have cancer or specific risk factors, it does not typically alter the prescription of contraception, as the benefits of contraception generally outweigh its risks. The choice of contraceptive method continues to depend on an individual's unique benefit-risk balance, considering factors such as age, individual and family history.

There is no need to modify the standard follow-up procedures.

b. Contraception during cancer treatment

It is advisable to wait for a minimum period of six months to one year after completing cancer treatment, and sometimes even longer depending on the specific cancer-related circumstances, before considering pregnancy. Contraception is essential for all sexually active non menopausal women undergoing cancer treatment. The choice of contraception may be limited by factors such as the patient's immune system status, risk of blood clots, and tolerance to gastrointestinal treatments.

In cases where a patient's immune system is compromised, such as with blood disorders or myelosuppressive treatments, the use of condoms is recommended to reduce the risk of STDs. Inserting an IUD should be approached with caution in immunocompromised women due to the heightened risk of genital infections shortly after insertion. To minimize this risk, testing for Chlamydiae and gonococci by PCR can be considered before IUD insertion. However, the effectiveness of IUDs in this context has not been thoroughly evaluated. An LNG-IUD, which operates independently of the body's inflammatory response, may be a preferred option.

Prescribing CHC should take into account potential drug interactions with other medications. For patients undergoing treatments that induce vomiting, it is advisable to opt for hormonal contraceptives delivered through implants, patches, or rings, or non-hormonal alternatives.

Thromboembolic risk tends to increase during cancer treatment due to various factors, including the disease itself, chemotherapy, surgery, and limited mobility. Given the elevated risk of thromboembolism associated with CHC, it is recommended to avoid their use throughout the treatment period. Macrodose progestins, administered at anti-gonadotropic levels, may be a viable alternative for hormone-independent cancers as they can induce amenorrhea while minimizing the risk of blood clots. In some cases, GnRH agonists may serve as an off-label contraceptive option during treatment.

It is advisable to refrain from using CHC during cancer treatment to avoid compounding the risk of thromboembolism. Periodic reevaluation of contraceptive options is necessary for women diagnosed with cancer.

c. Male antitumor treatment: are condoms necessary?

Two studies conducted prior to the year 2000 indicated the potential transmission of chemotherapy agents through seminal fluid.

However, the available data is insufficient to support a general recommendation for men undergoing cancer treatment to use condoms regularly, unless they are participating in research protocols evaluating new antitumor agents.

d. Contraception after cancer

Women who have previously undergone cancer treatment often report receiving inadequate information and practicing insufficient contraceptive use. It's worth noting that a delayed resumption of ovarian activity is possible in these cases.

For women who have undergone cancer treatment and were not menopausal at the time of diagnosis, contraception should be routinely considered. However, hormonal contraceptives are contraindicated after breast cancer due to the potential risk of relapse and limited data available. Non-hormonal contraception is recommended for women with a history of breast cancer, with the copper IUD being the preferred first-line contraceptive method due to its reversibility, long-lasting effectiveness, and excellent reliability. This recommendation holds irrespective of the time since treatment, hormone receptor status, and the histologic type of cancer (ductal/lobular/invasive/in situ).

In cases of endometrial cancer, conservative treatments that do not induce sterility are rarely indicated and are typically reserved for very early-stage tumors in young women who wish to preserve fertility (stage IA and grade 1 endometrioid tumors). While awaiting treatment for endometrial cancer, the use of CHC, injectable DMPA, progestin-only contraception, and either a copper IUD or LNG-IUD is possible. The 52-mg LNG-IUD can even be considered as a conservative treatment for atypical hyperplasia or grade 1 endometrial adenocarcinoma. CHC, DMPA, and progestin-only contraception can be used while waiting for treatment for endometrial cancer.

The 2017 guidelines for contraception following rare malignant ovarian tumors were issued by the national network specializing in rare gynecologic cancers (TMRG/GINECO). In cases where conservative treatment has been administered for borderline or germ-cell tumors, the use of hormonal contraception, irrespective of the specific type, is generally not considered contraindicated. However, after conservative treatment for an adult granulosa cell tumor, it is recommended to avoid contraceptives that contain estrogens. In instances of mucinous, high-grade serous, or high-grade endometrioid adenocarcinomas, hormonal contraceptives, regardless of their type, are typically not contraindicated. Nonetheless, it is advised against using hormonal contraceptives following the treatment of low-grade serous or endometrioid adenocarcinomas.

Regarding cervical intraepithelial neoplasms (CIN) or cervical cancer, discontinuing any type of contraception upon diagnosis while awaiting treatment is not recommended, given the positive benefit-risk balance in this situation. There is no evidence to contraindicate the use of hormonal or non-hormonal contraception, regardless of type, after conservative treatment of CIN or cervical cancer. For invasive cervical cancer, there is currently insufficient data to provide guidelines on the use of hormonal contraception.

There is no available evidence regarding contraception after colorectal cancer, but it's worth noting that oral contraception users have shown a reduced risk of colorectal cancer. Thus, there is no justification for limiting the use of hormonal or non-hormonal contraception after colorectal cancer.

Hormonal contraception's impact on liver function is a concern, especially for hepatocellular carcinoma, although no data in the literature report an association. Therefore, non-hormonal contraception is preferred.

There is no evidence to limit the use of hormonal or non-hormonal contraception after thyroid cancer. Similarly, there are no specific recommendations for hormonal contraception after lung cancer, and decisions should be made on a multidisciplinary basis.

For women who have had malignant central nervous system tumors, hormonal contraception is not contraindicated based on the currently inadequate data, with decisions adapted by histologic subtypes.

Women who have received strong thoracic irradiation, particularly for Hodgkin disease, have an elevated risk of breast cancer. Still, there is no available evidence to justify specific recommendations regarding hormonal contraception after thoracic irradiation.

e. Emergency contraception after hormone-dependent cancer (in particular, breast cancer)

Considering the potential consequences of pregnancy during cancer treatment, emergency contraceptives, including oral contraception, are permissible after the diagnosis of a hormone-dependent cancer. However, whenever feasible, a cautious approach suggests prioritizing the use of a non-hormonal copper IUD.

f. Contraception and family predisposition to cancer

1. **Hereditary Breast and Ovary Cancer Syndrome (BRCA1/2):** In 2017, Institut Nationol de Cancer (INCa) published guidelines for the monitoring and care of women carrying the BRCA1/2 gene mutation. These guidelines affirm that "women with the BRCA1 or 2 mutation who do not have breast cancer" can be offered hormonal contraception, whether it is combined or progestin-only, irrespective of the method of administration.

   When there is a history of breast cancer, prescription of hormonal treatments should be under the guidance of an oncologist, and detailed information about the breast cancer should be obtained prior to the consideration of hormonal contraception.

2. **Lynch Syndrome (HNPCC Syndrome - Hereditary Non-Polyposis Colon Cancer)**: Lynch syndrome, also known as HNPCC syndrome, is an autosomal dominant condition associated with a significantly increased risk of various

cancers, including colorectal, endometrial, ovarian, small intestine, upper urinary tract, hepatobiliary tract, and stomach cancers. Currently, there is insufficient data to evaluate the effectiveness of CHC, progestin-only contraception, or LNG-IUD in preventing colorectal cancers in individuals with Lynch syndrome. While there is some evidence suggesting a reduced risk of endometrial cancer in this syndrome, the data remain inconclusive. As of now, prophylactic surgery is considered the sole effective method of prevention for Lynch syndrome. Importantly, there are no specific contraindications to the use of either hormonal or non-hormonal contraception in individuals with Lynch syndrome.

G. Hormonal contraception in practice (except LNG-IUD)

CHC can be administered through various routes, including **oral, vaginal, or transdermal methods**. The administration can be continuous or intermittent. It's important to note that all combined contraceptives exhibit the same level of contraceptive effectiveness, regardless of how they are administered.

However, certain estrogen-progestin combinations carry a higher risk of venous thromboembolism, particularly when not taken orally.

For women who prefer oral contraceptives, first-line recommendations include those containing either LNG or norgestimate. Extended or continuous administration of CHC can be considered for specific medical indications (e.g., managing menstrual symptoms, functional menorrhagia, and endometriosis) and for personal convenience.

Progestin-only contraceptives are available in **oral form (minipill), for continuous use, as subcutaneous implants, or via quarterly intramuscular injections**. The etonogestrel implant is highly effective for contraception, even in obese women (maximum BMI observed in these studies: 56 kg/m2). As a Long-Acting Reversible Contraceptive (LARC) method, the implant can be recommended to women seeking effective contraception with minimal adherence requirements. There is no need to replace the etonogestrel contraceptive implant in obese women within the first 3 years of use.

Typically, hormonal contraceptives are initiated on the first day of a menstrual period. However, a "quick start" approach involves commencing hormonal contraception at other points in the menstrual cycle.

The option of initiating hormonal contraceptive use with a "quick start" approach can be extended to all women who express interest, provided they receive clear information regarding the necessary precautions. These precautions include:

1. Verifying that pregnancy is not already present

2. Combining hormonal contraception with an additional barrier method for the first 7 days
3. Informing the woman about the potential for vaginal bleeding during the initial month of use.

Common side effects: (particularly progestins):

1. vaginal bleeding
2. acne
3. weight gain
4. reduced libido which may increase the risk of discontinuation.

Vaginal bleeding while on contraceptives is frequently linked to suboptimal adherence but can also stem from infections, endometrial issues, or functional causes. Women experiencing vaginal bleeding while using hormonal contraception should undergo a comprehensive assessment, which may include a pelvic ultrasound and cytobacterial examination of discharge. An hCG assay should be conducted in cases of suspected poor adherence or clinical suspicion of pregnancy.

There is insufficient solid evidence to suggest that any particular combined oral contraceptive is better tolerated than others. In cases of poorly tolerated vaginal bleeding persisting for at least 3 months with no identified organic cause, it is advisable to consider changing the contraceptive method. Options may include increasing the estrogen dose, altering the type of progestin, or transitioning to a non-oral form of CHC (such as patches or a vaginal ring). However, neither modifying the progestin nor transitioning to multiphasic formulations is recommended.

In cases of vaginal bleeding persisting for at least three months with no identified organic cause while using a progestin-only oral contraceptive, adding estrogen treatment or another medication is not recommended, as its effectiveness is unproven.

If **acne** develops while using a second-generation CHC, it is reasonable to consider switching contraceptives or using a combination triphasic contraceptive containing 35 mg of EE and norgestimate. If these measures fail, consulting a dermatologist for specific acne treatment and/or using a CHC containing a different, anti-androgenic progestin can be discussed with the woman.

Any **reduction in libido** while using hormonal contraception should be explored through questioning, with a focus on assessing other psychological aspects of this concern. Discussing a change in contraceptive method can also be considered.

Hormonal contraceptives have not been found to be associated with **weight gain**. The use of the subcutaneous etonogestrel implant or injectable DMPA may slightly increase the risk of weight gain but is not a routine occurrence. In cases of

significant weight gain, a thorough evaluation should be conducted to explore other potential causes if appropriate.

Headaches that occur while using hormonal contraceptives could indicate a vascular risk and require appropriate management. The onset of new migraines or worsening of preexisting migraines while using CHC necessitates discontinuation of CHC. If menstrual migraines occur during the treatment-free interval while taking CHC, a continuous course of treatment can be suggested. Alternatively, percutaneous administration of relatively high-dose estrogen (at least 1.5 mg gel/day or patches dosed at 100 mg/24 h) during the treatment-free interval can be considered as an alternative to continuous CHC administration. Other contraceptives do not appear to significantly influence the natural course of migraines.

Some women using hormonal contraception have reported **mood disorders**. Data regarding the link between hormonal contraception and mood disorders are diverse and contradictory. There is no substantial evidence establishing hormonal contraception as a risk factor for mood disorders. Any changes in mood while using hormonal contraception should be explored through questioning, with a focus on assessing other psychological aspects of this concern. Discussing a change in contraceptive method can also be considered.

H. Contraceptives for adolescents

It is imperative to intricately balance the comprehensive well-being of adolescents, considering not only their general equilibrium, weight stability, and adequate calcium intake but also to remain mindful of the importance of STD prevention and vaccination against HPV. Employing condoms in conjunction with regular contraceptive use is indispensable, as they serve as a vital barrier against.

The initial contraceptive consultation represents a pivotal moment when dealing with adolescents, offering an opportunity for sex education and guidance on contraceptives to empower them to avoid unplanned pregnancies. During this visit, it is essential to ensure the patient's privacy by allowing her to be seen alone for at least a portion of the consultation.

The clinical evaluation should encompass a general assessment, measuring height, calculating body mass index, checking blood pressure, and assessing for signs of hyperandrogenemia, such as acne or hirsutism. A gynecological examination is not mandatory during the first visit unless a patient's medical history or symptoms warrant it.

Women employing contraceptive methods other than condoms should receive guidance on condom usage and the associated risk of.

Providing teenagers with genuine contraceptive options and delivering objective information about various contraceptive methods is of paramount importance. Emphasizing the exceptional effectiveness of LARCs is a pivotal aspect of this education.

In the absence of contraindications, if the initial prescription is for a CHC, it is advisable to select progestins like LNG or norgestimate.

Initiating contraception through vaginal (ring) or percutaneous (patch) routes, both of which employ third-generation progestins, is not preferred as first-line options. However, depending on the individual circumstances, these alternatives may be considered after conducting a thorough benefit-risk assessment.

Adolescence represents the life stage with the lowest vascular risk. For some experts, prescribing a pill with **30 mcg of ethinyl estradiol (EE)** may carry greater importance to ensure improved protection in case of missed pills, especially for very young women, and to maintain bone mineralization.

Existing literature does not provide substantial evidence to justify recommending any specific contraceptive method to adolescents, except when particular contraindications apply. It is recommended to present all contraception modalities collectively and then proceed in alignment with established guidelines.

LARCs such as IUDs and implants, are not contraindicated and offer highly favorable effectiveness profile.

I. Contraceptives after the age of 40 years

The available data in the literature for women in the 50 and older age group are limited. Various recent consensus statements and guidelines have been published. Despite the decline in fertility as women age, effective contraception remains crucial if pregnancy is not desired, as pregnancies in this age group carry higher risks, and elective abortions for unwanted pregnancies are more common.

