BACTERIAL GENITAL TRACT INFECTIONS

CHI Formulary Indication Review

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INDICATION UPDATE

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ADDENDUM to the CHI Original Bacterial Genital Tract Infections Clinical Guidance- Issued May 2020

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- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
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Abbreviations

AAFP	American Academy of Family Physicians
BPG	Benzathine Penicillin G
BV	Bacterial Vaginosis
CDC	Centers for Disease Control and Prevention
CHI	Council of Health Insurance
CSF	Cerebrospinal Fluid
EMA	European Medicines Agency
EPT	Expedited Partner Therapy
FDA	Food and Drug Administration
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
HAV	Hepatitis A Virus
HBV	Hepatitis B Virus
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
IM	Intramuscular
IUSTI	International Union against Sexually Transmitted Infections
IV	Intravenous
MIC	Minimum Inhibitory Concentration
MSM	Men who have Sex with Men
MTZ	Metronidazole
N/A	Not Applicable
NAAT	Nucleic Acid Amplification Test
NGU	Non-Gonococcal Urethritis
PID	Pelvic Inflammatory Disease
PO	Per Os (Orally)
RCT	Randomized Controlled Trial
RTI	Respiratory Tract Infection
SA	Saudi Arabia

SFDA	Saudi Food and Drug Authority
STD	Sexually Transmitted Disease
STI	Sexually Transmitted Infection
TDZ	Tinidazole
TOC	Test-of-Cure
UK	United Kingdom
WHO	World Health Organization

Executive Summary

Bacterial Genital Tract Infections are a category of communicable diseases characterized by the invasion and proliferation of pathogenic bacteria within the anatomical structures of the genital tract, which may include the male and female reproductive organs. These infections are typically transmitted through sexual contact and can manifest as a spectrum of local clinical signs and symptoms, such as urethritis, cervicitis, vaginitis, pelvic inflammatory disease (PID), or prostatitis. Signs and symptoms resulting from systemic dissemination can also be present.

They can result in a variety of complications, including infertility, ectopic pregnancies, and an increased risk of HIV transmission. Diagnosis is typically based on clinical evaluation, microbiological testing, and laboratory analysis of genital specimens, followed by appropriate antimicrobial treatment to resolve the infection[1].

Based on the etiology of genital tract infections, they can be categorized into three distinct types:

1. **Sexually Transmitted Infections (STIs):** These conditions are transmitted primarily through unprotected sexual intercourse. Prominent examples of STIs encompass gonorrhea, chlamydia, syphilis, and chancroid.
2. **Endogenous Infections:** These ailments arise due to the overgrowth of specific microorganisms that naturally inhabit the genital tract of healthy women. This category includes conditions such as vulvovaginal candidiasis (non-bacterial) and bacterial vaginosis, among others.
3. **Iatrogenic Infections:** These infections stem from improperly conducted medical procedures. Common triggers for iatrogenic infections include suboptimal childbirth practices and unsafe abortion procedures[1].

Bacterial genital tract infections can be influenced by various risk factors that increase an individual's susceptibility to contracting these infections. Some common risk factors for bacterial genital tract infections include unprotected sexual activity, multiple sexual partners, history of previous infections, young age, immunosuppression, lack of hygiene and proper care, childbirth and gynecological procedures, close contact with infected individuals and lack of vaccination[2].

According to the latest report of the World Health Organization (WHO), in 2016, the estimated global incident cases of four types of RTIs (chlamydia, gonorrhea, trichomoniasis, and syphilis) was 376.4 million, with an increasing trend compared to 2012. Furthermore, the majority of RTI patients were in developing regions[3].

Limited information is available regarding Bacterial genital tract infections in Islamic countries, where religion prohibits non-marital sexual activity and homosexuality. The scarcity of data is believed to stem from the anticipated low occurrence of STIs

in these regions, coupled with the strong religious and cultural disapproval of non-marital sexual relations and homosexuality. In a study conducted in 2006, A total of 39049 STIs were reported to the Ministry of Health in Saudi Arabia. Reported STIs included nongonococcal urethritis (37.3%), trichomoniasis (28.1%), gonococcal urethritis (14.2%), syphilis (8.7%), human immunodeficiency virus (7.5%), genital warts (3.5%), genital herpes (6%), and chancroid (0.2%). The average annual incidence of STIs per 100,000 population for Saudis and non-Saudis, respectively, was as follows: 14.8 and 7.5 for nongonococcal urethritis, 9.4 and 10.4 for trichomoniasis, 5.2 and 4.2 for gonorrhea, 1.7 and 6.4 for syphilis, 0.6 and 8.0 for HIV, 1.4 and 0.7 for genital warts, 0.1 and 0.4 for genital herpes, and 0.1 and 0.1 for chancroid. The incidence of STIs was somewhat steady over the surveillance period except for nongonococcal urethritis which gradually increased. Even though the incidence of STIs in SA is limited, appropriate preventive strategies that conform to the Islamic rules and values are essential and should be of highest priority for policymakers because of the potential of such infections to spread particularly among the youth[4].

STDs impose a significant burden of morbidity and mortality in the United States. They range from diseases that, for the most part, cause temporary discomfort and inconvenience to illnesses that impair fertility, result in long-term morbidity, or shorten life. Conservatively, the subset of STDs examined costs the nation *at least* 4 billion annually according to literature review[5].

The goals of therapy for bacterial genital infections are to effectively treat the infection, alleviate symptoms, prevent complications, and reduce the risk of transmitting the infection to others. Drug therapy is an integral component for the management of Bacterial Genital Tract Infections. The specific goals and drug therapy for bacterial genital infections depend on the type of infection. Bacterial Genital Tract Infections drug therapy typically involves antibiotics. The choice of antibiotic and the duration of treatment may vary depending on several factors, including the patient's age, allergies, and local antibiotic resistance patterns. Commonly prescribed antibiotics for Bacterial Genital Tract Infections include: Cephalosporins, Macrolides: Erythromycin, Azithromycin, Clarithromycin and Clindamycin. It's essential to adhere to the prescribed treatment regimen, complete the full course of antibiotics, and avoid sexual activity until treatment is completed to prevent reinfection or transmission. Sexual partners should be informed, tested, and treated as necessary to prevent reinfection and further spread of the infection[1].

CHI issued Bacterial Genital Tract Infections clinical guidance after thorough review of renowned international and national clinical guidelines in May 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior CHI Bacterial Genital Tract Infections clinical guidance and seeks to offer guidance for the effective management of Bacterial Genital Tract Infections. It provides an **update on the Bacterial Genital Tract Infections Guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update are summarized, being **the issuance of updated versions of previously reviewed guidelines** namely CDC STI treatment guidelines **(2021).**

Moreover, **new guidelines are added to the report** such as

- WHO Guidelines for the management of symptomatic sexually transmitted infections **(2021)**
- AAFP; Vaginitis: Diagnosis and Treatment **(2018)**
- AAFP Pelvic Inflammatory Disease: Diagnosis, Management, and Prevention **(2019)**
- British Association for Sexual Health and HIV national guideline for the management of infection with Mycoplasma genitalium **(2018)**
- UK national guideline for the management of infection with Neisseria gonorrhoeae **(2018)**
- United Kingdom National Guideline for the Management of Pelvic Inflammatory Disease **(2019 Interim Update)**
- European guideline on the management of syphilis **(2020)**
- European guideline for the diagnosis and treatment of gonorrhea in adults **(2020)**
- European (IUSTI/WHO) International Union against sexually transmitted infections (IUSTI) World Health Organisation (WHO) guideline on the management of vaginal discharge **(2018)**
- European guideline for the management of chancroid **(2017)**
- European guideline for the management of pelvic inflammatory disease **(2017)**
- European guideline on the management of Mycoplasma genitalium infections **(2021)**
- Brazilian Protocol for Sexually Transmitted Infections, **2020**: infections that cause cervicitis

- Brazilian Protocol for Sexually Transmitted infections, **2020**: pelvic inflammatory disease
- Australian STI Management Guidelines for use in Primary Care; Pelvic Inflammatory Disease (**2021**)

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is important to note that there has been **no withdrawal** of drugs.

Moreover, there has been **a newly FDA approved drug** for the treatment of bacterial genital tract infections: **Xaciato (clindamycin phosphate) vaginal gel.** However, it has not yet been approved by the SFDA.

Additionally, there have been **updates** regarding previously mentioned drugs in terms of drug information and prescribing edits since May 2020 (table 1).

Table 1. Prescribing Edits Modifications for Bacterial Genital Tract Infections Medications

DRUGS	PE MODIFICATIONS
Azithromycin	Remove PA Add ST: effective as alternative for treating primary, secondary syphilis, and early latent syphilis, should not be used as first-line treatment for syphilis and used with caution only when treatment with penicillin or doxycycline is not feasible. azithromycin should not be used in MSM, persons with HIV, or pregnant women, and this should be confirmed by the prescriber
Levofloxacin	Add AGE: not recommended for children < 18 years of age unless there are no suitable alternative antibiotics due to potential for musculoskeletal and joint-related side effects

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in the bacterial genital tract infections therapeutic management.

Below is a table summarizing the major changes based on the different Bacterial Genital Tract Infections guidelines used to issue this report:

Table 2. General Recommendations for the Management of Bacterial Genital Tract Infections

Management of Bacterial Genital Tract Infections		
General Recommendations	**Level of Evidence/Grade of Recommendation**	**Reference**
Prevention of STIs: • HPV vaccination is recommended up to age 26 for those not previously vaccinated at ages 11 or 12. • Administer the HBV vaccination series to all adolescents and young adults who missed it during childhood. • Offer the HAV vaccination series to adolescents and young adults, especially those who did not receive it in childhood.	Not graded[6]	CDC STI Treatment Guidelines[6]
Treatment for **chancroid** include azithromycin, ceftriaxone, ciprofloxacin, and erythromycin base. Azithromycin and ceftriaxone offer the advantage of single-dose therapy. Ciprofloxacin presents a low risk to the fetus during pregnancy but has potential for toxicity during breastfeeding.	Not graded[6]	CDC STI Treatment Guidelines[6]
Granuloma Inguinale (Donovanosis): it is recommended to give azithromycin as a first-line therapy. Alternative regimens are doxycycline, erythromycin base and trimethoprim-sulfamethoxazole.	Not graded[6]	CDC STI Treatment Guidelines[6]

Pregnant and lactating women with granuloma inguinale should be treated with a macrolide regimen (erythromycin or azithromycin) rather than doxycycline (associated with teeth discoloration).		
Recommended treatment regimens for primary & secondary **syphilis consist of benzathine penicillin G given IM in a single dose as opposed to 3 doses at weekly intervals for late latent syphilis and tertiary syphilis.** This drug is used for both children and adults with corresponding doses. In case of pregnancy, pregnant women with primary or secondary syphilis who are allergic to penicillin should be desensitized and treated with penicillin G.	Not graded[6] Strong recommendation; moderate-certainty evidence[7]	CDC STI Treatment Guidelines[6] WHO[7]
Recommended regiment for **nongonococcal urethritis** consists of doxycycline with alternative being azithromycin. Usually, it is always considered to check for compliance to medication whenever a patient presents with recurrent urethritis because it could be the cause of mistreatment. Once this has been ruled out, alternative treatment options can be considered.	Not graded[6]	CDC STI Treatment Guidelines[6]
Presumptive treatment for cervicitis caused by Chlamydia and Gonorrhea is recommended for women at increased risk (e.g., those under 25, those with a new or high-risk sex partner, or if follow-up isn't possible or testing isn't available). In case treatment	Not graded[6] Not graded[8]	CDC STI Treatment Guidelines[6] Journal of the Brazilian Society of Tropical Medicine[8]

for cervicitis is considered, options include doxycycline as first line and azithromycin as an alternative treatment. For women at lower risk for STIs, deferring treatment until diagnostic test results are available is an option. If treatment is deferred and Chlamydia and Gonorrhea tests are negative, a follow-up visit to check cervicitis resolution can be considered.		
Chlamydial infections should be treated on the spot to prevent adverse reproductive health complications and continued sexual transmission. It is also essential to treat sexual partners and pregnant women to prevent any further spread of the infection. Treatment options for adults include doxycycline and alternatives could be azithromycin and levofloxacin. Doxycycline is contraindicated during the second and third trimesters of pregnancy because of risk for tooth discoloration. Hence, pregnant women should be treated with azithromycin preferably.	Not graded[6]	CDC STI Treatment Guidelines[6]
Chlamydial infections for neonates and infants should be treated with erythromycin base or ethyl succinate. For children <45 kg: Erythromycin base or ethyl succinate are considered. For children ≥45 kg, consider azithromycin or doxycycline treatment.	Not graded[6]	CDC STI Treatment Guidelines[6]

For **gonococcal infections** of the cervix, urethra or rectum among adolescents and adults, high dose intramuscular (IM) ceftriaxone is the preferred regimen. In case ceftriaxone is not available, alternative cephalosporins can be used such as ceftizoxime [500 mg IM], cefoxitin [2 g IM with probenecid 1 g orally], or cefotaxime [500 mg IM]) or high dose cefixime combined with azithromycin. Spectinomycin IM single dose have also been used together with azithromycin single dose. In cases of penicillin allergies or if the above options are not available, high-dose azithromycin with gentamicin can be used. All of the above alternative regimens are not superior to ceftriaxone, and some are associated with inferior clearance in cases of pharyngeal gonorrhea infection. Pregnant women should be treated with ceftriaxone. Provide immediate treatment for individuals with confirmed urethral discharge to address N. gonorrhoeae and C. trachomatis infections on the same day. When dealing with patients suspected of treatment failure for certain infections, the initial treatment regimen (ceftriaxone 500 mg IM) should be administered again, with the inclusion of doxycycline if chlamydia infection is also suspected. This is because	Not graded[6] Conditional recommendation; low-certainty evidence[7] Not graded[9] Grade 1A[10] Grade 1C[11]	CDC STI Treatment Guidelines[6] WHO[7] British Association for Sexual Health and HIV National Guideline[10] European Guidelines[11]

reinfections are more common than actual treatment failures.		
Two-stage therapy approaches, ideally using resistance-guided therapy, are recommended for treatment of **Mycoplasma Genitalium.** If patients are macrolide sensitive, recommend doxycycline therapy followed by azithromycin. In case patients are macrolide resistant, doxycycline therapy followed by moxifloxacin is recommended. The role of doxycycline therapy is to reduce bacterial load to allow a better cure rate with subsequent Moxifloxacin or Azithromycin.	Not graded[6] Grade 1D[12] Grade 1B[13]	CDC STI Treatment Guidelines [6] British Association for Sexual Health and HIV National Guideline[12] European guideline[13]
Third-line treatment for persistent M. genitalium infection after azithromycin and moxifloxacin treatment include pristinamycin, minocycline or nitroimidazoles (tinidazole or metronidazole)	Grade 1B for pristinamycin[13] Grade 2B for mynocycline[13]	European guideline[13]
Treatment for **BV** is recommended for women with symptoms. Recommended regimens include metronidazole oral and intravaginal as well as clindamycin intravaginal. Alternatives to those regimens are clindamycin oral, oral secnidazole and oral tinidazole. Suggest treating for bacterial vaginosis if vaginal discharge is present (for example, tenacious or thin) or based on the results of microscopy, if available.	Not graded[6] Strong recommendation; moderate-certainty evidence[7] Not graded[14] Grade A[15] Grade A[16]	CDC STI Treatment Guidelines [6] WHO[7] AAFP[15] IUSTI/WHO[16]
The use of probiotics as an adjunctive or replacement therapy in women with BV is not currently	Not graded[6]	CDC STI Treatment Guidelines [6]

recommended. The use of high dose vitamin D supplementation among symptomatic women with BV was not associated with a decrease in BV recurrence.		
Physicians should explain potential adverse effects with oral metronidazole use for **BV**, including a possible disulfiram-like reaction with alcohol consumption or gastrointestinal symptoms.	Grade A[15]	AAFP[15]
PID treatment regimens should provide empiric, broad-spectrum coverage of likely pathogens. All regimens used to treat PID should also be effective against *N. gonorrhoeae* and *C. trachomatis* because negative endocervical screening for these organisms does not rule out upper genital tract infection. **Recommended parenteral treatment regimens include:** • Ceftriaxone plus doxycycline plus metronidazole • Cefotetan plus doxycycline • Cefoxitin plus doxycycline **Alternative parenteral regimens include:** • Ampicillin-sulbactam plus doxycycline • Clindamycin plus gentamicin • Azithromycin plus metronidazole can be considered in mild to moderate PID if N. gonorrhoeae is excluded or unlikely **Recommended IM/oral treatment regimens include:**	Not graded[6] Grade B[17] Not graded[18] Grade 1A[19]	CDC STI Treatment Guidelines[6] AAFP[17] Journal of the Brazilian Society of Tropical Medicine[18] British Association for Sexual Health and HIV National Guideline[19]

• Ceftriaxone plus doxycycline plus metronidazole • Cefoxitin and probenecid plus doxycycline with metronidazole • Other parenteral third-generation cephalosporin (ceftizoxime or cefotaxime) plus doxycycline with metronidazole		
For acute **epididymitis** most likely caused by chlamydia or gonorrhea: Ceftriaxone IM in a single dose plus doxycycline. For acute epididymitis most likely caused by chlamydia, gonorrhea, or enteric organisms (men who practice insertive anal sex): Ceftriaxone IM in a single dose plus levofloxacin. For acute epididymitis most likely caused by enteric organisms only: Levofloxacin monotherapy.	Not graded[6]	CDC STI Treatment Guidelines[6]
Treating sexual partners is essential to prevent the spread of chancroid, urethritis, cervicitis, chlamydial infections, gonococcal infections, Mycoplasma Genitalium, ensure proper care, and reduce the risk of reinfection. It is a crucial aspect of comprehensive disease management and public health. For BV, treatment of sexual partner is not recommended. For PID, the most recent sexual partner (<60 days) should be treated.	Not graded[6]	CDC STI Treatment Guidelines[6]

At the end of the report, a **key recommendation synthesis section** is added highlighting the latest updates in **Bacterial Genital Tract Infections clinical and therapeutic management.**

Section 1.0 Summary of Reviewed Clinical Guidelines & Evidence

This section is divided into two parts; one part includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Bacterial Genital Tract Infections report, and the other part includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

The following segment contains the updated versions of the guidelines mentioned in the May 2020 CHI Bacterial Genital Tract Infections Report and the corresponding recommendations:

Table 3. Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated versions**
1.1 CDC STI treatment guidelines **(2015)**	CDC STI treatment guidelines **(2021)**
1.2 WHO Guidelines on the Treatment of Neisseria gonorrhoeae Infection **(2016)**	N/A*

**: not available (no new updates for those guidelines)*

1.1.1 CDC STI Treatment Guidelines (2021)

The Centers for Disease Control and Prevention (CDC) published in 2021 Sexually Transmitted Infections (STI) treatment guidelines to provide current evidence-based prevention, diagnostic and treatment recommendations that replace the 2015 guidance[6]. While the guidance covered fungal and viral infections as well, this report will solely focus on STIs due to bacterial pathogens.

Missing recommendations:

Primary prevention:

- Primary prevention and anticipatory guidance for recognizing symptoms and behaviors associated with STIs are strategies that should be incorporated into all types of health care visits for adolescents and young adults. The following recommendations for primary prevention of STIs (i.e., vaccination and counseling) are based on published clinical guidelines for sexually active

adolescents and young adults from federal agencies and medical professional organizations.

- HPV vaccination is recommended through age 26 years for those not vaccinated previously at the routine age of 11 or 12 years
- The HBV vaccination series is recommended for all adolescents and young adults who have not previously received the universal HBV vaccine series during childhood.
- The HAV vaccination series should be offered to adolescents and young adults as well as those who have not previously received the universal HAV vaccine series during childhood.

Chancroid:

Table 4. Recommended Regimens for Chancroid

Azithromycin 1 g orally in a single dose
or
Ceftriaxone 250 mg IM in a single dose
or
Ciprofloxacin 500 mg orally 2 times/day for 3 days
or
Erythromycin base 500 mg orally 3 times/day for 7 days

- Azithromycin and ceftriaxone offer the advantage of single-dose therapy. Worldwide, several isolates with intermediate resistance to either ciprofloxacin or erythromycin have been reported. However, because cultures are not routinely performed, and chancroid is uncommon, data are limited regarding prevalence of *H. ducreyi* antimicrobial resistance.
- Patients should be reexamined 3–7 days after therapy initiation. If treatment is successful, ulcers usually improve symptomatically within 3 days and objectively within 7 days after therapy. If no clinical improvement is evident, the clinician should consider whether the diagnosis is correct, another STI is present, the patient has HIV infection, the treatment was not used as instructed, or the *H. ducreyi* strain causing the infection is resistant to the prescribed antimicrobial.
- The time required for complete healing depends on the size of the ulcer; large ulcers might require >2 weeks. In addition, healing can be slower for uncircumcised men who have ulcers under the foreskin. Clinical resolution of fluctuant lymphadenopathy is slower than that of ulcers and might require

needle aspiration or incision and drainage, despite otherwise successful therapy.

- Regardless of whether disease symptoms are present, sex partners of patients with chancroid should be examined and treated if they had sexual contact with the patient during the 10 days preceding the patient's symptom onset.
- Data indicate ciprofloxacin presents a low risk to the fetus during pregnancy but has potential for toxicity during breastfeeding. Alternative drugs should be used if the patient is pregnant or lactating. No adverse effects of chancroid on pregnancy outcome have been reported.