International literature consensus supports the use of CHC by women aged 40 and older, barring specific contraindications. CHC can offer non-contraceptive benefits during this phase of a woman's life, such as potential prevention of bone demineralization and reduction of conditions like menorrhagia, dysmenorrhea, and early symptoms of estrogen deficiency. No study provides evidence justifying strict age-based contraindications for any particular contraceptive method.

Progestin-only contraceptives, except for DMPA, can be considered due to their neutrality regarding vascular risk factors. However, this population may experience issues such as spotting, potential exacerbation of hyper-estrogenic symptoms, and difficulty managing signs of hypo-estrogenism. DMPA in women over 40 has adverse effects on vascular, blood glucose, and bone health.

IUDs are both effective and well-tolerated, especially after the age of 40. Clinicians should educate women aged 40 and older about fertility, pregnancy risks, and vascular, metabolic, and carcinogenic risks to help them evaluate the benefit-risk balance of different contraceptive options.

The risks and benefits of oral contraception should be reevaluated in women aged 40 or older.

Progesterone-only oral contraceptives can be offered as a first-line option for women over 40 due to their minimal impact on vascular, metabolic, and bone indicators, provided that women are informed about potential side effects.

DMPA is not recommended as a first-line contraceptive for women older than 40, particularly those with vascular risk factors, where it may be either a contraindication or a relative contraindication (for osteoporosis).

A copper IUD placed after a woman turns 40 can remain in place until menopause. The LNG-IUD is particularly suitable for managing menorrhagia or dysmenorrhea during perimenopause. An LNG-IUD placed after the age of 45 can also be left in place until menopause, potentially offering benefits through the menopausal period, when combined with percutaneous estrogen.

Women should be informed about various barrier methods of contraception. Conversely, natural methods based on fertility awareness and tracking ovulation, which becomes unpredictable with age, are particularly unreliable for women over 40.

Emergency contraception (using progestins or a selective progesterone receptor modulator (SPRM) does not exhibit specific considerations for this age group.

Permanent contraception (sterilization) for either men or women can become a viable option after the age of 40.

Beyond the age of 50, the primary question is when contraception can be discontinued?

Women using non-hormonal contraception should be advised to continue it until they experience a full year of amenorrhea after reaching 50.

Cessation is essential for women still using CHC. Hormone assays are not recommended for women on hormonal contraception. Instead, a treatment transition should be considered while maintaining contraception through a barrier method. In the absence of menopause, non-hormonal or progestin-only contraception (excluding DMPA) should be established. Among women using progestin-only contraception (oral, subcutaneous, or intrauterine), a transition period can be proposed, during which contraception through a barrier method helps confirm the persistence of ovarian activity.

J. Natural and barrier methods

In total, 4.6% of women report utilizing natural contraceptive methods based on identifying their fertile periods. These methods rely on either symptom observation (such as the Billings' cervical mucus method, Two Day method, Temperature method, or Symptothermal method) or calendar-based calculations of fertile days (like the Ogino-Knaus method or Standard Day method). The evidence supporting the effectiveness of these methods is limited, with the quality of studies ranging from moderate to low.

Women should be informed about the comparatively lower effectiveness rates of these methods when compared to hormonal contraception and intrauterine devices. Those who choose to use these methods should receive precise instructions on their proper usage, including the fact that abstaining from vaginal penetration enhances their effectiveness and that the use of a potentially error-prone barrier method diminishes their effectiveness. Data regarding the reliability and effectiveness of LH peak monitors and detection kits are insufficient.

The MAMA method is grounded in lactational amenorrhea, which occurs due to breastfeeding under specific conditions. Women employing the MAMA method for contraception should be educated that its effectiveness reaches 98% until six months after childbirth if amenorrhea persists and if exclusive breastfeeding is maintained. They must also be informed that the risk of pregnancy increases if they decrease the frequency of feedings (e.g., by discontinuing night feedings or introducing other foods or a pacifier) after six months or if menstruation resumes.

The withdrawal method (coitus interruptus) necessitates that the man withdraws from the vagina and genital area before ejaculation. Sperm must not come into contact with the vagina or vulva. This method's effectiveness is low. It is not recommended as a standalone contraceptive method, nor as an alternative or backup to barrier methods.

Barrier methods can be either physical (e.g., male and female condoms, cervical caps, and diaphragms) or chemical (spermicides), sometimes used in combination.

Condoms offer dual protection, preventing both unintended pregnancies and most STDs, including HIV. Their effectiveness is high when used in strict accordance with guidelines.

Cervical caps and diaphragms must remain in place for at least six hours after the last intercourse. However, they do not provide protection against STDs and HIV.

Spermicides used alone have a low effectiveness rate. Nonoxynol-9-based products are discouraged due to their potential to cause vaginal lesions, increasing the risk of HIV transmission.

Conclusion:

Healthcare professionals should offer patients detailed instructions on using male and female condoms. For optimal effectiveness, cervical caps and diaphragms are recommended to be used with spermicidal creams. The spermicidal gel must be applied for each instance of successive intercourse. Products containing nonoxynol-9 are not recommended.

Natural and barrier methods can be used either simultaneously or as alternative backup methods, particularly when adherence to other methods is suboptimal. Their use is preferable to completely foregoing contraception. Only condoms (male and female) provide protection against most STDs and HIV.

Women should also be informed about the availability of emergency contraception.

K. Non-contraceptive benefits of contraceptives

a. Non-contraceptive benefits of CHC

These additional effects remain consistent regardless of whether CHC is administered orally, vaginally, or transdermally, as all of them influence the endometrium in response to natural female hormones.

Prevention of Some Cancers:

CHC is associated with a protective effect against endometrial cancer and ovarian cancer. This protection is positively linked to the duration of CHC use and persists for more than three decades after discontinuation. CHC is also linked to a reduced risk of colon cancer. Physicians are advised to inform women about these protective effects regarding endometrial, ovarian, and colon cancer when responding to questions about cancer risks associated with CHC.

Menstrual Cycle Disorders:

CHC reduces the volume of functional menorrhagia and alleviates dysmenorrhea and premenstrual syndrome. Women seeking contraception and experiencing menorrhagia, dysmenorrhea, or premenstrual syndrome should be offered CHC after a clinical evaluation of these conditions and in the absence of contraindications.

Endometriosis:

CHC plays a significant role in managing painful endometriosis and preventing postoperative recurrence. It is considered a first-line treatment among hormone therapies, with its effects observed during treatment and disappearing upon cessation. Continuous administration benefits are not well-documented, except in cases of surgery or intense dysmenorrhea.

CHC is recommended as a first-line treatment for the medical management of painful endometriosis. For women not planning pregnancy, postoperative hormonal therapy is advised to reduce the risk of painful recurrence and improve quality of life.

CHC is indicated to reduce the risk of recurrence after surgical removal of endometriomas. Continuation of CHC is recommended as long as it is well-tolerated and pregnancy is not desired. For women with dysmenorrhea, continuous CHC prescription is preferred, with adherence to thromboembolic risk guidelines.

Benign Diseases of the Breast and Uterus:

CHC use has been associated with a reduction in the incidence of fibrocystic breast changes without atypia and breast fibroadenomas, with this reduction correlated with duration of use. Similarly, the incidence of uterine myomas has decreased in CHC users, with a reduction proportional to the duration of use. While benign breast and uterine lesions are not direct indications for CHC, nor is it automatically contraindicated (in the absence of atypia), the individual benefit-risk balance must be assessed.

Rheumatoid Arthritis:

The use of CHC for at least seven years is associated with around a 20% reduction in the incidence of rheumatoid arthritis, with a greater risk reduction observed with longer CHC use.

Acne:

CHC is clinically effective in treating acne, although its effectiveness compared to other treatments is a subject of debate. Its effect ceases when CHC treatment is discontinued. In 2015, the French Society of Dermatology issued specific acne guidelines that do not take a definitive stance on CHC as a first-line treatment due to the complex benefit-risk balance. If there is no need for contraception, prescribing CHC as the first-line treatment for acne is not recommended.

b. Non-contraceptive benefits of progestin-only contraceptives

This section focuses exclusively on progestin-only contraceptives authorized for marketing as contraceptives, which include LNG or desogestrel minipills, etonogestrel implants, and DMPA. Intrauterine systems containing LNG (such as the 52-mg LNG-IUD) are also considered within the context of IUDs.

There has been a limited number of studies evaluating the potential non-contraceptive benefits of progestin-only contraception, and the level of evidence supporting these benefits is generally low. The 2017 clinical practice guidelines from CNGOF (French National College of Obstetricians and Gynecologists) addressed the role of progestins in managing endometriosis.

Progestin-only contraceptives can be considered as a second-line option for managing painful endometriosis in women who do not wish to become pregnant or for whom CHC are contraindicated. There is currently no study assessing the effectiveness of progestin-only contraceptives in the medical treatment of myomas. The only study examining the risk of myomas in progestin-only contraceptive users suggests a lower risk in present or past users of DMPA.

There is no available study that has examined the impact of minipills or the etonogestrel implant on the reduction of menorrhagia, encompassing all underlying causes. However, two randomized studies indicate that the 52-mg LNG-IUD is more effective in this regard compared to DMPA or typical medical treatments.

Regarding the potential preventive or therapeutic effects of microprogestin contraceptives on functional uterine bleeding, no studies have provided conclusive evidence. Several small prospective studies do suggest a modest increase in hemoglobin levels among users of the etonogestrel implant.

Dysmenorrhea:

The etonogestrel implant and continuous desogestrel contraceptives may alleviate dysmenorrheic pelvic pain or chronic pelvic pain due to venous congestion (for the implant only).

Overall, the non-contraceptive benefits of progestin-only contraception, whether in oral or implant form, are not definitively established. The available studies are limited, and the level of evidence remains low. Predicting which women might benefit from these effects is particularly challenging, as the response, especially regarding hemorrhage, can be contrary to the desired outcome.

c. Non-contraceptive Benefits of the LNG-IUD

The benefits of the LNG-IUD extend beyond contraception and have been well-documented in various medical conditions, making it not just a contraceptive but also a therapeutic agent. Its marketing authorization recognizes this unique characteristic, and the 52-mg LNG-IUD is already included in some recommended treatment regimens.

Most studies have primarily assessed the LNG-IUD for its therapeutic effects, with fewer focusing on its non-contraceptive benefits during contraceptive use. These studies confirm its value for women experiencing specific symptoms of pain or excessive bleeding.

Menorrhagia: For women dealing with menorrhagia (heavy menstrual bleeding), the LNG-IUD stands out as the most effective treatment option in terms of improving quality of life and minimizing complications. Women treated with endometrectomy face twice the risk of complications and experience less effectiveness in comparison.

Consequently, the LNG-IUD is notably effective in treating menorrhagia and preventing anemia.

Dysmenorrhea: The utilization of the 52-mg LNG-IUD is linked to a substantial decrease in the severity of dysmenorrhea compared to other methods. The LNG-IUD is recommended for its contraceptive properties and its beneficial effects on menorrhagia and dysmenorrhea. However, it's important to thoroughly assess these conditions before prescribing the LNG-IUD, and any decision should be made with the woman's informed consent.

Endometriosis: The LNG-IUD has been found to reduce pain levels in women with untreated endometriosis. It also lowers the risk of painful recurrence and enhances the quality of life for women who have undergone surgery, with similar effects to GnRH analogs (GnRHa). For women not intending to conceive, the contraceptive use of the LNG-IUD is recommended as a first-line treatment, alongside CHC, after surgery for painful endometriosis.

d. Non-Contraceptive Benefits of Copper Intrauterine Devices

Several publications have highlighted the positive non-contraceptive effects of copper IUDs, particularly in two aspects:

Reducing the risk of endometrial cancer, even though the exact mechanism remains unclear.

Serving as a co-factor in protecting against epidermoid or adenomatous cervical cancer. This effect may be more pronounced in populations at higher risk.

IUDs may influence the natural progression of cervical cancer by inhibiting the development of precancerous cervical lesions in women infected with Papillomavirus or by enhancing their clearance.

The utilization of copper IUDs is associated with a significant decrease in the risk of endometrial and cervical cancers. However, this action alone does not suffice to recommend their use solely for prophylactic purposes.

L. Conclusion

Research in the field of contraceptives is advancing on multiple fronts to enhance their tolerability and accessibility for a broader range of women while promoting consistent use. This research encompasses various aspects, including innovative methods of administration, the development of new compounds, and novel combinations of existing components. While this list is not exhaustive and continues to evolve, noteworthy advancements include:

1. Reduction in the ethinyl estradiol dose to as low as 10 micrograms.
2. Introduction of a new "natural" estrogen, estetrol.

3. Shortening or even eliminating the treatment-free interval, with or without the use of placebos.
4. Development of injectable CHC containing estradiol cypionate and medroxyprogesterone acetate.
5. Introduction of new transdermal systems featuring progestins like LNG or gestodene.
6. Creation of a vaginal ring with a one-year duration of effectiveness.
7. Exploration of over-the-counter availability for progestin-only contraception.

While research into contraceptive vaccines and male contraceptives faces certain challenges and limitations, these areas have not yielded significant breakthroughs to date.

In practice, male contraceptives remain primarily limited to barrier methods such as condoms or permanent sterilization, such as vasectomy.

Looking ahead, the future of contraception, as far as we can anticipate it today, largely hinges on optimizing the utilization of existing contraceptive options.

1.3.2 Faculty of Sexual and Reproductive Health (FSRH) Guideline on Combined Hormonal Contraception (2019, Amended 2023)

The UK-based faculty of sexual and reproductive health (FSRH) published its clinical guidelines on the use of CHCs in January 2019, subsequently amended in July 2023[5]. NICE has accredited the process used by the FSRH to produce this guideline. An explanation of the classification of evidence level and grading of recommendations can be found in table 15. Main recommendations are summarized in table 16.

Table 15. FSRH Classification of Evidence Level and Grading of Recommendations

Grade	Definition
A	At least one meta-analysis, systematic review or randomised controlled trial (RCT) rated as 1++, and directly applicable to the target population; or A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results.
B	A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+.

C	A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++.
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+.
✓	Good Practice Point based on the clinical experience of the guideline development group.

Table 16. FSRH Recommendations for the Use of Combined Hormonal Contraception

Summary of recommendations	
How is CHC used	
✓	Tailored combined hormonal contraceptive (CHC) regimens can reduce the frequency of withdrawal bleeds and can reduce withdrawal symptoms associated with the hormone-free interval (HFI); however, unscheduled bleeding is common.
✓	Women should be given information about both standard and tailored CHC regimens to broaden contraceptive choice.
✓	Women should be advised that use of tailored CHC regimens is outside the manufacturer's license but is supported by the Faculty of Sexual & Reproductive Healthcare (FSRH).
✓	Women should have access to clear information (either written or digital) to support tailored CHC use.
When can CHC be started?	
D	CHC containing ethinylestradiol (EE) can be started by medically eligible women up to and including Day 5 of a natural menstrual cycle without the need for additional contraceptive protection.
D	CHC containing EE can be quick started by medically eligible women at any other time (with advice to use additional contraceptive precaution for 7 days) if: It is reasonably certain that the woman is not pregnant OR A high sensitivity urine pregnancy test is negative (even if there is a risk of pregnancy from unprotected sexual intercourse [UPSI] in the last 21

	days). A follow up high sensitivity urine pregnancy test is required 21 days after the last UPSI.
How effective is CHC?	
C	Contraceptive effectiveness of all CHC is similar.
✓	If used perfectly, CHC is very effective for contraception. With typical use, CHC is less effective for contraception than long-acting reversible contraception (LARC).
✓	Women requesting CHC should be informed about the effectiveness (with both typical and perfect use) of CHC and other contraceptive methods, including the superior effectiveness of LARC.
Is contraceptive effectiveness of CHC affected by obesity/weight?	
C	Most evidence suggests no association between weight/body mass index (BMI) and effectiveness of combined oral contraceptives (COC).
D	Limited evidence suggests a possible reduction in patch effectiveness in women ≥90 kg.
Is contraceptive effectiveness of CHC affected by bariatric surgery?	
D	Women who have had bariatric surgery should be advised that the effectiveness of COC could be reduced.
Enzyme-inducing drugs	
D	Women using enzyme-inducing drugs should be informed that the contraceptive effectiveness of CHC could be reduced during use of the enzyme-inducer and for 28 days after stopping.
D	Women using enzyme-inducing drugs should be offered a reliable contraceptive method that is unaffected by enzyme-inducers.
Lamotrigine	
D	Women taking lamotrigine should be advised that CHC may interact with lamotrigine; this could result in reduced seizure control or lamotrigine toxicity. The risks of using CHC could outweigh the benefits.
Antibiotics (non enzyme-inducing)	
D	Additional contraceptive precautions are not required when antibiotics that do not induce enzymes are used in conjunction with CHCs.
Progestogen receptor modulators	
D	Women should be advised to wait 5 days after taking ulipristal acetate for emergency contraception (UPA-EC) before starting CHC. Women should be made aware that they must use condoms reliably or abstain

	from sex during the 5 days waiting and then until their contraceptive method is effective.
Severe diarrhea or vomiting	
✓	Women using COC should be advised that contraceptive effectiveness could be reduced by vomiting or severe diarrhoea.
Non-contraceptive health benefits associated with CHC use	
✓	Use of CHC for contraception may also be associated with non-contraceptive health benefits
B	Use of CHC can reduce heavy menstrual bleeding (HMB) and menstrual pain and improve acne.
C	Use of CHC may be beneficial for women with premenstrual syndrome (PMS) symptoms.
A	Use of CHC (particularly continuous CHC regimens) can reduce risk of recurrence of endometriosis after surgical management.
B	CHC can be used for management of acne, hirsutism and menstrual irregularities associated with polycystic ovary syndrome (PCOS).
C	CHC use is associated with a significant reduction in risk of endometrial and ovarian cancer that increases with duration of CHC use and persists for many years after stopping CHC.
C	Use of CHC is associated with a reduced risk of colorectal cancer
Health risks associated with CHC use	
✓	Women should be informed about the health risks associated with use of CHC.
Venous thromboembolism (VTE) (including deep vein thrombosis and pulmonary embolism)	
C	Current use of CHC is associated with increased risk of VTE; some CHC formulations are associated with a greater risk of VTE than others, dependent on progestogen type and estrogen dose.
C	Women should be advised that use of CHC is associated with an increased risk of VTE, but the absolute risk of VTE for an individual CHC user remains very small.
Arterial thromboembolic disease	
C	Current use of CHC is associated with a very small increased risk of myocardial infarction (MI) and ischaemic stroke that appears to be greater with higher doses of estrogen in COC.

C	Women should be informed that current use of CHC is associated with an increased risk of MI and ischaemic stroke but that that these events are still extremely uncommon in CHC users.
✓	Use of CHC by women with significant additional risk factors for arterial disease should be strongly cautioned or avoided.
Breast cancer	
C	Women should be advised that current use of CHC is associated with a small increased risk of breast cancer which reduces with time after stopping CHC.
Cervical cancer	
C	Women should be advised that current use of CHC for more than 5 years is associated with a small increased risk of cervical cancer; risk reduces over time after stopping CHC and is no longer increased by about 10 years after stopping.
Assessment of suitability of CHC for an individual woman	
C	Use of suitable self-completed checklists for medical eligibility appears to be accurate and acceptable to women.
✓	Assessment of medical eligibility for CHC should include medical conditions, lifestyle factors and family medical history
✓	A drug history should identify: • any prescribed or non-prescribed drug that could affect the effectiveness of the contraceptive • any prescribed or non-prescribed drug that could itself be affected by the contraceptive
C	A recent, accurate blood pressure recording should be documented for all women prior to first CHC prescription.
D	BMI should be documented for all women prior to CHC prescription.
D	Pelvic examination is not required prior to initiation of CHC.
D	Breast examination, cervical screening, testing for thrombophilia, hyperlipidemia or diabetes mellitus and liver function tests are not routinely required prior to initiation of CHC.
✓	Women for whom CHC is unsuitable should be offered alternative effective contraception.
Choosing type and formulation of CHC	
✓	COC containing ≤30 µg EE in combination with levonorgestrel or norethisterone is a reasonable first-line choice of CHC to minimise cardiovascular risk.

Other important supporting information	
✓	Women should be provided with written information or a link to a trusted online resource to support safe, effective CHC use.
Duration of CHC prescription	
C	HCP can prescribe up to 12 months' supply of CHC for women who are initiating or continuing CHC.
Follow-up	
✓	Women should be advised that routine annual review of their contraception is recommended during CHC use.
✓	Medical eligibility, drug history, method adherence and method satisfaction should be reassessed at follow up. BMI and blood pressure should be recorded.
CHC use during travel	
C	Women using CHC should be advised about reducing periods of immobility during travel.
CHC use at high altitude	
D	Women trekking to high altitudes (above 4500 m or 14 500 feet) for periods of more than 1 week may be advised to consider switching to a safer alternative contraceptive method.
Surgery/periods of immobilization	
D	Women should be advised to stop CHC and to switch to an alternative contraceptive method at least 4 weeks prior to planned major surgery or expected period of limited mobility.
How long can women use CHC?	
D	CHC can be used by medically eligible women for contraception until age 50 years.
Use of CHC as an alternative to hormone replacement therapy (HRT)	
D	CHC can be considered for use by medically eligible women until age 50 as an alternative to HRT for relief of menopausal symptoms and prevention of loss of bone mineral density as well as for contraception.

1.3.3 Faculty of Sexual and Reproductive Health (FSRH) Guideline on Progestogen-Only Pills (2022, Amended 2023)

The same classification of evidence level and grading of recommendations detailed in table 15 above is applied for the recommendations below:

Table 17. FSRH Recommendations for the Use of Progestogen-Only Pills

Summary of recommendations	
Incorrect POP use	
✓	Contraceptive effectiveness of the progestogen-only pill (POP) relies on correct use.
✓	A traditional POP is considered missed if it is taken more than 3 hours late, a desogestrel (DSG) POP if it is taken more than 12 hours late, and a drospirenone (DRSP) POP if more than 24 hours late.
How effective are POPs?	
D	The risk of pregnancy during the first year of typical POP use has been estimated at about 9% If used perfectly, POPs may be more than 99% effective.
D	The available evidence is too limited to inform whether there is a significant difference in contraceptive effectiveness between traditional POPs and DSG/DRSP POPs.
What can affect effectiveness of the POP?	
Vomiting	
✓	Contraceptive effectiveness could be affected if a POP user vomits within a few hours of pill-taking.
Weight/BMI	
✓	Double-dose POP for contraception is not required for individuals who are overweight or individuals with obesity
D	The available evidence suggests that effectiveness of the POP is not affected by body weight or body mass index (BMI).
Bariatric surgery	
D	There is insufficient evidence to inform whether contraceptive effectiveness of POPs is affected by bariatric surgery. Users may therefore wish to consider effective non-oral contraception after bariatric surgery.
Drug interactions	
✓	Contraceptive effectiveness of POPs could be reduced by concomitant use of enzymeinducing drugs
Who can and cannot use POP?	
All POP	
D	The FSRH supports the use of all POPs by medically eligible individuals between menarche and age 55 years.

D	Breast cancer, arterial thromboembolism that occurred during use of a POP, decompensated cirrhosis and hepatocellular tumours are UKMEC3 or UKMEC4 conditions for use of all POPs.
Additional specific considerations for DRSP POP	
✓	The manufacturer advises that the DRSP POP should not be used by individuals with severe renal insufficiency or acute renal failure.
✓	The guideline development group (GDG) suggests that DRSP POP should also generally be avoided by: • Individuals with known hyperkaliemia or untreated hypoaldosteronism (eg, Addison's disease). • Individuals currently using potassium-sparing diuretics, aldosterone antagonists or potassium supplements.
✓	The GDG suggests that DRSP POP should be used with caution by individuals with mild/moderate renal impairment or treated hypoaldosteronism (eg, treated Addison's disease).
✓	The GDG suggests that for individuals with significant risk factors for chronic kidney disease, measurement of urea & electrolytes (U&E) and blood pressure should be considered prior to prescription of the DRSP POP, particularly if aged over 50 years.
What health risks are and are not associated with use of POP?	
Risk of venous thromboembolism	
C	The published evidence is very limited but suggests no increase in risk of venous thromboembolic events associated with use of POPs.
Risk of arterial thromboembolism	
C	The published evidence is very limited but suggests no increase in risk of thrombotic stroke or myocardial infarction associated with use of POPs.
Risk of breast cancer	
D	The available evidence suggests a possible association between current or recent use of hormonal contraception (including POP) and a small increase in risk of breast cancer; absolute risk remains very small.
Risk of ectopic pregnancy	
C	The use of all effective methods of contraception, including POPs, reduces the risk of all pregnancies (including ectopic pregnancies) compared to use of no contraception.
What are the side effects of POP?	
Change in bleeding pattern	

C	Individuals considering use of a traditional POP should be advised that bleeding pattern is unpredictable; but as a guide, over a 3-month period ending at about 12 months of use: • Fewer than 1 in 10 (only about 2%) LNG POP users may be amenorrhoeic. • About 1 in 10 LNG POP users may have infrequent bleeding (1–2 bleeding/spotting episodes). • About 8 in 10 LNG POP users may have normal frequency bleeding (3–5 bleeding/spotting episodes). • About 1 in 10 LNG POP users may have frequent bleeding (6 or more bleeding/spotting episodes). • Fewer than 1 in 10 LNG POP users may have prolonged bleeding (bleeding/spotting episode(s) lasting >14 days)
C	Individuals considering use of a DSG POP should be advised that bleeding pattern is unpredictable; but as a guide, over a 3-month period ending at about 12 months of use: • About 4 in 10 DSG POP users may have normal frequency bleeding (3–5 bleeding spotting/episodes). • About 2–3 in 10 DSG POP users may be amenorrhoeic. • About 3 in 10 DSG POP users may have infrequent bleeding (14 days).
C	Individuals considering use of a DRSP POP should be advised that bleeding pattern is unpredictable; they may or may not have "scheduled" bleeding/spotting during the 4-day HFI and they may or may not have "unscheduled" bleeding/spotting at other times. Both scheduled and unscheduled bleeding/spotting may reduce in frequency over the first year of use. Over a 3-month period at around 6–9 months of use: • The total number of days of bleeding/spotting (scheduled plus unscheduled) may be similar to the number of days of bleeding/spotting with the DSG POP. • About 2–3 in 10 DRSP POP users may be amenorrhoeic. • Fewer than 1 in 10 DRSP POP users may have frequent bleeding. • Fewer than 1 in 10 DRSP POP users may have bleeding episode(s) lasting >14 days.
Mood change	
C	The available evidence does not establish a causal relationship between POP use and depression.
Headache	

D	Evidence is too limited to confirm or exclude any causative association between POP use and headache.
Acne	
D	A causal association cannot be confirmed or excluded by the very limited evidence relating to POP use and acne.
Weight	
D	Whilst users of POP may gain some weight during use, there is not clear evidence that POP use causes significant weight gain.
When can the POP be started?	
✓	It is established practice that traditional and DSG POP can be started on days 1–5 of a natural menstrual cycle, by day 5 after abortion or by day 21 after childbirth without requirement for additional contraceptive precautions. At any other time, traditional and DSG POP can be quick started according to Quick Starting Guidance, with advice to use additional contraceptive precautions for 2 days and to take a follow-up pregnancy test if required.
✓	To align with manufacturer guidance for the new DRSP POP, the GDG recommends that additional contraceptive precautions are required unless DRSP POP is started on day 1 of a natural menstrual cycle, day 1 after abortion or by day 21 after childbirth. If started at any other time, additional contraceptive precautions are required for 7 days with advice to take a follow-up pregnancy test if appropriate.
Breastfeeding	
A	The available evidence indicates that progestogen-only methods of contraception have no adverse effects on lactation, infant growth or development.
What drug interactions are important to consider?	
Enzyme-inducing drugs	
✓	Individuals using enzyme-inducing drugs should be informed that the contraceptive effectiveness of all POPs could be reduced during use of the enzyme-inducer and for 28 days after stopping the enzyme-inducer.
✓	Individuals using enzyme-inducing drugs should be offered a reliable contraceptive method that is unaffected by enzyme-inducers.
Ulipristal acetate (UPA)	
D	The ability of ulipristal acetate emergency contraception (UPA-EC) to delay ovulation could be reduced if a POP is started within 5 days of taking the UPA.