Granuloma Inguinale (Donovanosis)

- Treatment has been reported to halt progression of lesions, and healing typically proceeds inward from the ulcer margins.
- Prolonged therapy is usually required to permit granulation and re-epithelialization of the ulcers. Relapse can occur 6–18 months after apparently effective therapy.

Table 5. Treatment Regimens for Granuloma Inguinale (Donovanosis)

Recommended Regimen for Granuloma Inguinale (Donovanosis)
Azithromycin 1 g orally once/week or 500 mg daily for > 3 weeks and until all lesions have completely healed
Alternative Regimens
Doxycycline 100 mg orally 2 times/day for at least 3 weeks and until all lesions have completely healed
or
Erythromycin base 500 mg orally 4 times/day for > 3 weeks and until all lesions have completely healed
or
Trimethoprim-sulfamethoxazole one double-strength (160 mg/800 mg) tablet orally 2 times/day for > 3 weeks and until all lesions have completely healed

- The addition of another antibiotic to these regimens can be considered if improvement is not evident within the first few days of therapy.
- Persons who have had sexual contact with a patient who has granuloma inguinale within the 60 days before onset of the patient's symptoms should be examined and offered therapy. However, the value of empiric therapy in the absence of clinical signs and symptoms has not been established.

- Use of doxycycline in pregnancy might be associated with discoloration of teeth; however, the risk is not well defined. Doxycycline is compatible with breastfeeding. Sulfonamides can be associated with neonatal kernicterus among those with glucose-6-phospate dehydrogenase deficiency and should be avoided during the third trimester and while breastfeeding. For these reasons, pregnant and lactating women with granuloma inguinale should be treated with a macrolide regimen (erythromycin or azithromycin).

Syphilis

- Parenteral penicillin G has been used effectively for achieving clinical resolution (i.e., the healing of lesions and prevention of sexual transmission) and for preventing late sequelae. However, no comparative trials have been conducted to guide selection of an optimal penicillin regimen. Substantially fewer data are available for nonpenicillin regimens.
- Available data demonstrate that use of additional doses of benzathine penicillin G, amoxicillin, or other antibiotics do not enhance efficacy of this recommended regimen when used to treat primary and secondary syphilis, regardless of HIV status.

Table 6. Regimens for Primary and Secondary Syphilis*

Recommended Regimen for Primary and Secondary Syphilis* Among Adults
Benzathine penicillin G 2.4 million units IM in a single dose
* Recommendations for treating syphilis among persons with HIV infection and pregnant women are discussed elsewhere in this report (see Syphilis Among Persons with HIV Infection; Syphilis During Pregnancy).
Recommended Regimen for Syphilis Among Infants and Children
Benzathine penicillin G 50,000 units/kg body weight IM, up to the adult dose of 2.4 million units in a single dose

- Infants and children aged ≥ 1 month who receive a syphilis diagnosis should have birth and maternal medical records reviewed to assess whether they have congenital or acquired syphilis. Infants and children aged ≥1 month with primary and secondary syphilis should be managed by a pediatric infectious disease specialist and evaluated for sexual abuse (e.g., through consultation with child protective services)
- Clinical and serologic evaluation should be performed at 6 and 12 months after treatment; more frequent evaluation might be prudent if opportunity for follow-up is uncertain or if repeat infection is a clinical concern.

- Pregnant women with primary or secondary syphilis who are allergic to penicillin should be desensitized and treated with penicillin G. Skin testing or oral graded penicillin dose challenge might be helpful in identifying women at risk for acute allergic reactions.
- Data to support use of alternatives to penicillin in treating primary and secondary syphilis are limited. However, multiple therapies might be effective for nonpregnant persons with penicillin allergy who have primary or secondary syphilis.
- Doxycycline (100 mg orally 2 times/day for 14 days) and tetracycline (500 mg orally 4 times/day for 14 days) have been used for years and can be effective. Compliance is likely to be better with doxycycline than tetracycline because tetracycline can cause more gastrointestinal side effects and requires more frequent dosing.
- Limited clinical studies, along with biologic and pharmacologic evidence, indicate that ceftriaxone (1 g daily either IM or IV for 10 days) is effective for treating primary and secondary syphilis; however, the optimal dose and duration of ceftriaxone therapy have not been defined.
- Persons with a penicillin allergy whose compliance with therapy or follow-up cannot be ensured should be desensitized and treated with benzathine penicillin G. Skin testing for penicillin allergy might be useful in circumstances in which the reagents and expertise are available for performing the test adequately.

Latent syphilis:

- Because latent syphilis is not transmitted sexually, the objective of treating persons in this disease stage is to prevent medical complications of syphilis. Latent syphilis can also be vertically transmitted to a fetus; therefore, the goal of treating a pregnant woman is to prevent congenital syphilis. Although clinical experience supports the effectiveness of penicillin in achieving this goal, limited evidence is available for guiding choice of specific regimens or duration.
- Available data demonstrate that additional doses of benzathine penicillin G, amoxicillin, or other antibiotics in early latent syphilis do not enhance efficacy, regardless of HIV status.

Table 7. Treatment Regimens for Latent Syphilis

Recommended Regimens for Latent Syphilis* Among Adults
Early latent syphilis: Benzathine penicillin G 2.4 million units IM in a single dose
Late latent syphilis: Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals
* Recommendations for treating syphilis in persons with HIV and pregnant women are discussed elsewhere in this report.

Tertiary syphilis:

- Tertiary syphilis refers to gummas, cardiovascular syphilis, psychiatric manifestations (e.g., memory loss or personality changes), or late neurosyphilis.
- Persons with gummas and cardiovascular syphilis who are not allergic to penicillin and have no evidence of neurosyphilis by clinical and CSF examination should be treated with the following regimen.

Table 8. Treatment Regimen for Tertiary Syphilis

Recommended Regimen for Tertiary Syphilis Among Adults
Tertiary syphilis with normal CSF examination: Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

Neurosyphilis, Ocular Syphilis, and Otosyphilis

Table 9. Treatment Regimen for Neurosyphilis, Ocular Syphilis and Otosyphilis

Recommended Regimen for Neurosyphilis, Ocular Syphilis, or Otosyphilis Among Adults
Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion for 10–14 days
Alternative Regimen
Procaine penicillin G 2.4 million units IM once daily **plus** **Probenecid** 500 mg orally 4 times/day, both for 10–14 days

Urethritis

- Ideally, treatment should be pathogen based; however, diagnostic information might not be immediately available. Presumptive treatment should be initiated **at NGU diagnosis**.
- Doxycycline is highly effective for chlamydial urethral infections and is also effective for chlamydial infections of the rectum; it also has some activity against *M. genitalium*. In contrast, reports have increased of azithromycin treatment failures for chlamydial infection, and the incidence of macrolide resistance in *M. genitalium* also has been rapidly rising.

Table 10. Treatment Regimens for Urethritis

Recommended Regimen for Nongonococcal Urethritis
Doxycycline 100 mg orally 2 times/day for 7 days
Alternative Regimens
Azithromycin 1 g orally in a single dose
or
Azithromycin 500 mg orally in a single dose; then 250 mg orally daily for 4 days

- All sex partners of men with NGU within the preceding 60 days should be referred for evaluation and testing and presumptive treatment with a drug regimen effective against chlamydia. All partners should be evaluated and treated according to the management section for their respective pathogen; EPT could be an alternate approach if a partner is unable to access timely care. To avoid reinfection, sex partners should abstain from sexual intercourse until they and their partners are treated.
- The objective diagnosis of persistent or recurrent NGU should be made before considering additional antimicrobial therapy. Symptomatic recurrent or persistent urethritis might be caused by treatment failure or reinfection after successful treatment.
- The initial step in recurrent urethritis is assessing compliance with treatment or potential re-exposure to an untreated sex partner. If the patient did not comply with the treatment regimen or was re-exposed to an untreated partner, retreatment with the initial regimen can be considered. If therapy was appropriately completed and no re-exposure occurred, therapy is dependent on the initial treatment regimen. Ideally, diagnostic testing among men with recurrent or persistent symptoms, including those with gonorrhea, chlamydia, *M. genitalium*, and trichomoniasis, can be used to guide further management decisions.

- *T. vaginalis* is also known to cause urethritis among men who have sex with women. In areas where *T. vaginalis* is prevalent, men who have sex with women with persistent or recurrent urethritis should be tested for *T. vaginalis* and presumptively treated with metronidazole 2 g orally in a single dose or tinidazole 2 g orally in a single dose; their partners should be referred for evaluation and treatment, if needed.
- If *T. vaginalis* is unlikely (MSM with NGU or negative *T. vaginalis* NAAT), men with recurrent NGU should be tested for *M. genitalium* by using an FDA-cleared NAAT. Treatment for *M. genitalium* includes a two-stage approach, ideally using resistance-guided therapy. If *M. genitalium* resistance testing is available it should be performed, and the results should be used to guide therapy (see *Mycoplasma genitalium*). If *M. genitalium* resistance testing is not available, doxycycline 100 mg orally 2 times/day for 7 days followed by moxifloxacin 400 mg orally once daily for 7 days should be used. The rationale for this approach is that although not curative, doxycycline decreases the *M. genitalium* bacterial load, thereby increasing likelihood of moxifloxacin success. Higher doses of azithromycin have not been effective for *M. genitalium* after azithromycin treatment failures. Men with persistent or recurrent NGU after treatment for *M. genitalium* or *T. vaginalis* should be referred to an infectious disease or urology specialist.

Cervicitis

- Multiple factors should affect the decision to provide presumptive therapy for cervicitis. Presumptive treatment with antimicrobials for *C. trachomatis* and *N. gonorrhoeae* should be provided for women at increased risk (e.g., those aged <25 years and women with a new sex partner, a sex partner with concurrent partners, or a sex partner who has an STI), if follow-up cannot be ensured, or if testing with NAAT is not possible. Trichomoniasis and BV should be treated if detected.
- For women at lower risk for STIs, deferring treatment until results of diagnostic tests are available is an option. If treatment is deferred and *C. trachomatis* and *N. gonorrhoeae* NAATs are negative, a follow-up visit to determine whether the cervicitis has resolved can be considered.

Table 11. Treatment Regimens for Cervicitis

Recommended Regimen for Cervicitis*
Doxycycline 100 mg orally 2 times/day for 7 days
* Consider concurrent treatment for gonococcal infection if the patient is at risk for gonorrhea or lives in a community where the prevalence of gonorrhea is high (see Gonococcal Infections).
Alternative Regimen
Azithromycin 1 g orally in a single dose

- Management of sex partners of women treated for cervicitis should be tailored for the specific infection identified or suspected. All sex partners during the previous 60 days should be referred for evaluation, testing, and presumptive treatment if chlamydia, gonorrhea, or trichomoniasis was identified.
- EPT and other effective partner referral strategies are alternative approaches for treating male partners of women who have chlamydial or gonococcal infection. To avoid reinfection, sex partners should abstain from sexual intercourse until they and their partners are treated.
- Diagnosis and treatment of cervicitis for pregnant women does not differ from that for women who are not pregnant.
- Among women with persistent cervicitis who were previously treated with doxycycline or azithromycin, testing for *M. genitalium* can be considered and treatment initiated on the basis of results of diagnostic testing. For women with persistent symptoms that are clearly attributable to cervicitis, referral to a gynecologic specialist can be considered for evaluation of noninfectious causes.

Chlamydial Infection Among Adolescents and Adults

- Treating persons with *C. trachomatis* prevents adverse reproductive health complications and continued sexual transmission.
- Furthermore, treating their sex partners can prevent reinfection and infection of other partners.
- Treating pregnant women usually prevents transmission of *C. trachomatis* to neonates during birth.
- Treatment should be provided promptly for all persons with chlamydial infection; treatment delays have been associated with complications (e.g., PID) in a limited proportion of women.

Table 12. Treatment Regimens for Chlamydial Infections

Recommended Regimen for Chlamydial Infection Among Adolescents and Adults
Doxycycline 100 mg orally 2 times/day for 7 days
Alternative Regimens
Azithromycin 1 g orally in a single dose
or
Levofloxacin 500 mg orally once daily for 7 days

- To minimize disease transmission to sex partners, persons treated for chlamydia should be instructed to abstain from sexual intercourse for 7 days after single-dose therapy or until completion of a 7-day regimen and resolution of symptoms if present. To minimize risk for reinfection, patients also should be instructed to abstain from sexual intercourse until all their sex partners have been treated.
- Sex partners should be referred for evaluation, testing, and presumptive treatment if they had sexual contact with the partner during the 60 days preceding the patient's onset of symptoms or chlamydia diagnosis. Although the exposure intervals defining identification of sex partners at risk are based on limited data, the most recent sex partner should be evaluated and treated, even if the time of the last sexual contact was >60 days before symptom onset or diagnosis.
- Clinical experience and published studies indicate that azithromycin is safe and effective during pregnancy.
- Doxycycline is contraindicated during the second and third trimesters of pregnancy because of the risk for tooth discoloration. Human data reveal that levofloxacin presents a low risk to the fetus during pregnancy but has potential for toxicity during breastfeeding; however, data from animal studies increase concerns regarding cartilage damage to neonates.

Table 13. Treatment Regimens for Chlamydial Infections in Pregnant Women

Recommended Regimen for Chlamydial Infection During Pregnancy
Azithromycin 1 g orally in a single dose
Alternative Regimen
Amoxicillin 500 mg orally 3 times/day for 7 days

Chlamydial Infection among Neonates

Table 14. Treatment Regimen for Chlamydial Infections among Neonates

Recommended Regimen for Chlamydial Infection Among Neonates
Erythromycin base or ethyl succinate 50 mg/kg body weight/day orally, divided into 4 doses daily for 14 days*
* An association between oral erythromycin and azithromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported among infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for IHPS signs and symptoms.

- Although data regarding use of azithromycin for treating neonatal chlamydial infection are limited, available data demonstrate that a short therapy course might be effective.
- Topical antibiotic therapy alone is inadequate for treating ophthalmia neonatorum caused by chlamydia and is unnecessary when systemic treatment is administered.
- Mothers of infants who have ophthalmia caused by chlamydia and the sex partners of these women should be evaluated and presumptively treated for chlamydia.

Chlamydial Infection among Infants and Children

Table 15. Treatment Regimens for Chlamydial Infections in Infants and Children

Recommended Regimens for Chlamydial Infection Among Infants and Children
For infants and children weighing <45 kg: Erythromycin base or ethyl succinate 50 mg/kg body weight/day orally divided into 4 doses daily for 14 days.
Data are limited regarding the effectiveness and optimal dose of azithromycin for treating chlamydial infection among infants and children weighing <45 kg.
For children weighing ≥ 45 kg but aged < 8 years: Azithromycin 1 g orally in a single dose
For children aged ≥ 8 years: Azithromycin 1 g orally in a single dose
or
Doxycycline 100 mg orally 2 times/day for 7 days

Gonococcal Infection among Adolescents and Adults

Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum

Table 16. Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum

Recommended Regimen for Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum Among Adults and Adolescents
Ceftriaxone 500 mg* IM in a single dose for persons weighing <150 kg
If chlamydial infection has not been excluded, treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.
* For persons weighing ≥ 150 kg, 1 g ceftriaxone should be administered.
Alternative Regimens if Ceftriaxone Is Not Available
Gentamicin 240 mg IM in a single dose
plus
Azithromycin 2 g orally in a single dose
or
Cefixime* 800 mg orally in a single dose
* If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.

- Recent sex partners (i.e., persons having sexual contact with the infected patient < 60 days preceding onset of symptoms or gonorrhea diagnosis) should be referred for evaluation, testing, and presumptive treatment. If the patient's last potential sexual exposure was > 60 days before onset of symptoms or diagnosis, the most recent sex partner should be treated.
- Treatment of the sexual partner with cefixime 800 mg as a single dose is recommended, provided that concurrent chlamydial infection has been excluded. If a chlamydia test result has not been documented, the partner may be treated with a single dose of oral cefixime 800 mg plus oral doxycycline 100 mg 2 times/day for 7 days.
- If adherence with multiday dosing is a considerable concern, azithromycin 1 g can be considered but has lower treatment efficacy among persons with rectal chlamydia.
- Patients with suspected treatment failures should first be retreated routinely with the initial regimen used (ceftriaxone 500 mg IM), with the addition of doxycycline if chlamydia infection exists, because reinfections are more likely than actual treatment failures. However, in situations with a higher likelihood

of treatment failure than reinfection, relevant clinical specimens should be obtained for culture (preferably with simultaneous NAAT) and antimicrobial susceptibility testing before retreatment.

- Dual treatment with single doses of IM gentamicin 240 mg plus oral azithromycin 2 g can be considered, particularly when isolates are identified as having elevated cephalosporin MICs.
- Persons with suspected treatment failure after treatment with the alternative regimen (cefixime or gentamicin) should be treated with ceftriaxone 500 mg as a single IM dose or as a single dose with or without an antichlamydial agent on the basis of chlamydia infection status.
- Pregnant women infected with *N. gonorrhoeae* should be treated with ceftriaxone 500 mg in a single IM dose plus treatment for chlamydia if infection has not been excluded. When cephalosporin allergy or other considerations preclude treatment with this regimen, consultation with an infectious disease specialist or an STD clinical expert is recommended. Gentamicin use is cautioned during pregnancy because of risk for neonatal birth defects, nephrotoxicity, or ototoxicity.

Gonococcal Infection among Infants and Children

Table 17. Treatment Regimens for Gonococcal Infection among Infants/Children

Recommended Regimen for Uncomplicated Gonococcal Vulvovaginitis, Cervicitis, Urethritis, Pharyngitis, or Proctitis Among Infants and Children Weighing ≤45 kg
Ceftriaxone 25–50 mg/kg body weight IV or IM in a single dose, not to exceed 250 mg IM
Recommended Regimen for Uncomplicated Gonococcal Vulvovaginitis, Cervicitis, Urethritis, Pharyngitis, or Proctitis Among Children Weighing >45 kg
Treat with the regimen recommended for adults

Disseminated gonococcal infection

Treatment of Arthritis and Arthritis-Dermatitis Syndrome

Recommended Regimen for Gonococcal-Related Arthritis and Arthritis-Dermatitis Syndrome

- Ceftriaxone 1 g IM or IV every 24 hours.

If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.

Alternative Regimens

- Cefotaxime 1 g IV every 8 hours

  or

- Ceftizoxime 1 g every 8 hours

If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.

Treatment of Gonococcal Meningitis and Endocarditis

Recommended Regimen for Gonococcal Meningitis and Endocarditis

- Ceftriaxone 1–2 g IV every 24 hours

If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days

Mycoplasma genitalium

- *M. genitalium* lacks a cell wall, and thus antibiotics targeting cell-wall biosynthesis (e.g., ß-lactams including penicillins and cephalosporins) are ineffective against this organism. Because of the high rates of macrolide resistance with treatment failures and efficient selection of additional resistance, a 1-g dose of azithromycin should not be used.
- Two-stage therapy approaches, ideally using resistance-guided therapy, are recommended for treatment. Resistance-guided therapy has demonstrated cure rates of >90% and should be used whenever possible; however, it requires access to macrolide-resistance testing.
- As part of this approach, doxycycline is provided as initial empiric therapy, which reduces the organism load and facilitates organism clearance, followed by macrolide-sensitive *M. genitalium* infections treated with high-dose azithromycin; macrolide-resistant infections are treated with moxifloxacin.

Table 18. Treatment Regimen for M. genitalium

Recommended Regimens if *M. genitalium* Resistance Testing Is Available
If macrolide sensitive: Doxycycline 100 mg orally 2 times/day for 7 days, followed by **azithromycin** 1 g orally initial dose, followed by 500 mg orally daily for 3 additional days (2.5 g total)
If macrolide resistant: Doxycycline 100 mg orally 2 times/day for 7 days followed by **moxifloxacin** 400 mg orally once daily for 7 days
Recommended Regimen if *M. genitalium* Resistance Testing Is Not Available

If *M. genitalium* is detected by an FDA-cleared NAAT: Doxycycline 100 mg orally 2 times/day for 7 days, followed by **moxifloxacin** 400 mg orally once daily for 7 days

- Although the majority of *M. genitalium* strains are sensitive to moxifloxacin, resistance has been reported, and adverse side effects and cost should be considered with this regimen. In settings without access to resistance testing and when moxifloxacin cannot be used, an alternative regimen can be considered, based on limited data: doxycycline 100 mg orally 2 times/day for 7 days, followed by azithromycin (1 g orally on day 1 followed by 500 mg once daily for 3 days) and a test of cure 21 days after completion of therapy.
- Because of the high prevalence of macrolide resistance and high likelihood of treatment failure, this regimen should be used only when a test of cure is possible, and no other alternatives exist. If symptomatic treatment failure or a positive test of cure occurs after this regimen, expert consultation is recommended.
- Data are limited regarding use of minocycline in instances of treatment failure.
- Sex partners of patients with symptomatic *M. genitalium* infection can be tested, and those with a positive test can be treated to possibly reduce the risk for reinfection. If testing the partner is not possible, the antimicrobial regimen that was provided to the patient can be provided.

Bacterial Vaginosis

- Treatment for BV is recommended for women with symptoms. Established benefits of therapy among nonpregnant women are to relieve vaginal symptoms and signs of infection. Other potential benefits of treatment include reduction in the risk for acquiring *C. trachomatis, N. gonorrhoeae*, *T. vaginalis*, *M. genitalium*, HIV, HPV, and HSV-2. No data are available that directly compare the efficacy of oral and topical medications for treating BV.