✓	The ability of UPA-EC to delay ovulation could theoretically be reduced if a POP has been taken in the preceding 7 days.
✓	Individuals should be advised to wait 5 days after taking UPA-EC before starting a POP. They should be made aware that they must use condoms reliably or abstain from sex during the 5 days waiting and then for 2 days after starting the levonorgestrel (LNG) and DSG POP and 7 days for DRSP POP.
What should be done in an initial consultation?	
✓	Assessment of medical eligibility for POP use should include a comprehensive assessment of medical conditions and drug history.
✓	Individuals requesting POP should be informed about the effectiveness with both typical and perfect use of POP and other contraceptive methods, including the superior effectiveness of long-acting reversible contraception (LARC).
✓	Individuals should be provided with accessible information or a link to a trusted online resource to support safe, effective POP use.
Duration of POP prescription	
D	A 12-month supply of traditional, DSG or DRSP POP can be provided to medically eligible individuals who are initiating or continuing POP, with information to seek advice if there are any changes to their medical history.
Use of a self-completed checklist to assess medical eligibility for POP	
C	Use of suitable self-completed checklists for medical eligibility appears accurate and acceptable to users of oral contraception.
Pharmacy provision of POP	
✓	Specific approved brands of DSG POP can now be bought by the user as Pharmacy Medicines (from a pharmacy, without a prescription, under the supervision of a pharmacist).
Follow-up	
✓	After initiation of POP, users should generally be reviewed annually. This can usually be achieved without an in-person consultation.
How long can POP use be continued?	
✓	POP can be used for contraception by medically eligible individuals until age 55 years.
Return of fertility	
D	The limited available evidence suggests that there is no delay in return to fertility following POP use.

1.4 International Guidelines

The WHO international guidelines[6] did not provide any new information beyond what has already been discussed in the previously mentioned guidelines from Saudi Arabia, the United States, and Europe.

1.5 Systematic Reviews & Meta Analyses

Table 18 below details two systematic reviews and meta-analysis issued in **2022-2023** on the subject of contraception.

Table 18. Systematic Review and Meta-Analyses

Study	Author (year)	Primary Objective	Outcomes	Results
1	Fitzpatrick et al. (2023)[7]	Combined and progestogen-only hormonal contraceptives and breast cancer risk	Risk of breast cancer	• Modest elevation in the risk of breast cancer associated with current or recent use of progestogen-only contraceptives. • This increase in risk does not appear to differ based on the method of administration and is comparable in magnitude to the risk associated with CHC.
2	Brabaharan et al. (2022)[8]	Association of hormonal contraceptive use with adverse health outcomes	Adverse health outcomes	• No significant associations with adverse outcomes (Cardiovascular and cancer-related risks) were substantiated through high-quality evidence. • High-quality evidence supporting a connection between the utilization of a

				levonorgestrel-releasing intrauterine system and a reduction in the development of endometrial polyps, particularly in cases associated with the use of tamoxifen.

Section 2.0 Drug Therapy

2.1 Hormonal Contraceptives

2.1.1 Levonorgestrel (Systemic)[9]

Table 19. Levonorgestrel (Systemic) Drug Information

SCIENTIFIC NAME **Levonorgestrel**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	Z30
Drug Class	Contraceptive
Drug Sub-class	Progestin
ATC Code	G03AD01
Pharmacological Class (ASHP)	Contraceptive; Progestin
DRUG INFORMATION	
Dosage Form	Tablet, 30mcg
Route of Administration	Oral
Dose (Adult) [DDD]*	**Contraception:** 30 mcg (1 tablet) daily **Emergency contraception:** Oral (1.5 mg tablet): One 1.5 mg tablet as soon as possible within 72 hours of unprotected sexual intercourse or known or suspected contraceptive failure
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	**Emergency contraception:** Oral (0.75 or 1.5 mg tablet): Administer as soon as possible within 72 hours of having unprotected sex. Consider repeating the dose if vomiting occurs

	within 2 hours. Some products require a second be given within 12 hours of the first dose; consult individual product labeling.
Maximum Daily Dose Pediatrics*	N/A
Adjustment	**Altered Kidney Function:** There are no dosage adjustments provided in the manufacturer's labeling. **Hepatic Impairment:** Contraception (30 mcg tablet): Use is contraindicated in severe impairment with abnormal liver function values. Emergency contraception (0.75 or 1.5 mg tablet): There are no dosage adjustments provided in the manufacturer's labeling
Prescribing edits*	Age, G
AGE (Age Edit)	Not indicated for use post menopause
CU (Concurrent Use Edit)	N/A
G (Gender Edit)	Female only
MD (Physician Specialty Edit)	N/A
PA (Prior Authorization)	N/A
QL (Quantity Limit)	N/A
ST (Step Therapy)	N/A
EU (Emergency Use Only)	N/A
PE (Protocol Edit)	N/A
SAFETY	
Main Adverse Drug Reactions (most common and most serious)	**Most common:** Bleeding irregularities, Depression **Most serious**: Carbohydrate intolerance, Ectopic pregnancy, Thromboembolism
Drug Interactions*	**Category X:** Fusidic Acid (Systemic) Mobocertinib Taurursodiol Tranexamic Acid Ulipristal

Special Population	**Older Adults:** Not indicated for use post menopause. **Pediatric:** Emergency contraception (0.75 or 1.5 mg tablet): Females: Refer to adult dosing. Not for use prior to menarche.
Pregnancy	Not for use in patients confirmed to be pregnant. Adverse effects to the mother or fetus have not been observed following inadvertent exposure during pregnancy
Lactation	Levonorgestrel is present in breast milk. Patients who are breastfeeding may use oral levonorgestrel for emergency contraception
Contraindications	**Emergency contraceptive products (0.75 or 1.5 mg tablets):** **OTC labeling**: When used for self-medication, do not use if you are already pregnant; do not use for regular birth control. **Contraceptive products (30 mcg tablet):** Hypersensitivity to levonorgestrel or any component of the formulation; known or suspected pregnancy; severe hepatic disease as long as liver function values have not returned to normal; active or history of thromboembolism (stroke, MI); known or suspected sex-steroid dependent malignancies (eg, breast cancer); active or history of hepatic tumors; undiagnosed vaginal bleeding; severe diabetes with vascular changes.
Monitoring Requirements	Evaluate for pregnancy, spontaneous abortion, or ectopic pregnancy if normal (expected) menstrual period is delayed for ≥1 week following emergency contraception, or if lower abdominal

	pain or persistent irregular bleeding develops (ACOG 2015). **Nursing Physical Assessment:** Educate patient to not use if already pregnant. Educate patient on importance of frequent self-breast exams and yearly gynecological exams and to be evaluated for pregnancy if normal menstrual period is delayed for >1-week, lower abdominal pain develops, or persistent irregular bleeding occurs.
Precautions	**Hepatic disease**: Use as a continuous contraceptive is contraindicated with severe hepatic disease **Hypertension**: When used as a continuous contraceptive, consider discontinuation of therapy if significant/sustained hypertension develops **Appropriate use**: Emergency contraceptive product not intended to be used for routine contraception and is not effective in terminating an existing pregnancy. **Body weight**: Levonorgestrel may be less effective in patients with a BMI ≥30 kg/m compared to ulipristal acetate **Fertility**: Barrier contraception is recommended immediately following emergency contraception. **HIV infection protection**: Emergency contraceptives do not protect against HIV infection or other STD. **Laboratory changes**: The use of estrogen and/or progestin may change the results of some laboratory tests (eg, coagulation factors, lipids, glucose tolerance, binding

	proteins).
Black Box Warning	N/A
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Contraception options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations below are for Levonorgestrel (systemic).**

Table 20. Levonorgestrel (Systemic) HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Levonorgestrel (systemic)	NICE	N/A
	CADTH	November 29, 2018 - ulipristal should be recommended for those with a BMI equal to or greater than 25 who are seeking emergency contraception instead of levonorgestrel[10].
	HAS[11]	May 3, 2017 – Positive Recommendation: Opinion in favor of maintaining reimbursement in the emergency contraception[12].
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT- Levonorgestrel

Levonorgestrel tablet, with a dosage of 1.5 mg, serves as an emergency contraceptive intended to avert pregnancy in cases of birth control method malfunction or unprotected sexual activity. It functions as a secondary option for preventing pregnancy and is not suitable for routine contraceptive use. Treatment for emergency contraception should begin as soon as possible: One 1.5 mg tablet within 72 hours. Levonorgestrel tablet 1.5 mg is not recommended as a primary birth control method or if the woman is already pregnant.

2.1.2 Levonorgestrel (IUD)[13]

Table 21. Levonorgestrel (IUD) Drug Information

SCIENTIFIC NAME **Levonorgestrel**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	Z30
Drug Class	Contraceptive
Drug Sub-class	Progestin
ATC Code	G03AD01
Pharmacological Class (ASHP)	Contraceptive; Progestin
DRUG INFORMATION	
Dosage Form	IUD
Route of Administration	Vaginal
Dose (Adult) [DDD]*	Intrauterine Device, Intrauterine: Kyleena: 19.5 mg Liletta (52 MG): 20.1 mcg/day Mirena (52 MG): 20 mcg/day Skyla: 13.5 mg **Abnormal uterine bleeding, nonacute** (52 mg devices: Mirena, Liletta [off-label use]): Treatment of abnormal uterine bleeding (ie, heavy menstrual bleeding) in patients who also choose to use an IUD for contraception **Contraception:** **Kyleena**: Replace by the end of 5 years. Initially releases levonorgestrel ~17.5 mcg/day after 24 days, then rate subsequently decreases; the average release rate over 5 years is

	levonorgestrel ~9 mcg/day. Do not leave device in place for >5 years. **Liletta**: Replace by the end of 8 years. Initially releases levonorgestrel ~20 mcg/day, then rate subsequently decreases; the average release rate over 8 years is levonorgestrel ~13.5 mcg/day. Do not leave in place for >8 years. **Mirena:** Replace by the end of 8 years. Initially releases levonorgestrel 21 mcg/day, then rate subsequently decreases to ~11 mcg/day after 5 years and 7 mcg/day after 8 years. Do not leave device in place for >8 years. **Skyla:** Replace by the end of 3 years. Initially releases levonorgestrel ~14 mcg/day after 24 days, then rate subsequently decreases; mean release rate over 3 years is levonorgestrel ~6 mcg/day. Do not leave device in place for >3 years. **Emergency contraception (off-label use):** levonorgestrel 52 mg IUD may be an option for emergency contraception following unprotected intercourse within the last 5 days (120 hours) in patients also desiring an IUD **Dysmenorrhea (off-label use):** 52 mg device: Refer to dosing for "Contraception" **Endometrial hyperplasia, treatment (off-label use):** 52 mg device **Estrogen therapy-associated endometrial hyperplasia, prevention (off-label use)** (alternative agent): 52 mg device
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	**Contraception** (Kyleena, Liletta, Mirena, Skyla): Postmenarche patients: Intrauterine device (IUD) **Heavy menstrual bleeding** (Mirena):

	Postmenarche patients: Intrauterine device (IUD)
Maximum Daily Dose Pediatrics*	N/A
Adjustment	**Altered Kidney Function:** There are no dosage adjustments provided in the manufacturer's labeling. **Hepatic Impairment:** There are no dosage adjustments provided in the manufacturer's labeling; use of the intrauterine device is contraindicated with active hepatic disease or hepatic tumor
Prescribing edits*	Age, G
AGE (Age Edit)	Not indicated for use post menopause
CU (Concurrent Use Edit)	N/A
G (Gender Edit)	Female only
MD (Physician Specialty Edit)	N/A
PA (Prior Authorization)	N/A
QL (Quantity Limit)	N/A
ST (Step Therapy)	N/A
EU (Emergency Use Only)	N/A
PE (Protocol Edit)	N/A
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Bleeding irregularities, Device expulsion. Ectopic pregnancy **Most serious**: • Bradycardia/syncope • Pelvic inflammatory disease: or endometritis (may be asymptomatic), and actinomycosis • Seizure
Drug Interactions*	**Category X:** Ulipristal
Special Population	**Older Adults:** Not indicated for use post menopause. **Pediatric:** Postmenarche patients

Pregnancy	Use during pregnancy or a suspected pregnancy is contraindicated
Lactation	Levonorgestrel is present in breast milk. Following pregnancy, insert following removal of the placenta, or do not insert for at least 6 weeks postpartum or until involution of the uterus is complete. Insert immediately postpartum in patients who are breastfeeding, including patients who had a cesarean delivery. Risk of infection is not increased; risk of expulsion may be increased.
Contraindications	Hypersensitivity to levonorgestrel or any component of the formulation; pregnancy or suspected pregnancy; postcoital contraception; congenital or acquired uterine anomaly, including fibroids that distort the uterine cavity and would be incompatible with correct IUD placement; acute pelvic inflammatory disease or history of pelvic inflammatory disease; postpartum endometritis or infected abortion within past 3 months; known or suspected cervical malignancy; untreated acute cervicitis or vaginitis uterine bleeding of unknown etiology; acute hepatic disease or hepatic tumors (benign or malignant); current or history of known or suspected breast cancer or other hormone-sensitive cancer **Canadian labeling**: Additional contraindications (not in US labeling): Bacterial endocarditis; recent trophoblastic disease while human chorionic gonadotropin (hCG) hormone levels are elevated; cervical dysplasia; known immunodeficiency or hematologic malignancy (Mirena)

Monitoring Requirements	**Prior to insertion**: Assessment of pregnancy status; bimanual examination and cervical inspection; weight; STI screen. Evaluate any unexplained vaginal bleeding; exclude endometrial polyps or cancers. Complete medical and social history, which may determine conditions influencing an IUD use for contraception. **Following insertion**: Transvaginal ultrasound may be used to check placement. Assess changes in health status (including medications) at routine follow-up visits. Reexamine following insertion (4 to 6 weeks) and then yearly or more frequently if necessary. Monitor for significant changes in menstrual bleeding during prolonged use, Pap smear, BP, serum glucose in patients with diabetes. Evaluate patients presenting with lower abdominal pain for ectopic pregnancy **Endometrial hyperplasia, treatment (off-label use):** Endometrial sampling every 3 to 6 months, although most appropriate frequency has not been determined
Precautions	**Cervical or endometrial cancer**: Do not use an IUD for pregnancy prevention in patients diagnosed with cervical or endometrial cancer prior to IUD insertion **Depression**: Use with caution in patients with depression; may be more susceptible to recurrence of depressive episodes; consider removal of IUD for serious recurrence **Gestational trophoblastic disease**:

	Do not initiate therapy with a levonorgestrel IUD in patients with persistently elevated beta-hCG concentrations or malignant disease with evidence or suspicion of intrauterine disease due to risks of infection, hemorrhage, or perforation. **Sepsis**: Do not insert levonorgestrel IUD in patients with postpartum sepsis or immediately following a septic abortion
Black Box Warning	N/A
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Contraception options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations below are for Levonorgestrel (IUD).**

Table 22. Levonorgestrel (IUD) HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Levonorgestrel (IUD)	NICE	N/A
	CADTH	N/A
	HAS	February 08, 2017 – Positive Recommendation: Opinion in favor of maintaining reimbursement in the emergency contraception[14].
	IQWIG	N/A
	PBAC	March 2007 The PBAC suggested inclusion as a limited-access option due to cost-effectiveness, when compared to hysterectomy. This recommendation is made with the expectation that, over a five-year timeframe, the potential average savings per patient would amount to roughly less than $5,000 in cases where hysterectomy was not performed during that period[15].