Table 19. Treatment Regimens for Bacterial Vaginosis

Recommended Regimens for Bacterial Vaginosis
Metronidazole 500 mg orally 2 times/day for 7 days
or
Metronidazole gel 0.75% one full applicator (5 g) intravaginally, once daily for 5 days
or
Clindamycin cream 2% one full applicator (5 g) intravaginally at bedtime for 7 days

Alternative Regimens
Clindamycin 300 mg orally 2 times/day for 7 days
or
Clindamycin ovules 100 mg intravaginally once at bedtime for 3 days*
or
Secnidazole 2 g oral granules in a single dose†
or
Tinidazole 2 g orally once daily for 2 days
or
Tinidazole 1 g orally once daily for 5 days
* Clindamycin ovules use an oleaginous base that might weaken latex or rubber products (e.g., condoms and diaphragms). Use of such products within 72 hours after treatment with clindamycin ovules is not recommended. † Oral granules should be sprinkled onto unsweetened applesauce, yogurt, or pudding before ingestion. A glass of water can be taken after administration to aid in swallowing.

- Metronidazole does not inhibit acetaldehyde dehydrogenase, as occurs with disulfiram. Ethanol alone or ethanol-independent side effects of metronidazole might explain the suspicion of disulfiram-like effects. Thus, refraining from alcohol use while taking metronidazole (or tinidazole) is unnecessary. Clindamycin cream is oil based and might weaken latex condoms and diaphragms for 5 days after use.
- Women should be advised to refrain from sexual activity or to use condoms consistently and correctly during the BV treatment regimen. Douching might increase the risk for relapse, and no data supports use of douching for treatment or symptom relief.
- Routine treatment of sex partners is not recommended.
- BV treatment is recommended for all symptomatic pregnant women because symptomatic BV has been associated with adverse pregnancy outcomes, including premature rupture of membranes, preterm birth, intra-amniotic infection, and postpartum endometritis. Studies have been undertaken to determine the efficacy of BV treatment among this population, including two trials demonstrating that oral metronidazole was efficacious during pregnancy by using the 250 mg 3 times/day regimen; however, oral metronidazole administered as a 500 mg 2 times/day regimen can also be used. One trial involving a limited number of participants revealed treatment

with oral metronidazole 500 mg 2 times/day for 7 days to be equally effective as metronidazole gel 0.75% for 5 days, with cure rates of 70% by using Amsel criteria to define cure. Another trial demonstrated a cure rate of 85% by using Gram-stain criteria after treatment with oral clindamycin 300 mg 2 times/day for 7 days.

Pelvic Inflammatory Disease

- PID treatment regimens should provide empiric, broad-spectrum coverage of likely pathogens.
- Multiple parenteral and oral antimicrobial regimens have been effective in achieving clinical and microbiologic cure in randomized clinical trials with short-term follow-up. However, only a limited number of studies have assessed and compared these regimens with regard to infection elimination in the endometrium and fallopian tubes or determined the incidence of long-term complications (e.g., tubal infertility and ectopic pregnancy) after antimicrobial regimens.
- The optimal treatment regimen and long-term outcome of early treatment of women with subclinical PID are unknown. All regimens used to treat PID should also be effective against *N. gonorrhoeae* and *C. trachomatis* because negative endocervical screening for these organisms does not rule out upper genital tract infection.
- Anaerobic bacteria have been isolated from the upper genital tract of women who have PID, and data from in vitro studies have revealed that some anaerobes (e.g., *Bacteroides fragilis*) can cause tubal and epithelial destruction. BV is often present among women who have PID.
- Addition of metronidazole to IM or oral PID regimens more effectively eradicates anaerobic organisms from the upper genital tract. Until treatment regimens that do not cover anaerobic microbes have been demonstrated to prevent long-term sequelae (e.g., infertility and ectopic pregnancy) as successfully as the regimens that are effective against these microbes, using regimens with anaerobic activity should be considered. Treatment should be initiated as soon as the presumptive diagnosis has been made because prevention of long-term sequelae is dependent on early administration of recommended antimicrobials. For women with PID of mild or moderate clinical severity, parenteral and oral regimens appear to have similar efficacy. The decision of whether hospitalization is necessary should be based on provider judgment and whether the woman meets any of the following criteria:
    - Surgical emergencies (e.g., appendicitis) cannot be excluded

- Tubo-ovarian abscess
- Pregnancy
- Severe illness, nausea and vomiting, or oral temperature >38.5°C (101°F)
- Unable to follow or tolerate an outpatient oral regimen
- No clinical response to oral antimicrobial therapy

Table 20. Treatment Regimens for Pelvic Inflammatory Disease

Recommended Parenteral Regimens for Pelvic Inflammatory Disease
Ceftriaxone 1 g by every 24 hours
plus
Doxycycline 100 mg orally or IV every 12 hours
plus
Metronidazole 500 mg orally or IV every 12 hours
or
Cefotetan 2 g IV every 12 hours
plus
Doxycycline 100 mg orally or IV every 12 hours
or
Cefoxitin 2 g IV every 6 hours
plus
Doxycycline 100 mg orally or IV every 12 hours
Alternative Parenteral Regimens
Ampicillin-sulbactam 3 g IV every 6 hours
plus
Doxycycline 100 mg orally or IV every 12 hours
or
Clindamycin 900 mg IV every 8 hours
plus
Gentamicin loading dose IV or IM (2 mg/kg body weight), followed by a maintenance dose (1.5 mg/kg body weight) every 8 hours; single daily dosing (3–5 mg/kg body weight) can be substituted
Recommended Intramuscular or Oral Regimens for Pelvic Inflammatory Disease
Ceftriaxone 500 mg* IM in a single dose

plus
Doxycycline 100 mg orally 2 times/day for 14 days with **metronidazole** 500 mg orally 2 times/day for 14 days
or
Cefoxitin 2 g IM in a single dose and **probenecid** 1 g orally administered concurrently in a single dose
plus
Doxycycline 100 mg orally 2 times/day for 14 days with **metronidazole** 500 mg orally 2 times/day for 14 days
or
Other parenteral third-generation cephalosporin (e.g., ceftizoxime or cefotaxime)
plus
Doxycycline 100 mg orally 2 times/day for 14 days with **metronidazole** 500 mg orally 2 times/day for 14 days
* For persons weighing ≥ 150 kg, 1 g of ceftriaxone should be administered

- Because of the pain associated with IV infusion, doxycycline should be administered orally when possible. Oral and IV administration of doxycycline and metronidazole provide similar bioavailability. Oral metronidazole is well absorbed and can be considered instead of IV for women without severe illness or tubo-ovarian abscess when possible.
- After clinical improvement with parenteral therapy, transition to oral therapy with doxycycline 100 mg 2 times/day and metronidazole 500 mg 2 times/day is recommended to complete 14 days of antimicrobial therapy.
- Persons who have had sexual contact with a partner with PID during the 60 days preceding symptom onset should be evaluated, tested, and presumptively treated for chlamydia and gonorrhea, regardless of the PID etiology or pathogens isolated. If the last sexual intercourse was >60 days before symptom onset or diagnosis, the most recent sex partner should be treated
- Pregnant women suspected of having PID are at high risk for maternal morbidity and preterm delivery. These women should be hospitalized and treated with IV antimicrobials in consultation with an infectious disease specialist.

Epididymitis

- To prevent complications and transmission of STIs, presumptive therapy for all sexually active men is indicated at the time of the visit before all laboratory test results are available.
- Selection of presumptive therapy is based on risk for chlamydial and gonococcal infections or enteric organisms. Treatment goals for acute epididymitis are 1) microbiologic infection cure, 2) improvement of signs and symptoms, 3) prevention of transmission of chlamydia and gonorrhea to others, and 4) decreased potential for chlamydial or gonococcal epididymitis complications (e.g., infertility or chronic pain).
- Although the majority of men with acute epididymitis can be treated on an outpatient basis, referral to a specialist and hospitalization should be considered when severe pain or fever indicates other diagnoses (e.g., torsion, testicular infarction, abscess, or necrotizing fasciitis) or when men are unable to comply with an antimicrobial regimen. Age, history of diabetes, fever, and elevated C-reactive protein can indicate more severe disease requiring hospitalization.

Table 21. Treatment Regimens for Epididymitis

Recommended Regimens for Epididymitis
For acute epididymitis most likely caused by chlamydia or gonorrhea: Ceftriaxone 500 mg* IM in a single dose
plus
Doxycycline 100 mg orally 2 times/day for 10 days
For acute epididymitis most likely caused by chlamydia, gonorrhea, or enteric organisms (men who practice insertive anal sex): Ceftriaxone 500 mg* IM in a single dose
plus
Levofloxacin 500 mg orally once daily for 10 days
For acute epididymitis most likely caused by enteric organisms only: Levofloxacin 500 mg orally once daily for 10 days
* For persons weighing ≥150 kg, 1 g of ceftriaxone should be administered

- Levofloxacin monotherapy should be considered if the infection is most likely caused by enteric organisms only, and gonorrhea has been ruled out by Gram, MB, or GV stain. This includes men who have undergone prostate biopsy, vasectomy, and other urinary tract instrumentation procedures.

- Treatment should be guided by bacterial cultures and antimicrobial susceptibilities. As an adjunct to therapy, bed rest, scrotal elevation, and nonsteroidal anti-inflammatory drugs are recommended until fever and local inflammation have subsided. Complete resolution of discomfort might not occur for a few weeks after completion of the antibiotic regimen.
- Men who have acute epididymitis confirmed or suspected to be caused by *N. gonorrhoeae* or *C. trachomatis* should be advised to abstain from sexual intercourse until they and their partners have been treated and symptoms have resolved. All men with acute epididymitis should be tested for HIV and syphilis.
- Men who have acute sexually transmitted epididymitis confirmed or suspected to be caused by *N. gonorrhoeae* or *C. trachomatis* should be instructed to refer all sex partners during the previous 60 days before symptom onset for evaluation, testing, and presumptive treatment (see Chlamydial Infections; Gonococcal Infections). If the last sexual intercourse was >60 days before onset of symptoms or diagnosis, the most recent sex partner should be evaluated and treated. Arrangements should be made to link sex partners to care. EPT is an effective strategy for treating sex partners of men who have or are suspected of having chlamydia or gonorrhea for whom linkage to care is anticipated to be delayed. Partners should be instructed to abstain from sexual intercourse until they and their sex partners are treated, and symptoms have resolved.

1.2 Additional Guidelines

This part includes the added guidelines to the previous CHI Bacterial Genital Tract Infections report, along with their recommendations.

Table 22. List of Additional Guidelines

Additional Guidelines
International Guidelines
WHO Guidelines for the management of symptomatic sexually transmitted infections **(2021)**
Brazilian Protocol for Sexually Transmitted Infections, **2020**: infections that cause cervicitis
Brazilian Protocol for Sexually Transmitted infections, **2020**: pelvic inflammatory disease
Australian STI Management Guidelines for use in Primary Care; Pelvic Inflammatory Disease (**2021**)

North American Guidelines
AAFP; Vaginitis: Diagnosis and Treatment **(2018)**
AAFP Pelvic Inflammatory Disease: Diagnosis, Management, and Prevention **(2019)**
European Guidelines
British Association for Sexual Health and HIV national guideline for the management of infection with Mycoplasma genitalium **(2018)**
UK national guideline for the management of infection with Neisseria gonorrhoeae **(2018)**
United Kingdom National Guideline for the Management of Pelvic Inflammatory Disease **(2019 Interim Update)**
European guideline on the management of syphilis **(2020)**
European guideline for the diagnosis and treatment of gonorrhea in adults **(2020)**
European (IUSTI/WHO) International Union against sexually transmitted infections (IUSTI) World Health Organization (WHO) guideline on the management of vaginal discharge **(2018)**
European guideline for the management of chancroid **(2017)**
European guideline for the management of pelvic inflammatory disease **(2017)**
European guideline on the management of Mycoplasma genitalium infections **(2021)**

1.2.1 International Guidelines

1.2.1.1 WHO Guidelines for the Management of Symptomatic Sexually Transmitted Infections (2021)

The STI Guideline Development Group of the WHO Department of Global HIV, Hepatitis and Sexually Transmitted Infections Programmes published in June 2021 updated guidelines for the management of symptomatic sexually transmitted infections, with the objective to provide updated, evidence-informed clinical and practical recommendations on the case management of people with symptoms of STIs and to support countries in updating their national guidelines for the case management of people with symptoms of STIs[7].

The 2021 WHO Guidelines have opted for the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) system:

Table 23. GRADE Approach

Strength of Recommendations	
Strong	Benefits clearly outweigh risks and burdens or vice versa. Usually stated as: **"we recommend"**
Conditional	Benefits probably outweigh risks and burden, or vice versa, but there is appreciable uncertainty.
Weak	Benefits closely balanced with risks and burdens. Usually stated as: **"we suggest"**
Evidence Level (Quality of Evidence)	
High	One or more well-designed and well-executed randomized controlled trials (RCTs) that yield consistent and directly applicable results. This level also means that further research is very unlikely to change our confidence in the estimate of effect.
Moderate	RCTs with important limitations (i.e., biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, from well-designed cohort or case-control analytic studies, and from multiple time series with or without intervention is in this category. This level also means that further research will probably have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Observational studies would typically be rated as low quality because of the risk for bias. This level also means that further research is very likely to have an important impact on our confidence in the estimate of effect and will probably change the estimate.
Very low	Evidence is conflicting, of poor quality, or lacking, and hence the balance of benefits and harms cannot be determined. Any estimate of effect is very uncertain as evidence is either unavailable or does not permit a conclusion.

The WHO has issued the recommendations below[7]:

Urethral discharge management

Settings with quality-assured molecular testing in a laboratory with a fully operational quality management system and results available on the same day of the visit

- For people with symptom of urethral discharge from the penis, management is recommended to be based on the results of quality-assured molecular assays. However, in settings with limited or no molecular tests or laboratory capacity, recommend syndromic treatment to ensure treatment on the same day of the visit. (Strong recommendation; moderate certainty evidence)
- Treat according to the test results on the same day. If urethral discharge is present but tests are negative, treat for nongonococcal and non-chlamydial urethritis (such as Mycoplasma genitalium or Trichomonas vaginalis). (Strong recommendation; moderate certainty evidence)
- When treatment based on molecular assays is not feasible on the same day of the visit, recommend syndromic treatment of infection with N. gonorrhoeae and C. trachomatis and using the test results to support managing the partner when tests are available. (Strong recommendation; moderate certainty evidence)
- Treat people with recurrent or persistent urethral discharge based on a repeat molecular assay (such as NAAT) after 21 days, testing for N. gonorrhoeae, C. trachomatis as well as M. genitalium and T. vaginalis and testing for antimicrobial-resistant N. gonorrhoeae. (Strong recommendation; moderate certainty evidence)

Settings in which same-day treatment is not feasible with molecular testing or with limited or no molecular testing

- Treat people who have urethral discharge confirmed on examination for N. gonorrhoeae and C. trachomatis to ensure same-day treatment. (Conditional recommendation; low-certainty evidence)
- Treat people with recurrent or persistent urethral discharge for treatment failure based on WHO guidelines and review. (Conditional recommendation; low-certainty evidence)

Table 24. Treatment Regimens for Urethral Discharge Syndrome

Therapy for uncomplicated *Neisseria gonorrhoeae* *Plus* Therapy for *Chlamydia trachomatis*		
Infections covered	**First-line options**	**Effective substitutes**
In settings in which local antimicrobial resistance data are not available, the WHO STI guideline suggests dual therapy for gonorrhea.		
N. gonorrhoeae	**Ceftriaxone 250 mg**, intramuscularly, single dose *Plus* **Azithromycin 1 gram**, orally, single dose	**Cefixime 400 mg**, orally, single dose *Plus* **Azithromycin 1 gram**, orally, single dose
C. trachomatis	**Doxycycline 100 mg**, orally, twice daily for seven days (to be given only if gonorrhea therapy did not include azithromycin)	**Azithromycin 1 gram**, orally, single dose *or* **Erythromycin 500 mg**, orally, 4 times a day for 7 days *or* **Ofloxacin 200–400 mg**, orally, twice a day for 7 days. (to be given only if gonorrhea therapy did not include azithromycin)
In settings in which local antimicrobial resistance data reliably confirm the susceptibility of *N. gonorrhoeae* to the antimicrobial agent, singe therapy may be given.		
N. gonorrhoeae	**Ceftriaxone 250 mg**, intramuscularly, single dose	**Cefixime 400 mg**, orally, single dose *or* **Spectinomycin 2 grams**, intramuscularly, single dose (availability makes this antibiotic impractical)
Additional therapeutic options for recurrent or persistent infections		
T. vaginalis	**Metronidazole 2 grams**, orally, single doses	**Metronidazole 400 or 500 mg**, twice daily for 7 days
M. genitalium	**Azithromycin 500 mg**, orally on day 1, 250 mg daily on days 2–5	

Vaginal discharge management

- For people with symptoms of vaginal discharge, recommend treatment for N. gonorrhoeae and/or C. trachomatis and/or T. vaginalis on the same visit. (Strong recommendation; Moderate certainty evidence)
- Suggest treatment based on the results of quality-assured molecular assays for N. gonorrhoeae and/or C. trachomatis and/or T. vaginalis. (Strong recommendation; Moderate certainty evidence)
- In settings in which treatment based on the results of molecular assay in the same visit is not feasible or that have limited or no molecular testing, suggest treatment based on testing with quality-assured rapid point-of-care tests or on syndromic treatment. (Strong recommendation; Moderate certainty evidence)

Settings in which treatment is based on quality-assured molecular assays in a laboratory with a fully operational quality management system and results available on the same day of the visit

- Recommend treating N. gonorrhoeae and/or C. trachomatis and/or T. vaginalis based on the results of quality-assured molecular assays on a self-collected, or clinician-collected, vaginal swab or on a urine specimen. (Strong recommendation; Moderate certainty evidence)
- Suggest treating for bacterial vaginosis if vaginal discharge is present (for example, tenacious or thin) or based on the results of microscopy, if available. (Strong recommendation; Moderate certainty evidence)
- Suggest treating for candidiasis, where indicated by type of discharge (such as curd-like with vaginal itching) or by the results of microscopy, if available. (Strong recommendation; Moderate certainty evidence)

Settings in which same-day treatment is not feasible with molecular testing or with limited or no molecular testing

- Suggest treating based on a quality-assured rapid test with a minimum sensitivity of 80% and specificity of 90%, if available, to confirm or exclude infection with N. gonorrhoeae and C. trachomatis
- If the availability of a low-cost rapid test or molecular assay is limited, suggest performing a speculum examination and treating for N. gonorrhoeae and C. trachomatis if there is evidence of cervicitis and performing a low-cost rapid test or molecular assay for people with a negative speculum examination who are at high risk of infection with N. gonorrhoeae and C. trachomatis and treating based on the test results

- If a rapid test is not available, suggest treating people who have signs of cervicitis on speculum examination for infection with N. gonorrhoeae and C. trachomatis
- If a rapid test is not available and a speculum examination is not feasible or acceptable, suggest treating people for N. gonorrhoeae and C. trachomatis, all people at high risk of STIs and all people who have vaginal discharge on genital examination
- Suggest treating people for bacterial vaginosis and T. vaginalis if vaginal discharge is present or based on the results of microscopy, if available.
- Suggest treating people for candidiasis, where indicated by type of discharge (such as curd-like with vaginal itching) or by the results of microscopy, if available. (Conditional recommendation; low-certainty evidence for all of the above)

Table 25. Treatment Options for Vaginal Infections

Therapy for bacterial vaginosis and trichomoniasis			
Infections covered	**First-line options**	**Effective substitutes**	**Note: In pregnancy, metronidazole should, ideally, be avoided in the first trimester**
Bacterial vaginosis	**Metronidazole 400 mg or 500 mg,** orally, twice daily for 7 days	**Clindamycin 300 mg,** orally, twice daily for 7 days *or* **Metronidazole 2 grams,** orally, single dose	**Metronidazole 200 mg or 250 mg,** orally, 3 times a day for 7 days *or* **Metronidazole gel** 0.75%, one full applicator (5 grams) intravaginally, twice a day for 7 days *or* **Clindamycin 300 mg,** orally, twice daily for 7 days
T. vaginalis	**Metronidazole 2 grams,** orally, in a single dose *or* **Metronidazole 400 mg or 500 mg,** orally,	**Tinidazole 2 grams orally,** single dose *or* **Tinidazole 500 mg orally,** twice daily for 5 days	**Metronidazole 200 mg or 250 mg,** orally, 3 times a day for 7 days *or* **Metronidazole gel** 0.75%, one full applicator (5 grams)

	twice daily for 7 days		intravaginally, twice a day for 7 days

Table 26. Treatment Options for Cervical Infection

Therapy for uncomplicated *N. gonorrhoeae* ***Plus*** **Therapy for *C. trachomatis***			
Infections covered	**First-line options**	**Effective substitutes**	**Options for pregnant women or during breastfeeding**
In settings in which local antimicrobial resistance data are not available, the WHO STI guidelines suggest dual therapy for gonorrhea.			
*N. gonorrhoeae*a	**Ceftriaxone 250 mg,** intramuscularly single dose *plus* **Azithromycin 1 gram,** orally, single dose	Cefixime 400 mg, orally, single dose *plus* Azithromycin 1 gram, orally, single dose	**Ceftriaxone 250 mg,** intramuscularly, single dose *plus* **Azithromycin 1 gram,** orally, single dose *or* **Cefixime 400 mg,** orally, single dose *plus* **Azithromycin 1 gram,** orally, single dose
C. trachomatis	**Doxycycline 100 mg,** orally, twice daily for 7 days (to be given only if gonorrhea therapy did not include azithromycin)	**Azithromycin 1 gram,** orally, single dose *or* **Erythromycin 500 mg,** orally, 4 times a day for 7 days *or* **Ofloxacin 200–400 mg,** orally, twice daily for 7 days (to be given only if gonorrhea	**Erythromycin 500 mg,** orally, 4 times a day for 7 days *or* **Azithromycin 1 gram,** orally, single dose (to be given only if gonorrhea therapy did not include azithromycin)

		therapy did not include azithromycin)	
M. genitalium	**Azithromycin 500 gram,** orally day 1, 250 mg daily, days 2–5 (absence of macrolide resistance)	**Azithromycin 500 gram,** orally, day 1, 250 mg daily, days 2–5 (absence of macrolide resistance)	