CONCLUSION STATEMENT- Levonorgestrel IUD[16]

Levonorgestrel IUD 52 mg is indicated for prevention of pregnancy for up to 8 years; replace after the end of the eighth year. It is indicated for the treatment of heavy menstrual bleeding for up to 5 years in women who choose to use intrauterine contraception as their method of contraception; replace after the end of the fifth year if continued treatment of heavy menstrual bleeding is needed. Levonorgestrel IUD is contraindicated for women with a prior transcervical tubal sterilization procedure, postmenopausal woman, Known or suspected pregnancy, and PID.

2.1.3 Desogestrel[17]

Table 23. Desogestrel Drug Information

SCIENTIFIC NAME **Desogestrel**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	Z30
Drug Class	Contraceptive
Drug Sub-class	Progestin
ATC Code	G03AC09
Pharmacological Class (ASHP)	Contraceptive; Progestin
DRUG INFORMATION	
Dosage Form	Tablet, 75mcg
Route of Administration	Oral
Dose (Adult) [DDD]*	75 mcg
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	Contraception: Females: Refer to adult dosing. Not to be used prior to menarche.
Maximum Daily Dose Pediatrics*	N/A
Adjustment	**Altered Kidney Function:** There are no dosage adjustments provided in the manufacturer's labeling. **Hepatic Impairment:**

	Mild to moderate impairment: There are no dosage adjustments provided in manufacturer's labeling (has not been studied); use with caution. Severe impairment: Use is contraindicated
Prescribing edits*	Age, G
AGE (Age Edit)	Not indicated for use post menopause
CU (Concurrent Use Edit)	N/A
G (Gender Edit)	Female only
MD (Physician Specialty Edit)	N/A
PA (Prior Authorization)	N/A
QL (Quantity Limit)	N/A
ST (Step Therapy)	N/A
EU (Emergency Use Only)	N/A
PE (Protocol Edit)	N/A
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Bleeding irregularities, Depression, Acne, decreased Libido **Most serious**: Breast cancer, Ectopic pregnancy, Thromboembolism
Drug Interactions*	**Category X:** Encorafenib Erdafitinib Fusidic Acid (Systemic) Mobocertinib Omaveloxolone Pexidartinib Taurursodiol Tranexamic Acid Ulipristal
Special Population	**Older Adults:** Not indicated for use post menopause. **Pediatric:** Contraception: Females: Refer to adult dosing. Not to be used prior to menarche.
Pregnancy	In general, the use of hormonal contraceptives, when inadvertently

	used early in pregnancy, have not been associated with teratogenic effects. Discontinue therapy if pregnancy occurs.
Lactation	Etonogestrel, the active metabolite of desogestrel, is present in breast milk. According to the manufacturer, desogestrel may be used in nursing women; monitor growth and development
Contraindications	Hypersensitivity to desogestrel or any component of the formulation; undiagnosed abnormal vaginal bleeding; known or suspected progestogen-dependent malignancies; active venous thromboembolic disorder; severe hepatic disease.
Monitoring Requirements	Assessment of pregnancy status (prior to therapy); weight; assess potential health status changes at routine visits; blood pressure; glycemic control in diabetic patients; abnormal vaginal bleeding
Precautions	**Lactose**: Tablets may contain lactose; avoid use in patients with galactose intolerance, congenital lactase deficiency, or glucose-galactose malabsorption syndromes. **HIV infection protection**: Use does not protect against HIV infection or other STDs. **Laboratory changes**: The use of estrogen and/or progestin may change the results of some laboratory tests (eg, coagulation factors; lipids; glucose tolerance; binding proteins; biochemical parameters of liver, thyroid, adrenal, and renal function).
Black Box Warning	N/A

REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Contraception options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations below are for Desogestrel.**

Table 24. Desogestrel HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Desogestrel	NICE	N/A
	CADTH	N/A
	HAS	June 2012 Third-generation oral contraceptives should only be prescribed as a second-line option after first and second-generation oral contraceptives due to a higher risk of venous thromboembolism[18].
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT- Desogestrel[19]

Desogestrel is an oral progestin indicated for contraception. Its effectiveness may decrease in case of missed pills, vomiting, severe diarrhea, or when certain treatments are taken concurrently with them. One tablet 75 mcg should be taken every day at approximately the same time without interruption. The grace period for missed doses for Desogestrel is 12 hours, similar to a low-dose combined oral contraceptive. Contraception with Desogestrel should be discontinued in the event of newly appearing or uncontrolled high blood pressure under treatment. Amenorrhea, menstrual irregularities, intermenstrual bleeding, and spotting may occur during treatment.

2.1.4 Drospirenone[20]

Table 25. Drospirenone Drug Information

SCIENTIFIC NAME **Drospirenone**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	Z30
Drug Class	Contraceptive
Drug Sub-class	Progestin
ATC Code	G03AC10
Pharmacological Class (ASHP)	Contraceptive; Progestin
DRUG INFORMATION	
Dosage Form	Tablet, 4mg
Route of Administration	Oral
Dose (Adult) [DDD]*	**Contraception:** Tablet, Oral: Slynd 4 mg (1 tablet) daily **Emergency contraception:** Oral (1.5 mg tablet): One 1.5 mg tablet as soon as possible within 72 hours of unprotected sexual intercourse or known or suspected contraceptive failure
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	Contraception: Postmenarche patients: Oral: One tablet once daily
Maximum Daily Dose Pediatrics*	N/A
Adjustment	**Altered Kidney Function:** Contraindicated in patients with renal impairment. **Hepatic Impairment:** Contraindicated in patients with hepatic impairment.

Prescribing edits*	Age, G
AGE (Age Edit)	Not indicated for use post menopause
CU (Concurrent Use Edit)	N/A
G (Gender Edit)	Female only
MD (Physician Specialty Edit)	N/A
PA (Prior Authorization)	N/A
QL (Quantity Limit)	N/A
ST (Step Therapy)	N/A
EU (Emergency Use Only)	N/A
PE (Protocol Edit)	N/A
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Headache, Acne vulgaris, Bleeding irregularities **Most serious**: Bone loss, Hyperkalemia, Thromboembolic disorders
Drug Interactions*	**Category X:** Fexinidazole Erdafitinib Fusidic Acid (Systemic) Mobocertinib Pexidartinib Taurursodiol Tranexamic Acid Ulipristal
Special Population	**Older Adults:** Not indicated for use post menopause. **Pediatric:** Contraception: Postmenarche patients: Oral: One tablet once daily in the order presented in the blister pack. Patients not currently using a hormonal contraceptive should start on the first day of the menstrual cycle. **Surgical patients**: Consider discontinuation in cases of prolonged immobilization due to surgery or illness
Pregnancy	Use is contraindicated in pregnancy
Lactation	Drospirenone is present in breast milk.

	Progestin-only contraceptives may be initiated immediately postpartum in breastfeeding patients if reasonably sure the patient is not pregnant. If >5 days since menstrual bleeding started, an additional method of contraception (nonhormonal) should be used for the next 2 days
Contraindications	Renal impairment; adrenal insufficiency; cervical cancer or progestin-sensitive cancers (presence or history of); liver tumors (benign or malignant); hepatic impairment; undiagnosed abnormal uterine bleeding. Hypersensitivity to drospirenone or any component of the formulation.
Monitoring Requirements	**Assessment of pregnancy status (prior to therapy**); personal or family history of thrombotic or thromboembolic disorders (prior to therapy); signs and symptoms of thromboembolic disorders; signs and symptoms of depression; glycemic control in patients with diabetes. **Weight** (optional; BMI at baseline may be helpful to monitor changes during therapy) **Pregnancy status** should be assessed if all doses have been taken on schedule and 2 consecutive menstrual periods are missed, or if patient has not adhered to the dosing schedule and 1 menstrual period is missed. **In patients taking concomitant medications that increase serum potassium,** monitor serum potassium prior to therapy and during the first treatment cycle; consider monitoring serum potassium in patients taking concomitant strong CYP3A4 inhibitors and other patients if clinically indicated.

	Nursing Physical Assessment/Monitoring Check ordered labs and report any abnormalities. Monitor for and educate patient to report any vision changes, signs of depression, abnormal vaginal bleeding, or signs of thromboembolism (eg, swelling in arms or legs, chest pain, weakness on one side). Educate patient on importance of frequent self-breast exams and yearly gynecological exams. Educate diabetic patients on the importance of closely watching blood sugar.
Precautions	**Depression:** Use with caution in patients with depression; discontinue if serious depression recurs. **Diabetes:** May decrease insulin sensitivity and increase risk for hyperglycemia in patients with diabetes. **Hepatic impairment:** Discontinue if jaundice develops during therapy or if liver function becomes abnormal. **HIV infection protection**: Progestin only contraceptives do not protect against HIV infection or other STDs.
Black Box Warning	N/A
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Contraception options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations below are for Drospirenone.**

Table 26. Drospirenone HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Drospirenone	NICE	N/A
	CADTH	June 2023: Manufacturer Requested Reimbursement but still not approved
	HAS	N/A
	IQWIG	September 2019: Third- and fourth-generation birth control pills (such as those containing desogestrel, dienogest, gestodene and drospirenone) appear to increase the risk of thrombosis more than older first- and second-generation pills do (such as those containing levonorgestrel or norgestimate)
	PBAC	N/A

CONCLUSION STATEMENT- Drospirenone

Drospirenone is a progestin indicated for Contraception: Tablet, Oral: Slynd 4 mg (1 tablet) daily or for Emergency contraception: Oral (1.5 mg tablet): One 1.5 mg tablet as soon as possible within 72 hours of unprotected sexual intercourse or known or suspected contraceptive failure.

It is a POP with a better bleeding profile than traditional POPs. DRSP-only pill represents a real step forward in oral contraception with only progestins, even if the bleeding patterns during its use are still different to estrogen-containing products.

DRSP is a potent progestin analogue of spironolactone, with antiandrogenic and anti-mineralocorticoid properties.

Monitor serum potassium prior to therapy and during the first treatment cycle; consider monitoring serum potassium in patients taking concomitant strong CYP3A4 inhibitors (ketoconazole, itraconazole, voriconazole, indinavir, boceprevir clarithromycin) and other medicines that may also increase potassium levels in blood.

Drospirenone is contraindicated in case of kidney disease or kidney failure, reduced adrenal gland function, cervical cancer or any cancer that is sensitive to female hormones, liver disease, including liver tumors, unexplained vaginal bleeding.

2.1.5 Etonogestrel[21]

Table 27. Etonogestrel Drug Information

SCIENTIFIC NAME **Etonogestrel**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	Z30
Drug Class	Contraceptive
Drug Sub-class	Progestin
ATC Code	G03AC08
Pharmacological Class (ASHP)	Contraceptive; Progestin
DRUG INFORMATION	
Dosage Form	Implant
Route of Administration	Subcutaneous:
Dose (Adult) [DDD]*	Nexplanon: 68 mg Insert 1 implant in the inner side of the upper, nondominant arm. Remove no later than 3 years after the date of insertion; may be replaced with a new implant at the time of removal if continued contraceptive protection is desired
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	Contraception: Females: Refer to adult dosing. Not to be used prior to menarche.
Maximum Daily Dose Pediatrics*	N/A
Adjustment	**Altered Kidney Function:** There are no dosage adjustments provided in the manufacturer's labeling. **Hepatic Impairment:** Use is contraindicated
Prescribing edits*	Age, G

AGE (Age Edit)	Not indicated for use post menopause
CU (Concurrent Use Edit)	N/A
G (Gender Edit)	Female only
MD (Physician Specialty Edit)	N/A
PA (Prior Authorization)	N/A
QL (Quantity Limit)	N/A
ST (Step Therapy)	N/A
EU (Emergency Use Only)	N/A
PE (Protocol Edit)	N/A
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Weight gain, Acne, Headache **Most serious**: Cervical cancer, Ovarian cysts, Retinal thrombosis, Thromboembolism
Drug Interactions*	**Category X:** Encorafenib Erdafitinib Fexinidazole Fusidic Acid (Systemic) Omaveloxolone Taurursodiol Tranexamic Acid:
Special Population	**Older Adults:** Not indicated for use post menopause. **Pediatric:** Contraception: Females: Refer to adult dosing. Not to be used prior to menarche.
Pregnancy	In general, the use of hormonal contraceptives, when inadvertently used early in pregnancy, have not been associated with teratogenic effects. Discontinue therapy if pregnancy occurs.
Lactation	Etonogestrel is present in breast milk. According to the manufacturer, the decision to breastfeed should consider the risk of infant exposure, the benefits

	of breastfeeding to the infant, and benefits of use to the mother.
Contraindications	Hypersensitivity to etonogestrel or any component of the formulation; breast cancer (known, suspected, or personal history of); progestin-sensitive cancer (current or a history of); hepatic tumors (benign or malignant) or active hepatic disease; pregnancy (known or suspected); thrombosis or thromboembolic disorders (current or history of); undiagnosed abnormal genital bleeding.
Monitoring Requirements	Assessment of pregnancy status (prior to therapy); weight (optional; body mass index [BMI] at baseline may be helpful to monitor changes during therapy); assess potential health status changes at routine visits. Monitor patient for vision changes; BP; signs and symptoms of thromboembolic disorders; signs or symptoms of depression; glycemic control in patients with prediabetes or diabetes; lipid profiles in patients being treated for hyperlipidemias. Bleeding irregularities including amenorrhea; adequate diagnostic measures should be performed to rule out malignancy in all cases of undiagnosed abnormal vaginal bleeding.
Precautions	**Cardiovascular disease**: Use with caution in patients with risk factors for cardiovascular disease (eg, hypertension, hypercholesterolemia, morbid obesity, diabetes, patients who smoke) **Depression**: Use with caution in patients with a history of depression;

	consider removing implant if serious depression occurs. **Diabetes:** May impair glucose tolerance; use caution in patients with diabetes or prediabetes. **Diseases exacerbated by fluid retention**: Use with caution in patients with diseases that may be exacerbated by fluid retention
Black Box Warning	N/A
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Contraception options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations below are for Etonogestrel.**

Table 28. Etonogestrel HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Etonogestrel	NICE[22]	September 2014: Etonogestrel implants have a very low failure rate (less than 1 pregnancy per 1000 implants fitted over 3 years)
	CADTH[23]	October 2020: CADTH recommends that etonogestrel implant should be reimbursed for the prevention of pregnancy for up to three years only if the following condition is met
	HAS[11]	March 2013: HAS has positioned Etonogestrel NEXPLANON as a second-line option for women with contraindications or intolerance to combined estrogen-progestin contraceptives and intrauterine devices, or for women facing challenges with oral contraceptive adherence
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT- Etonogestrel

Etonogestrel 68mg implant is indicated for women for the prevention of pregnancy. It is a long-acting (up to 3 years), reversible, contraceptive method. The implant must be removed by the end of the third year and may be replaced by a new implant at the time of removal, if continued contraceptive protection is desired.

Etonogestrel 68mg implant NEXPLANON is considered as a second-line option for women with contraindications or intolerance to combined estrogen-progestin contraceptives and intrauterine devices, or for women facing challenges with oral contraceptive adherence.

2.1.6 Ethinylestradiol and Etonogestrel[24]

Table 29. Ethinylestradiol and Etonogestrel (Ring) Drug Information

SCIENTIFIC NAME **Ethinylestradiol and Etonogestrel (Ring)**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	Z30
Drug Class	Contraceptive
Drug Sub-class	Estrogen and Progestin Combination
ATC Code	NUVARING VAGINAL RING: G03AC08 ORNIBEL0.120mg/0.015mg/24hRing: G02BB01
Pharmacological Class (ASHP)	Contraceptive; Estrogen and Progestin Combination
DRUG INFORMATION	
Dosage Form	Ring
Route of Administration	Vaginal
Dose (Adult) [DDD]*	**Contraception**: Vaginal: One ring, inserted vaginally and left in place continuously for 3 consecutive weeks, then removed for 1 week. A new ring is inserted 7 days after the last was removed (even if bleeding is not

	complete) and should be inserted at approximately the same time of day the ring was removed the previous week.
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	Contraception: Postmenarche patients: One ring, inserted vaginally and left in place continuously for 3 consecutive weeks, then removed for 1 week. A new ring is inserted 7 days after the last was removed (even if bleeding is not complete) and should be inserted at approximately the same time of day the ring was removed the previous week.
Maximum Daily Dose Pediatrics*	N/A
Adjustment	**Altered Kidney Function:** There are no dosage adjustments provided in the manufacturer's labeling. **Hepatic Impairment:** Use is contraindicated
Prescribing edits*	Age, G
AGE (Age Edit)	Not indicated for use post menopause
CU (Concurrent Use Edit)	N/A
G (Gender Edit)	Female only
MD (Physician Specialty Edit)	N/A
PA (Prior Authorization)	N/A
QL (Quantity Limit)	N/A
ST (Step Therapy)	N/A
EU (Emergency Use Only)	N/A
PE (Protocol Edit)	N/A
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Intermenstrual bleeding, Vaginitis, Headache **Most serious**: Cerebrovascular accident, Cervical erosion, Deep vein thrombosis
Drug Interactions*	**Category X:** Antihepaciviral Combination Products Dasabuvir Dehydroepiandrosterone

	Encorafenib Erdafitinib Exemestane Fezolinetant Fusidic Acid (Systemic) Glecaprevir and Pibrentasvir Hemin Indium 111 Capromab Pendetide Lactic Acid, Citric Acid, and Potassium Bitartrate Mobocertinib Omaveloxolone Ospemifene Pexidartinib Taurursodiol Ulipristal
Special Population	**Older Adults:** Not indicated for use post menopause. **Patients at high risk of arterial or venous thrombotic diseases:** contraindicated **Pediatric:** Contraception: Females: Refer to adult dosing. Not to be used prior to menarche.
Pregnancy	Use is contraindicated during pregnancy
Lactation	Etonogestrel and ethinyl estradiol are present in breast milk. The manufacturer recommends use of other forms of contraception until the child is weaned.
Contraindications	Hypersensitivity, including anaphylaxis and angioedema, to ethinyl estradiol, etonogestrel, or any component of the formulation; breast cancer (current or a history of); hepatic tumors (benign or malignant) or hepatic disease; pregnancy; undiagnosed abnormal uterine bleeding; concurrent use of hepatitis C drug combinations

	containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir. Contraindicated in patients at high risk of arterial or venous thrombotic diseases.
Monitoring Requirements	Assessment of pregnancy status (prior to therapy); personal or family history of thrombotic or thromboembolic disorders (prior to therapy); BP (prior to therapy and yearly); weight (optional; BMI at baseline may be helpful to monitor changes during therapy); assess potential health status changes at routine visits. Monitor patient for vision changes; blood pressure; signs or symptoms of depression; glycemic control in patients with diabetes. Nursing Physical Assessment/Monitoring: Check ordered labs and report any abnormalities. Educate patient on importance of frequent self-breast exams and yearly gynecological exams. Educate patients who smoke on increased risks of smoking while taking this drug.
Precautions	**Body weight**: Patients with a BMI ≥30 kg/m may have an increased risk of VTE. **Smoking**: Cigarette smoking increases the risk of serious cardiovascular events from combination hormonal contraceptive use. This risk increases with age, particularly in patients >35 years of age, and with the number of cigarettes smoked. **Surgical patients**: Whenever possible, use should be discontinued at least 4 weeks prior to and through 2 weeks following major surgery or other

	surgeries known to have an increased risk of thromboembolism or during periods of prolonged immobilization. **HIV infection protection**: Combination hormonal contraceptives do not protect against HIV infection or other STDs.
Black Box Warning	Cigarette smoking increases the risk of serious cardiovascular events from CHC use
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Contraception options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations below are for Ethinylestradiol and Etonogestrel (Ring).**

Table 30. Ethinylestradiol and Etonogestrel (Ring) HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Ethinylestradiol and Etonogestrel (Ring)	NICE	N/A
	CADTH[25]	November 2006: The increase cost of NUVARING over oral contraceptives is not justified
	HAS[11]	March 2013: NUVARING is a vaginal ring intended for contraception for women of childbearing age. Safety and efficacy have been established in women aged 18 to 40 years
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT- Ethinylestradiol and Etonogestrel[26]

Contraceptive vaginal rings (CVR) offer an effective contraceptive option, expanding the available choices of hormonal contraception.

The main advantages of CVRs are their effectiveness (similar or slightly better than the pill) They are user-friendly, eliminating the need for daily reminders, and users have the autonomy to start or stop them as needed. CVRs offer a consistent release

rate, enabling the use of lower doses while improving bioavailability. When compared to oral contraceptives, the combined ring also provides superior cycle control.

Ethinylestradiol and Etonogestrel NUVARING Etonogestrel 120mcg/day, ethinyl estradiol 15mcg/day is a vaginal ring intended for contraception for women of childbearing age. Safety and efficacy have been established in women aged 18 to 40 years. Its use is contraindicated in patients at high risk of arterial or venous thrombotic diseases.

2.1.7 Ethinylestradiol and Desogestrel[27]

Table 31. Ethinylestradiol and Desogestrel Drug Information

SCIENTIFIC NAME **Ethinylestradiol and Desogestrel**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	Z30
Drug Class	Contraceptive
Drug Sub-class	Estrogen and Progestin Combination
ATC Code	G03AA09
Pharmacological Class (ASHP)	Contraceptive; Estrogen and Progestin Combination
DRUG INFORMATION	
Dosage Form	MARVELON: Tablet, 150,30 µg REGULON: Tablet, 150,30 µg GRACIAL: Tablet, 0.025,0.03 mg CYBELLE: Film Coated Tablet, 150,30 µg
Route of Administration	Oral
Dose (Adult) [DDD]*	1 tablet once daily in the order presented in the blister pack.
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	Contraception: Post menarche patients: Oral: One tablet once daily.
Maximum Daily Dose Pediatrics*	N/A

Adjustment	**Altered Kidney Function:** There are no dosage adjustments provided in manufacturer's labeling (has not been studied); use with caution and monitor blood pressure closely. Consider other forms of contraception. **Hepatic Impairment:** Contraindicated in patients with hepatic impairment.
Prescribing edits*	Age, G
AGE (Age Edit)	Not indicated for use post menopause
CU (Concurrent Use Edit)	N/A
G (Gender Edit)	Female only
MD (Physician Specialty Edit)	N/A
PA (Prior Authorization)	N/A
QL (Quantity Limit)	N/A
ST (Step Therapy)	N/A
EU (Emergency Use Only)	N/A
PE (Protocol Edit)	N/A
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Depression, headache, fluid retention **Most serious**: Contact lens intolerance, Hypertension, Thromboembolic disorders
Drug Interactions*	**Category X:** Anastrozole Antihepaciviral Combination Products Dehydroepiandrosterone Encorafenib Erdafitinib Exemestane Fexinidazole Fezolinetant Fusidic Acid (Systemic) Glecaprevir and Pibrentasvir Hemin Indium 111 Capromab Pendetide

	Lactic Acid, Citric Acid, and Potassium Bitartrate Mobocertinib Omaveloxolone Ospemifene Pexidartinib Raloxifene Taurursodiol Tranexamic Acid Ulipristal
Special Population	Contact lens wearers: Any changes with lens tolerance or vision should be evaluated by an ophthalmologist. Body weight: BMI is ≥30 kg/m; use of combination hormonal contraceptives may increase the risk of VTE. Smoking: Cigarette smoking increases the risk of serious cardiovascular events from combination hormonal contraceptives use. This risk increases with age, particularly in patients >35 years of age, and with the number of cigarettes smoked. Surgical patients: Whenever possible, should be discontinued at least 4 weeks prior to and for 2 weeks following elective surgery associated with an increased risk of thromboembolism or during periods of prolonged immobilization.
Pregnancy	Use is contraindicated during pregnancy
Lactation	Contraceptive steroids may be present in breast milk. The manufacturer recommends use of other forms of contraception until the child is weaned.
Contraindications	Hypersensitivity to ethinyl estradiol, desogestrel, or any component of the formulation; breast cancer, hepatic

	tumors (benign or malignant) or hepatic disease, cholestatic jaundice of pregnancy or jaundice with prior oral contraceptive pill (OCP) use, pregnancy, undiagnosed abnormal genital bleeding; coadministration with hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir with or without dasabuvir. Use is also contraindicated in patients at high risk of arterial or venous thrombotic diseases.
Monitoring Requirements	Assessment of pregnancy status (prior to therapy); personal or family history of thrombotic or thromboembolic disorders (prior to therapy); BP (prior to therapy and yearly); weight. Monitor patient for vision changes; signs or symptoms of depression; glycemic control in patients with diabetes; lipid profiles in patients being treated for hyperlipidemias. Adequate diagnostic measures, including endometrial sampling, if indicated, should be performed to rule out malignancy in all cases of undiagnosed abnormal vaginal bleeding. <u>Nursing Physical Assessment/Monitoring</u> Check ordered labs and report any abnormalities. Educate patients on importance of frequent self-breast exams and yearly gynecological exams. Educate patients who smoke on increased risks of smoking while taking this drug.
Precautions	**Chloasma**: Combination hormonal contraceptives, as well as sun exposure and pregnancy, are triggers for chloasma. Patients with a susceptibility

	to chloasma or additional risk factors should avoid exposure to sun or UV radiation during therapy. **Cholestasis**: Risk of cholestasis may be increased with previous cholestatic jaundice of pregnancy or jaundice with prior oral contraceptive use. **Hepatic adenomas or carcinomas**: Use of combination hormonal contraceptives is associated with hepatic adenomas (rare); rupture may cause fatal intra-abdominal hemorrhage. Long term use may be associated with an increased risk of hepatocellular carcinoma (rare). **Lipid effects**: Combination hormonal contraceptives may adversely affect lipid levels, including serum triglycerides. Patients with hypertriglyceridemia or a family history of hypertriglyceridemia may be at increased risk of pancreatitis when using combination hormonal contraceptives. **Retinal thrombosis**: Discontinue if unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions occur and immediately evaluate for retinal thrombosis. **Thromboembolic disorders**: Discontinue use of combination hormonal contraceptives if an arterial or venous thromboembolic event occurs. **HIV infection protection**: CHC do not protect against HIV infection or other STDs
Black Box Warning	Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptives use
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Contraception options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations below are for Ethinylestradiol and Desogestrel (Tablet).**

Table 32. Ethinylestradiol and Desogestrel (Tablet) HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Ethinylestradiol and Desogestrel (Tablet)	NICE	N/A
	CADTH[28]	July 2011: No health technology assessments regarding the risk of VTE in women using a DSRP/EE COC versus women using CHC were identified.
	HAS[18]	June 2012: Third-generation oral contraceptives should only be prescribed as a second-line option after first and second-generation oral contraceptives due to a higher risk of venous thromboembolism
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT- Ethinylestradiol and Desogestrel (Tablet)[29]

Desogestrel and Ethinyl Estradiol Tablets, provide an oral contraceptive regimen of 21 white to off-white round tablets each containing 0.15 mg desogestrel, 0.02 mg ethinyl estradiol.