Management of lower abdominal pain among women

- For sexually active women with symptom of lower abdominal pain, suggest assessing for pelvic inflammatory disease and treating syndromically. (Conditional recommendation; low-certainty evidence)
- For sexually active women with lower abdominal pain with either of the following features on clinical examination (bimanual palpation):
    - cervical motion tenderness; or
    - lower abdominal tenderness:
- WHO suggests the following.
    - Treat for pelvic inflammatory disease on the same visit.
    - Test for infection with N. gonorrhoeae and C. trachomatis and, if available, M. genitalium, to support partner management when tests are available.
    - Schedule follow-up assessment three days later to assess for clinical improvement, and if the woman has not improved, refer for further assessment. Conditional recommendation; moderate-certainty evidence)

Table 27. Treatment Options for Pelvic Inflammatory Disease

Therapy for uncomplicated *N. gonorrhoeae* *plus* Therapy for *C. trachomatis* *plus* Therapy for anaerobic infections		
Infections covered	**First-line options**	**Effective substitutes**

In settings in which local antimicrobial resistance data are not available, the WHO STI guidelines suggest dual therapy for gonorrhea.		
N. gonorrhoeae	**Ceftriaxone 250 mg,** intramuscularly, single dose *plus* **Azithromycin 1 gram,** orally, single dose	**Cefixime 400 mg,** orally, single dose *plus* **Azithromycin 1 gram,** orally, single dose
C. trachomatis	**Doxycycline 100 mg,** orally, twice daily for 14 days	**Erythromycin 500 mg,** four times daily for 14 days (to be given only if gonorrhea therapy did not include azithromycin)
In settings in which local antimicrobial resistance data reliably confirm the susceptibility of *N. gonorrhoeae* to the antimicrobial agent, singe therapy may be given as below.		
N. gonorrhoeae	**Ceftriaxone 250 mg,** intramuscularly, single dose	**Cefixime 400 mg,** orally, single dose
The treatment for anaerobes must be included in either treatment option above.		
Anaerobes	**Metronidazole 400 mg or 500 mg**, orally, twice daily for 14 days	

Management of genital ulcer disease, including anorectal ulcers

- For people who present with genital ulcers (including anorectal ulcers), recommend treatment based on quality-assured molecular assays of the ulcer. However, in settings with limited or no molecular tests or laboratory capacity, recommend syndromic treatment to ensure treatment on the same day of the visit. (Strong recommendation; moderate certainty evidence)

Settings with quality-assured molecular testing in a laboratory with a fully operational quality management system and results available on the same day of the visit

- For people with confirmed anogenital ulcers, WHO recommends the following.
    1. Perform molecular assays (NAAT) from anogenital lesions to confirm or exclude herpes simplex virus and Treponema pallidum (syphilis).
    2. Perform molecular assays from anogenital lesions to confirm lymphogranuloma venereum in geographical settings and/or populations in which cases are reported or emerging.

3. Perform serological tests for syphilis, with appropriate interpretation for management depending on the test or tests used.
4. Treat for syphilis and/or herpes simplex virus according to the results available on the same day of the visit or treat syndromically and revise management according to the results when available.
5. Treat for lymphogranuloma venereum when the results are positive.
6. Treat for chancroid only in geographical settings where cases (Strong recommendation; moderate certainty evidence)

Settings in which same-day treatment is not feasible with molecular testing or with limited or no molecular testing

- For people with confirmed anogenital ulcers, suggest the following:
    1. Treat syndromically for syphilis and herpes simplex virus on the same day.
    2. Treat for herpes simplex virus if the ulcer is recurrent or vesicular and treat for syphilis if the person has no history of recent treatment for syphilis (in the past three months).
    3. Treat for chancroid only in geographical settings where cases are reported or emerging. (Conditional recommendation; moderate certainty evidence)

Table 28. Recommended Treatment Options for Genital Ulcer Disease

Infections covered	First-line options	Effective substitutes	For pregnant and breastfeeding women and people younger than 16 years
Syphilis (early) (treatment for primary, secondary, and early latent [less than two years since infection] syphilis)	**Benzathine penicillin 2.4 million units,** intramuscularly in a single dose	**Doxycycline 100 mg,** orally, twice a day for 14 days *or* **Erythromycin 500 mg,** 4 times a day for 14 days	**Benzathine penicillin 2.4 million units**, intramuscularly in a single dose *or* **Erythromycin 500 mg,** orally, 4 times a day for 14 days
Syphilis (late) (treatment for late latent and tertiary syphilis)	**Benzathine penicillin 2.4 million units** by intramuscular	**Procaine penicillin 1.2 million units** by	**Erythromycin 500mg** orally, 4 times a day for 30 days

	injection, once weekly for 3 consecutive weeks	intramuscular injection, once daily for 20 consecutive days *or* **Doxycycline 100 mg,** orally, twice daily for 30 days	

Management of anorectal discharge

- For people with symptom of anorectal discharge and report receptive anal sex, recommend management based on the results of quality-assured molecular assays. However, in settings with limited or no molecular tests or laboratory capacity, recommend syndromic treatment to ensure treatment on the same day of the visit (Strong recommendation; moderate certainty evidence)

Settings with quality-assured molecular testing in a laboratory with a fully operational quality management system and results available on the same day of the visit

Recommend the following:

- Perform molecular assays (NAAT) using a self-collected or clinician-collected anorectal swab to confirm or exclude infection with N. gonorrhoeae and/or C. trachomatis and treat the individual infections detected.
- Treat, additionally, for herpes simplex virus if there is anorectal pain.
- Follow the genital ulcer guidelines if ulceration is present. (Strong recommendation; moderate certainty evidence)

Settings in which same-day treatment is not feasible with molecular testing or with limited or no molecular testing

Suggest the following:

- Treat for N. gonorrhoeae and C. trachomatis if discharge is present.
- Treat, additionally, for herpes simplex virus if there is anorectal pain. (Conditional recommendation; moderate certainty evidence)

Table 29. Treatment Options for Anorectal Discharge

Recommended treatment regimens for anorectal infections		
Infections covered	**First-line options**	**Effective substitutes**
N. gonorrhoeae	**Ceftriaxone 250 mg,** intramuscularly, single dose *plus* **Azithromycin 1 gram,** orally, single dose	**Cefixime 400 mg,** orally, single dose *plus* **Azithromycin 1 gram,** orally, single dose
C. trachomatis	**Doxycycline 100 mg** orally, twice daily, for 7 days *or* **Doxycycline for 21 days** (to cover rectal lymphogranuloma venereum) if suspected or confirmed on NAAT (to be given only if dual therapy did not include azithromycin)	**Erythromycin 500 mg,** orally, 4 times a day for 14 days (to be given only if dual therapy did not include azithromycin)
Syphilis (if ulcer present)	**Benzathine penicillin 2.4 million units** intramuscularly, single dose People with a positive syphilis test and no ulcer: administer the same dose at weekly intervals for a total of three doses	**Doxycycline 100 mg** orally, twice daily for 14 days **Erythromycin 500 mg** 4 times a day, orally, for 14 days Extend treatment to 30 days if syphilis serology is positive

1.2.1.2 Brazilian Protocol for Sexually Transmitted Infections (2020): Infections That Cause Cervicitis

This publication expands on the clinical protocols published in 2020 by the Brazilian Ministry of Health for comprehensive care for people with STIs. The document was approved by the National Committee for Technology Incorporation to the Brazilian National Health System[8].

Cervicitis, also called endocervicitis, is an STI that causes inflammation and irritation of the cervix. The most common causative agents are *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. 70 to 80% of cervicitis cases are asymptomatic. The most typical claims are vaginal discharge, intermenstrual or postcoital bleeding, dyspareunia, dysuria, frequent urination, and chronic pelvic pain. The risk factors are sexually active women younger than 25 years old, new, or multiple sexual partners, partners with STI, previous history or presence of other STI, and irregular use of condoms.

The main recommendations for treatment are summarized in table 29.

Table 30. Treatment Regimens for Gonorrhea/Chlamydia

Gonorrhea/Chlamydia	Treatment
NON-complicated gonococcal infection (urethra, cervix, rectum, and pharynx)	Ceftriaxone 500mg, intramuscular (IM), a single dose plus Azithromycin 500mg, two pills, *per os* (PO), a single dose
Disseminated gonococcal infection	Ceftriaxone 1g, IM or intravenous (IV), per day, completing at least seven days of treatment plus Azithromycin 500mg, two pills, PO, a single dose
Chlamydia or mycoplasma infection	Azithromycin 500mg, two tablets, PO, a single dose, or Doxycycline 100mg, PO, twice a day, for seven days (except pregnant women)

1.2.1.3 Brazilian Protocol for Sexually Transmitted Infections (2020): Pelvic Inflammatory Disease

The main recommendations from the Brazilian protocol for the management of pelvic inflammatory disease are summarized below[18]:

- Treatment must start immediately, aiming at avoiding late complications, such as infertility, ectopic pregnancy, and chronic pelvic pain.
- Treatment of other common pelvic pain causes (ectopic pregnancy, acute appendicitis, ovarian cyst, and functional pain) is unlikely to be harmed by antimicrobial therapy for pelvic inflammatory disease. In addition to antibiotics, analgesic and anti-inflammatory drugs can be used for decreasing symptomatology.
- Outpatient treatment applies to women that present light clinical pictures without signs of pelvic peritonitis.
- Pregnant women with pelvic inflammatory disease have a high risk of miscarriage, chorioamnionitis, and premature delivery, and they must be hospitalized and undergo intravenous broad-spectrum antibiotic treatment immediately. Doxycycline and quinolones are a contraindication during pregnancy.