Third-generation oral contraceptives should only be prescribed as a second-line option after first and second-generation oral contraceptives due to a higher risk of venous thromboembolism.

COCs, including desogestrel and ethinyl estradiol tablets, are contraindicated in women who are over 35 years of age and smoke.

The use of oral contraceptives is associated with increased risks of several serious

conditions including myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease, although the risk of serious morbidity or mortality is very small in healthy women without underlying risk factors. The risk of

morbidity and mortality increases significantly in the presence of other underlying risk factors such as hypertension, hyperlipidemias, obesity, and diabetes.

2.1.8 Ethinylestradiol and Levonorgestrel[30]

Table 33. Ethinylestradiol and Levonorgestrel Drug Information

SCIENTIFIC NAME **Ethinylestradiol and Levonorgestrel**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	Z30
Drug Class	Contraceptive
Drug Sub-class	Estrogen and Progestin Combination
ATC Code	G03AA07
Pharmacological Class (ASHP)	Contraceptive; Estrogen and Progestin Combination
DRUG INFORMATION	
Dosage Form	LOGYNON: Tablet, 30,125 µg
Route of Administration	Oral
Dose (Adult) [DDD]*	**Contraception:** One tablet once daily in the order presented in the blister pack. **Emergency contraception (off-label use): Oral:** One dose followed by a second dose 12 hours later. Each dose should contain a minimum of ethinyl estradiol 0.1 mg and levonorgestrel 0.5 mg
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	**Contraception**, oral: Postmenarche patients: Oral: 1 tablet once daily **Emergency contraception** Postmenarche patients: Oral: 1 dose followed by a second dose 12 hours later.

	Each dose should contain a minimum of ethinyl estradiol 100 mcg and levonorgestrel 0.5 mg.
Maximum Daily Dose Pediatrics*	N/A
Adjustment	**Altered Kidney Function**: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied); use with caution and monitor blood pressure closely. **Hepatic Impairment:** Contraindicated in patients with hepatic impairment.
Prescribing edits*	Age, G
AGE (Age Edit)	Not indicated for use post menopause
CU (Concurrent Use Edit)	N/A
G (Gender Edit)	Female only
MD (Physician Specialty Edit)	N/A
PA (Prior Authorization)	N/A
QL (Quantity Limit)	N/A
ST (Step Therapy)	N/A
EU (Emergency Use Only)	N/A
PE (Protocol Edit)	N/A
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Dysmenorrhea, headache, Nausea **Most serious**: contact lens intolerance, Hypertension, Thromboembolic disorders
Drug Interactions*	**Category X:** Anastrozole Antihepaciviral Combination Products Dehydroepiandrosterone Encorafenib Erdafitinib Exemestane Fexinidazole Fezolinetant Fusidic Acid (Systemic)

	Glecaprevir and Pibrentasvir Hemin Indium 111 Capromab Pendetide Lactic Acid, Citric Acid, and Potassium Bitartrate Mobocertinib Omaveloxolone Ospemifene Pexidartinib Raloxifene Taurursodiol Tranexamic Acid
Special Population	**Body weight**: BMI is ≥30 kg/m; use of combination hormonal contraceptives may increase the risk of VTE. **Smoking**: Cigarette smoking increases the risk of serious cardiovascular events from combination hormonal contraceptives use. This risk increases with age, particularly in patients >35 years of age, and with the number of cigarettes smoked. **Surgical patients**: Whenever possible, should be discontinued at least 4 weeks prior to and for 2 weeks following elective surgery associated with an increased risk of thromboembolism or during periods of prolonged immobilization.
Pregnancy	Combination hormonal contraceptives are used to prevent pregnancy; discontinue treatment if pregnancy occurs
Lactation	Contraceptive steroids may be present in breast milk. The manufacturer recommends use of other forms of contraception until the child is weaned.
Contraindications	Hypersensitivity to ethinyl estradiol, levonorgestrel, or any component of the formulation; breast cancer; hepatic

	tumors, acute viral hepatitis or severe (decompensated) cirrhosis; hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir; liver disease; undiagnosed abnormal uterine bleeding. Patients at high risk of arterial or venous thrombotic diseases including: Cerebrovascular disease; coronary artery disease; diabetes mellitus with any of the following: age >35 years, duration >20 years, hypertension, vascular disease, or other end-organ damage; deep vein thrombosis or pulmonary embolism (current or history of); hypercoagulopathies (inherited or acquired); hypertension (uncontrolled)
Monitoring Requirements	**Contraception:** Assessment of pregnancy status (prior to therapy); personal or family history of thrombotic or thromboembolic disorders (prior to therapy); BP (prior to therapy and yearly); weight (optional; BMI at baseline may be helpful to monitor changes during therapy); assess potential health status changes at routine visits. Determining if reasonably certain a person is not pregnant: If the patient has no signs or symptoms of pregnancy and meets any one of the following criteria, a health care provider can be reasonably certain the person is not pregnant: • ≤7 days after the start of normal menses • No sexual intercourse since last menses • Correct and consistent use of reliable contraception

	• ≤7 days after spontaneous or induced abortion • <4 weeks postpartum • <6 months postpartum, amenorrheic, and exclusively breastfeeding or ≥85% of feeds are breastfeeds. If all doses have not been taken on schedule and one menstrual period is missed, consider the possibility of pregnancy. If 2 consecutive menstrual periods are missed, assess pregnancy status before a new dosing cycle is started. **Monitor patient for vision changes**; BP; signs and symptoms of thromboembolic disorders; signs or symptoms of depression; glycemic control in patients with diabetes; lipid profiles in patients being treated for hyperlipidemias. Perform adequate diagnostic measures to rule out malignancy in all cases of undiagnosed abnormal vaginal bleeding. **Emergency contraception**: Evaluate for pregnancy, spontaneous abortion or ectopic pregnancy if menses is delayed for ≥1 week following emergency contraception, or if lower abdominal pain or persistent irregular bleeding develops (ACOG 2015). **Nursing Physical Assessment/Monitoring** Check ordered labs and report any abnormalities. Educate patients on the importance of frequent self-breast exams and yearly gynecological exams. Educate patients who smoke on increased risks of smoking and taking this drug. Educate patient on the importance of taking medication at the

	same time every day and what to do in the case doses are missed.
Precautions	**Chloasma**: Combination hormonal contraceptives, as well as sun exposure and pregnancy, are triggers for chloasma. Patients with a susceptibility to chloasma or additional risk factors should avoid exposure to sun or UV radiation during therapy. **Cholestasis**: Risk of cholestasis may be increased with previous cholestatic jaundice of pregnancy or jaundice with prior oral contraceptive use. **Hepatic adenomas or carcinomas**: Use of combination hormonal contraceptives is associated with hepatic adenomas (rare); rupture may cause fatal intra-abdominal hemorrhage. Long term use may be associated with an increased risk of hepatocellular carcinoma (rare). **Lipid effects**: Combination hormonal contraceptives may adversely affect lipid levels, including serum triglycerides. Patients with hypertriglyceridemia or a family history of hypertriglyceridemia may be at increased risk of pancreatitis when using combination hormonal contraceptives. **Retinal thrombosis**: Discontinue if unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions occur and immediately evaluate for retinal thrombosis. **Thromboembolic disorders**: Discontinue use of combination hormonal contraceptives if an arterial or venous thromboembolic event occurs.

	HIV infection protection: CHC do not protect against HIV infection or other STDs.
Black Box Warning	**Cigarette smoke and serious cardiovascular events:** Cigarette smoking increases the risk of serious cardiovascular events from combined hormonal contraceptive use. **Obesity and venous thromboembolism risk (patch only):** Ethinyl estradiol and levonorgestrel is contraindicated in women with a BMI ≥30 kg/m
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Contraception options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations below are for Ethinylestradiol and Levonorgestrel (Tablet).**

Table 34. Ethinylestradiol and Levonorgestrel (Tablet) HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Ethinylestradiol and Levonorgestrel Tablet	NICE[31]	2019: Combination contraception methods, in the form of a pill, the vaginal ring, and the transdermal patch, have all been shown to regulate the menstrual cycle in premenopausal women, with the added benefit of reducing menstrual blood loss MBL
	CADTH[28]	July 2011: No health technology assessments regarding the risk of VTE in women using a DSRP/EE COC versus women using CHC were identified.
	HAS[32]	June 2014: LEVONORGESTREL/ ETHINYLESTRADIOL products do not provide any

		improvement in the medical service compared to other second-generation oral contraceptives
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT- Ethinylestradiol and Levonorgestrel

Ethinylestradiol and Levonorgestrel Tablets

COC is one of the first-line methods for women without specific risk factors (cardiovascular, cancer-related, hepatic, etc.). It is highly effective when used optimally. No data support favoring the prescription of a specific type of combined estrogen-progestin pill in terms of contraceptive effectiveness and cycle control.

COCs, including ethinyl estradiol tablets, are contraindicated in women who are over 35 years of age and smoke.

All COCs are associated with an increased risk of thromboembolic events. However, there is an additional risk of VTE with third-generation oral estrogen-progestin contraceptives compared to first and second-generation oral estrogen-progestin contraceptives (containing less than 50 micrograms of ethinylestradiol).

The risk of venous and arterial thromboembolic events varies depending on the dose of ethinylestradiol in COCs, with lower estrogen dosages being associated with a lower risk.

The use of oral contraceptives is associated with increased risks of several serious

conditions including myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease, although the risk of serious morbidity or mortality is very small in healthy women without underlying risk factors. The risk of morbidity and mortality increases significantly in the presence of other underlying risk factors such as hypertension, hyperlipidemias, obesity, and diabetes.

2.1.9 Medroxyprogesterone Acetate (DMPA)[33]

Table 35. Medroxyprogesterone Acetate (DMPA) Drug Information

SCIENTIFIC NAME MEDROXYPROGESTERONE ACETATE (DMPA)	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes

PMDA	Yes
Indication (ICD-10)	Z30
Drug Class	Contraceptive
Drug Sub-class	Progestin
ATC Code	L02AB02
Pharmacological Class (ASHP)	Hormonal contraceptive
DRUG INFORMATION	
Dosage Form	Suspension for injection
Route of Administration	Intramuscular
Dose (Adult) [DDD]*	Depo-Provera Contraceptive: IM: 150 mg every 3 months (every 13 weeks)
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	Contraception: Adolescents: First dose to be given only during first 5 days of normal menstrual period; only within 5 days postpartum if not breast-feeding, or only at sixth postpartum week if exclusively breast-feeding. IM (Depo-Provera): 150 mg every 3 months (every 13 weeks).
Maximum Daily Dose Pediatrics*	N/A
Adjustment	**Altered Kidney Function:** There are no dosage adjustments provided in the manufacturer's labeling. **Hepatic Impairment:** contraindicated in patients with hepatic impairment
Prescribing edits*	Age, G
AGE (Age Edit)	Adolescent post menarche
CU (Concurrent Use Edit)	N/A
G (Gender Edit)	Female only
MD (Physician Specialty Edit)	N/A
PA (Prior Authorization)	N/A
QL (Quantity Limit)	N/A
ST (Step Therapy)	N/A
EU (Emergency Use Only)	N/A
PE (Protocol Edit)	N/A

SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Menstrual bleeding irregularities, Weight gain, Headache **Most serious**: Bone loss, Anemia, Asthma
Drug Interactions*	**Category X:** Encorafenib Erdafitinib Fexinidazole Fusidic Acid (Systemic) Indium 111 Capromab Pendetide: Mobocertinib Omaveloxolone Pexidartinib Taurursodiol Tranexamic Acid Ulipristal
Special Population	**Reproductive Considerations** Depo-medroxyprogesterone 150 mg/mL injections are used for contraception. Use is not recommended as a long-term (ie, longer than 2 years) birth control method unless other options are considered inadequate.
Pregnancy	When used for contraception, consider the possibility of ectopic pregnancy in patients with severe abdominal pain; ectopic pregnancies have been reported with use of the DMPA contraceptive injection.
Lactation	The injectable DMPA contraceptives can be initiated immediately postpartum in patients who are breastfeeding.
Contraindications	Hypersensitivity to medroxyprogesterone or any component of the formulation, active thrombophlebitis, thromboembolic disorders or cerebral vascular disease,

	estrogen or progesterone-dependent tumor.
Monitoring Requirements	Monitor blood glucose, bone density depression. Evaluate abnormal bleeding that persists or is severe. Contraception: Assessment of pregnancy status (prior to therapy); weight, BMD with long-term use. If time interval between IM injections is >13 weeks, evaluate pregnancy status prior to injection. Appropriate dose scheduling.
Precautions	**Adrenal suppression:** May cause suppression of hypothalamic-pituitary-adrenal (HPA) axis, Cushingoid symptoms may occur. **Anaphylaxis/hypersensitivity reactions:** Anaphylaxis or anaphylactoid reactions have been reported with use of the injection; medication for the treatment of hypersensitivity reactions should be available for immediate use. **Asthma:** Use with caution in patients with asthma; may exacerbate disease. **Cardiovascular disease**: Manage risk factors for cardiovascular disease discontinue use immediately if adverse cardiovascular events occur or are suspected. **Epilepsy**: Use with caution in patients with epilepsy; may exacerbate disease. **Dietary Considerations:** Ensure adequate calcium and vitamin D intake
Black Box Warning	DMPA is not recommended as a long-term (ie, longer than 2 years) birth control method or medical therapy for endometriosis-associated pain unless other options are considered inadequate.

	Prolonged use of the drug can cause significant bone density loss
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of Contraception options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations below are for MEDROXYPROGESTERONE ACETATE (DMPA).**

Table 36. Medroxyprogesterone Acetate (DMPA) HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Medroxyprogesterone Acetate (DMPA)	NICE[34]	April 2021 For individuals of any age with substantial lifestyle or medical factors that increase the risk of osteoporosis, it is advisable to explore alternative contraceptive methods before resorting to intramuscular (IM) DPMA
	CADTH	N/A
	HAS[11]	March 2013 There is no significant difference in contraceptive effectiveness between a copper IUD with a surface area greater than 250 mm2 and a levonorgestrel-releasing IUD.
	IQWIG	N/A
	PBAC	N/A

CONCLUSION STATEMENT- MEDROXYPROGESTERONE ACETATE (DMPA)

MEDROXYPROGESTERONE ACETATE (DMPA) injections are given every three months and are available as 150 mg in 1 mL for intramuscular injection and 104 mg in 0.65 mL for subcutaneous injection. For progestin-only methods, the IUD and implant are the most effective options, followed by DPMA injections and then the pill. The progestin-only IUD, implant, and injectable are also more effective than combined oral contraceptives.

The DMPA injection can delay returning to fertility for as long as 18 months after it is stopped and should not be chosen by women thinking about pregnancy within the next two years. According to the US Boxed Warning for DPMA from Lexicomp, it is

not recommended for long-term use (>2 years) as a birth control method or as medical therapy for endometriosis-associated pain unless other options are considered inadequate. Prolonged use of DPMA may result in a loss of bone mineral density, and the incidence of probable dementia increased in women ≥65 years old taking conjugated estrogen in combination with DMPA.

DPMA is contraindicated in case of hypersensitivity to medroxyprogesterone or any component of the formulation, active thrombophlebitis, thromboembolic disorders or cerebral vascular disease, estrogen or progesterone-dependent tumor

2.2 Other Drugs

2.2.1 Copper IUD[35, 36]

The copper IUD (Cu-IUD) was approved by the FDA in 1984 and has been available in the US since 1988.

A Cu-IUD can be used within 5 days of unprotected intercourse as an emergency contraceptive.

A higher surface area of copper results in higher contraceptive efficacy. Compared with older copper IUDs, which typically had less than 350 mm2 of copper surface area, the Copper T-380A has been able to achieve superior contraception while maintaining a similar side-effect profile.

Although Copper T-380A is approved for use in the United States for 10 years and is licensed for use in the United Kingdom for 8 years, it has been shown to consistently maintain its efficacy for 12 years.

Adverse events that accompany the Copper T-380A use: perforation, expulsion, and infection.

2.2.2 Ulipristal[37]

Ulipristal acetate (UPA) developed for emergency contraception has been approved by the European Medicines Agency EMA in May 2009 and by the United States Food and Drug Administration (US FDA) in August 2010.

Ulipristal acetate for uterine fibroids: EMA recommends restricting use. On 12 November 2020, EMA recommended restricting use of medicines containing ulipristal acetate 5 mg as a result of cases of serious liver injury.

Ulipristal acetate is also authorized as a single-dose medicine for emergency contraception (ellaOne and other trade names). No concern has been raised about liver injury with these **single-dose** emergency contraception medicines and this recommendation does not affect them[38]. However, the **repeated** self-administration

could be associated with hepatotoxicity in unaware women, although further investigations are required to understand the underlying pharmacological mechanisms, to define the toxic thresholds of UPA and to assure women of the best protection[39].

2.2.3 Norelgestromin/Ethinylestradiol Transdermal Patch[40,41]

Norelgestromin/Ethinylestradiol tansdermal patch was approved by the FDA in February 2020 and by EMA in August 2022. It is indicated for the prevention of pregnancy in women who elect to use a transdermal patch as a method of contraception. It contains 6.00 mg norelgestromin (NGMN) and 0.75 mg ethinyl estradiol (EE).

The transdermal patch delivers EE and NGMN over a seven-day period while oral contraceptives (containing NGM 250 mcg / EE 35 mcg) are administered daily.

Transdermal hormonal contraceptives offer advantages for individuals who struggle with daily pill adherence. Healthy women in their teens and 20s, with a low risk of venous thromboembolism (VTE), may still be suitable candidates for norelgestromin patches, especially if they prefer higher doses for cycle regulation, acne improvement (as higher estrogen-containing options are often more effective for this), or when combined with medications that could interact to reduce hormone levels. Nevertheless, the availability of additional transdermal options with lower estrogen doses would be beneficial in clinical practice.

There is a concern regarding an increased risk of contraceptive failure in individuals using transdermal contraceptives who have a body mass index (BMI) ≥ 30 kg/m^2. As a result, the FDA approved the transdermal contraceptive patch only f in women whose body mass index (BMI) is < 30 kg/m2 and for whom a combined hormonal contraceptive is appropriate.

Section 3.0 Key Recommendations Synthesis

Contraception is a crucial aspect of women's reproductive health and family planning. The following synthesis outlines key considerations in the realm of contraceptive methods based on current medical literature and guidelines:

Choice and Education: Comprehensive patient education is fundamental. Women should have access to detailed information about various contraceptive options, enabling them to make informed decisions aligned with their unique needs and preferences.

First-Line Choices: For those opting for oral contraceptives, formulations containing LNG or norgestimate are recommended. However, the efficacy and convenience of LARCs like IUDs and implants make them suitable first-line options.

Quick Start: Initiating hormonal contraceptives promptly is possible after comprehensive counseling. Pregnancy verification and supplementary barrier method use for seven days are essential precautions.

Managing Vaginal Bleeding: In cases of persistent, poorly tolerated vaginal bleeding lasting at least three months, healthcare providers should investigate potential causes and consider altering the chosen contraceptive method.

Managing Side Effects: Addressing common side effects such as vaginal bleeding, acne, weight gain, and reduced libido is vital. Modifications to contraceptive methods or specialized treatments may be necessary for persistent side effects.

Weight Gain: Significant weight gain associated with contraceptive use should prompt a thorough evaluation to identify underlying factors.

Migraines: Healthcare providers should exercise vigilance when patients report headaches, particularly migraines, in connection with hormonal contraceptives. Discontinuation may be warranted in some cases.

Mood Disorders: Mood changes related to contraceptive use should be acknowledged and managed. If necessary, consider adjustments to the contraceptive method.

STD Prevention: Emphasize the importance of combining condoms with other contraceptives to ensure protection against sexually transmitted diseases.

Adolescents: Adolescents should receive comprehensive sex education and contraceptive guidance during their initial visit. Contraceptive discussions should be tailored to individual preferences and needs.

Women Over 40: Women over 40 should undergo a thorough evaluation of the risks and benefits of hormonal contraceptives, taking into account vascular,

metabolic, and carcinogenic risks. Progestin-only oral contraceptives may be a primary option due to their favorable risk profile.

Permanent Contraception: Discuss sterilization options for both men and women after the age of 40, offering a permanent solution for those no longer desiring fertility.

Cessation of Contraception: For older women, discontinuing contraception may be considered at a certain age. Guidance on non-hormonal or progestin-only methods should be provided as needed.

Natural and Barrier Methods: Educate women about the effectiveness and correct utilization of natural and barrier contraceptive methods. These methods can serve as backup options, particularly when adherence to other contraceptives is inconsistent.

Non-Contraceptive Benefits: Highlight the potential non-contraceptive benefits of hormonal contraceptives, such as reducing the risk of specific cancers and addressing menstrual cycle disorders.

Future Research: Recognize the ongoing research efforts aimed at enhancing contraceptive methods. Lower-dose formulations, novel compounds, and innovative delivery systems are being explored to improve tolerability and accessibility.

Section 4.0 Conclusion

A patient-centered approach that prioritizes informed decision-making is paramount in contraceptive care.

Healthcare providers should be equipped with the latest evidence and guidelines to guide women in selecting the most suitable contraceptive method based on their individual needs, age, and associated risks and benefits.

Contraception plays a pivotal role in women's reproductive health and family planning, and its provision should be approached with care and consideration.

The recommendations provided in this report are intended to assist in the management of contraception.

These recommendations should be used to support and not supplant decisions in individual patient management.

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Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses and sequence of therapy

Appendix B. Level of Evidence Description

I- Level of Evidence Adopted:

Grade of research	
A	Strongly recommend; good evidence
B	Recommend; at least fair evidence
C	No recommendation for or against; balance of benefits and harms too close to justify a recommendation
D	Recommend against; fair evidence is ineffective, or harm outweighs the benefit
E	Evidence is insufficient to recommend for or against routinely; evidence is lacking or of poor quality; benefits and harms cannot be determined
Level of evidence	
Level I	Meta-analysis of multiple studies
Level II	Experimental studies
Level III	Well-designed, quasi-experimental studies
Level IV	Well-designed, non-experimental studies
Level V	Case reports and clinical examples

Appendix C. PubMed Search

Query	Sort By	Filters	Search Details	Results
((((((((((((Contraception[MeSH Terms]) OR (Inhibition of Fertilization[Title/Abstract])) OR (Fertilization Inhibition[Title/Abstract])) OR (Fertility Control[Title/Abstract])) OR (Birth Control[Title/Abstract])) OR (Contraceptive Methods[Title/Abstract])) OR (Contraceptive Method[Title/Abstract])) OR (Female Contraception[Title/Abstract])) OR (Contraception, Female[Title/Abstract])) OR (Contraceptions, Female[Title/Abstract])) OR (Female Contraceptions[Title/Abstract])) OR (Male Contraception[Title/Abstract])) OR (Contraception, Male[Title/Abstract])) OR (Contraceptions, Male[Title/Abstract])) OR (Male Contraceptions[Title/Abstract])			"Contraception"[MeSH Terms] OR "inhibition of fertilization"[Title/Abstract] OR "fertilization inhibition"[Title/Abstract] OR "fertility control"[Title/Abstract] OR "birth control"[Title/Abstract] OR "contraceptive methods"[Title/Abstract] OR "contraceptive method"[Title/Abstract] OR "female contraception"[Title/Abstract] OR "contraception female"[Title/Abstract] OR (("contracept"[All Fields] OR "contracepted"[All Fields] OR "contracepting"[All Fields] OR "Contraception"[MeSH Terms] OR "Contraception"[All Fields] OR "Contraceptions"[All Fields] OR "contraceptive agents"[Pharmacological Action] OR "contraceptive agents"[Supplementary Concept] OR "contraceptive agents"[All Fields] OR "Contraceptive"[All Fields] OR "contraceptive devices"[MeSH Terms] OR ("Contraceptive"[All Fields] AND "devices"[All Fields]) OR "contraceptive devices"[All Fields] OR "contraceptive agents"[MeSH Terms] OR ("Contraceptive"[All Fields] AND "agents"[All Fields]) OR "contraceptives"[All Fields] OR "contraceptive s"[All Fields] OR "contraceptively"[All Fields]) AND "Female"[Title/Abstract]) OR (("femal"[All Fields] OR "Female"[MeSH Terms] OR "Female"[All Fields] OR "females"[All Fields] OR "female s"[All Fields] OR "femals"[All Fields]) AND "Contraceptions"[Title/Abstract])	67,289

	OR "male contraception"[Title/Abstract] OR "contraception male"[Title/Abstract] OR (("contracept"[All Fields] OR "contracepted"[All Fields] OR "contracepting"[All Fields] OR "Contraception"[MeSH Terms] OR "Contraception"[All Fields] OR "Contraceptions"[All Fields] OR "contraceptive agents"[Pharmacological Action] OR "contraceptive agents"[Supplementary Concept] OR "contraceptive agents"[All Fields] OR "Contraceptive"[All Fields] OR "contraceptive devices"[MeSH Terms] OR ("Contraceptive"[All Fields] AND "devices"[All Fields]) OR "contraceptive devices"[All Fields] OR "contraceptive agents"[MeSH Terms] OR ("Contraceptive"[All Fields] AND "agents"[All Fields]) OR "contraceptives"[All Fields] OR "contraceptive s"[All Fields] OR "contraceptively"[All Fields]) AND "Male"[Title/Abstract]) OR (("Male"[MeSH Terms] OR "Male"[All Fields]) AND "Contraceptions"[Title/Abstract])	

Appendix D. Treatment Algorithm

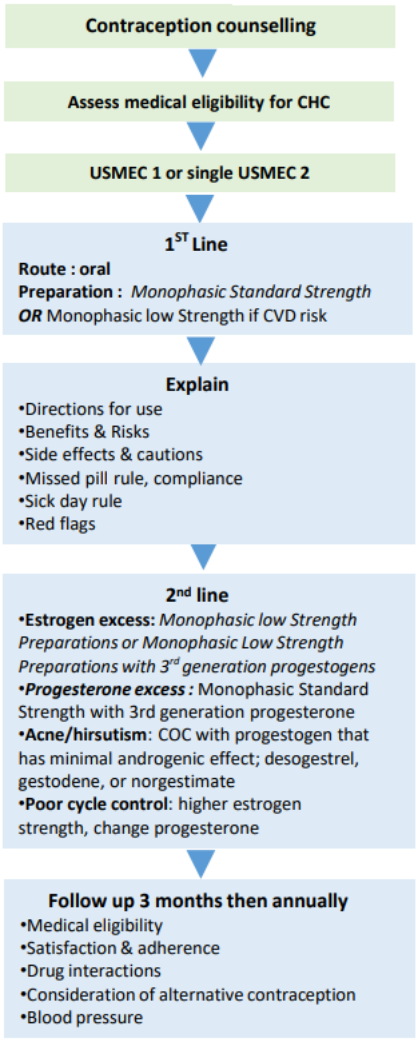

Figure 6. *How to choose combined hormonal contraceptives. Retrieved from the Saudi Society of Family and Community Medicine Contraception Clinical Practice Guidelines.*