Table 31. Treatment Regimens for Pelvic Inflammatory Disease

Treatment	First option	Second option	Third option
Outpatient	Ceftriaxone 500mg, intramuscular (IM), single dose plus Doxycycline 100mg, 1 pill, *per os* (PO), twice/day, for 14 days plus Metronidazole 250mg, 2 pills, PO, twice/day, for 14 days	Cefotaxime 500mg, IM, single dose plus Doxycycline 100mg, 1 pill, PO, twice/day, for 14 days plus Metronidazole 250mg, two pills, PO, twice/day, for 14 days	-
Hospital	Ceftriaxone 1g, intravenous (IV), once/day, for 14 days plus Doxycycline 100mg, 1 pill, PO, twice/day, for 14 days	Clindamycin 900mg, IV, three times/day, for 14 days plus Gentamicin (IV or IM): 3-5mg/kg, once/day for 14 days	Ampicillin/sulbactam 3g, IV, each 6 hours, for 14 days plus Doxycycline 100mg, one pill, PO, twice/day, for 14 days

	plus Metronidazole 400mg, IV, each 12 hours		

1.2.1.4 Australian STI Management Guidelines for use in Primary Care; Pelvic Inflammatory Disease (2021)

These guidelines published in 2022 were developed by the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) and endorsed by the Blood Borne Viruses and Sexually Transmitted Infections Standing Committee (BBVSS)[20].

The main recommendations related to pelvic inflammatory disease are summarized below.

Primary treatment choices: in the case of an infection, the recommended treatments differ depending on the severity.

For Mild to Moderate Cases (Outpatient Treatment):

- Ceftriaxone: 500 mg administered intramuscularly with 2 mL of 1% lignocaine, or 500 mg given intravenously as a single dose.
- In addition to Ceftriaxone:
    - Metronidazole: Take 400 mg orally twice daily for 14 days.
    - Doxycycline: Take 100 mg orally twice daily for 14 days.

For Severe Cases (Inpatient Treatment):

Inpatient treatment is necessary for severe cases, and the options are as follows:

- Ceftriaxone: Administer 2 g intravenously daily.
- Alternatively, Cefotaxime: Administer 2 g intravenously three times daily.
- Along with Ceftriaxone or Cefotaxime:
    - Azithromycin: Administer 500 mg intravenously daily.
    - Metronidazole: Administer 500 mg intravenously twice daily.

Treatment Recommendations:

- Commence treatment promptly based on a provisional diagnosis, without waiting for test results.
- For patients who are breastfeeding or may not comply with a doxycycline regimen, consider substituting with Azithromycin 1g as a single oral dose, followed by another dose one week later.

- Contemplate the removal of an intrauterine device (IUD) if there is no response to treatment within 48-72 hours. Weigh the decision in consideration of the risk of pregnancy and consider oral emergency contraception.
- Think about admitting the patient if:
    - The diagnosis is uncertain.
    - A surgical emergency cannot be ruled out.
    - There is suspicion or a confirmed diagnosis of a pelvic abscess.
    - The patient is severely ill or does not respond to outpatient management.
    - There is intolerance to oral therapy.
    - The patient is pregnant or lacks stable housing.

Other Immediate Measures:

- Advise the patient to abstain from sexual intercourse for one week following treatment or until symptoms improve.
- Provide rest and simple pain relief as needed, such as non-steroidal anti-inflammatory drugs or paracetamol.
- Implement contact tracing.
- Furnish the patient with an informational pamphlet.

1.2.2 North American Guidelines

1.2.2.1 AAFP - Vaginitis: Diagnosis and Treatment (2018)

The American Academy of Family Physicians (AAFP) published in 2018 a guidance on the diagnosis and treatment of vaginitis[15], with the levels of evidence as defined in table 31.

Table 32. AAFP Evidence Rating

Grade	Level of Evidence
A	Consistent, good-quality patient-oriented evidence
B	Inconsistent or limited-quality patient-oriented evidence
C	Consensus, disease-oriented evidence, usual practice, expert opinion, or case series.

The AAFP has issued the recommendations below[15]:

- Treatment of bacterial vaginosis is recommended for resolving symptoms, as well as reducing the risk of Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis, human immunodeficiency virus (HIV), and herpes simplex virus type 2 infections. Shifts in vaginal flora have been associated with increased risk of these infections, leading researchers to conclude that treatment of bacterial vaginosis may decrease susceptibility to these infections.
- **First-line therapy** includes seven-day courses of oral metronidazole (Flagyl), intravaginal metronidazole (Metrogel), or intravaginal clindamycin. No significant difference in effectiveness has been demonstrated among these regimens. Patient preference should be considered when choosing an agent.
- Physicians should explain potential adverse effects with each regimen, including a possible disulfiram-like reaction with alcohol consumption or gastrointestinal symptoms in persons taking oral metronidazole, or possible weakening of latex condoms with the use of topical therapies containing oil-based preparations.
- The U.S. Food and Drug Administration recently approved a single-dose oral therapy for bacterial vaginosis, secnidazole (Solosec), which will be available in 2018. The dosing involves one-time oral administration of a 2-g packet of granules mixed into applesauce, yogurt, or pudding. A primary adverse effect of this regimen is vulvovaginal candidiasis.
- **Bacterial Vaginosis in Pregnancy.** In the past, treatment for bacterial vaginosis during pregnancy was recommended to prevent preterm births. Further review of the evidence has demonstrated that antibiotic treatment does not prevent preterm birth for women with symptomatic or asymptomatic bacterial vaginosis.

Table 33. AAFP Clinical Recommendations for Bacterial Vaginosis

Clinical recommendation	Evidence rating
Symptoms alone cannot differentiate between the causes of vaginitis. Office-based or laboratory testing should be used with the history and physical examination findings to make the diagnosis.	**C**
Do not obtain culture for the diagnosis of bacterial vaginosis because it represents a polymicrobial infection.	**C**
Nucleic acid amplification testing is recommended for the diagnosis of trichomoniasis in symptomatic or high-risk women.	**C**

Treatment of bacterial vaginosis during pregnancy improves symptoms but does not reduce the risk of preterm birth.	**A**

Table 34. Treatment Regimen for Bacterial Vaginosis

Initial regimens	Alternative regimens	Pregnancy	Recurrence	Treatment of sex partners
Bacterial vaginosis				
Metronidazole (Flagyl), 500 mg orally twice daily for seven days* *or* Metronidazole 0.75% gel (Metrogel), one full applicator (5 g) intravaginally daily for five days *or* Clindamycin 2% cream, one full applicator (5 g) intravaginally at bedtime for seven days†	Tinidazole (Tindamax), 2 g orally once daily for two days *or* Tinidazole, 1 g orally once daily for five days *or* Clindamycin, 300 mg orally twice daily for seven days *or* Clindamycin (Cleocin Ovules), 100 mg intravaginally at bedtime for three days	Metronidazole, 500 mg orally twice daily for seven days	First recurrence: Retrial of same regimen *or* Trial of alternative initial regimen Multiple recurrences: Metronidazole 0.75% gel, intravaginally twice weekly for four to six months	Routine treatment of sex partners is not recommended

1.2.2.2 AAFP Pelvic Inflammatory Disease: Diagnosis, Management, and Prevention (2019)

The AAFP published in 2019 a guidance on the diagnosis, management, and treatment of pelvic inflammatory disease[17], with the levels of evidence as defined in table 31 above.

The main recommendations are listed below[17]:

- Empiric antibiotic treatment should be offered at the time of presentation to patients with PID symptoms (grade C).
- Women with mild to moderate PID may be treated in an outpatient setting without increased risk of sequelae (grade B).
- Patient-delivered or expedited partner therapy for STIs should be offered where legal to decrease rates of reinfection (Grade B).
- Annual screening for chlamydia and gonorrhea is recommended in all sexually active women younger than 25 years and any women who are at increased risk of STIs (grade B).

Table 35. Treatment Regimens for Pelvic Inflammatory Disease

Inpatient Treatment Regimens for Pelvic Inflammatory Disease
Recommended regimens
Cefotetan (Cefotan), 2 g IV every 12 hours *plus* Doxycycline, 100 mg orally or IV every 12 hours *OR* Cefoxitin, 2 g IV every six hours *plus* Doxycycline, 100 mg orally or IV every 12 hours *OR* Clindamycin, 900 mg IV every eight hours *plus* Gentamicin, loading dose of 2 mg per kg IV or IM, followed by a maintenance dosage of 1.5 mg per kg every eight hours. Single daily dosing of 3 to 5 mg per kg can be substituted
Alternative regimen
Ampicillin/sulbactam (Unasyn), 3 g IV every six hours *plus* Doxycycline, 100 mg orally or IV every 12 hours
Outpatient Treatment Regimens for Pelvic Inflammatory Disease
Ceftriaxone (Rocephin), 250 mg IM in a single dose *plus* Doxycycline, 100 mg orally twice a day for 14 days *with or without* Metronidazole (Flagyl), 500 mg orally twice a day for 14 days

OR Cefoxitin, 2 g IM, and probenecid, 1 g orally, administered concurrently in a single dose *plus* Doxycycline, 100 mg orally twice a day for 14 days *with or without* Metronidazole, 500 mg orally twice a day for 14 days *OR* Other parenteral cephalosporins: ceftizoxime (Cefizox) or cefotaxime (Claforan) *plus* Doxycycline, 100 mg orally twice a day for 14 days *with or without* Metronidazole, 500 mg orally twice a day for 14 days
CDC = Centers for Disease Control and Prevention; IM = intramuscularly; IV = intravenously

1.2.3 European Guidelines

1.2.3.1 British Association for Sexual Health and HIV National Guideline for the Management of Infection with *Mycoplasma genitalium* (2018)

This guideline is the first published by the British Association for sexual Health and HIV (BASHH) aimed to serve as a reference guide for the diagnosis and management of *Mycoplasma genitalium* in people aged 16 years and older[12].

Table 36. BASHH Grading Scheme for Recommendations.

Quality of evidence	
A	A body of evidence of high-quality meta-analyses, systematic reviews of and RCTs directly applicable to the target population
B	As above but relating to high quality case control or cohort studies with low risk of bias or confounding and high probability that a relationship is causal
C	As B but trials may have some flaws
D	Non-analytic evidence (e.g., case reports or series or expert opinion)
Strength of recommendation	
1	Strong
2	Weak

The British Association for Sexual Health and HIV National Guideline has issued the recommendations below:

Treatment regimens for uncomplicated infection:

- Doxycycline 100 mg two times daily for 7 days followed by azithromycin 1 g orally as a single dose then 500 mg orally once daily for 2 days (grade 1D)
- Moxifloxacin 400 mg orally once daily for 10 days (grade 1B)

Treatment regimens for complicated infection (PID, epididymo-orchitis):

- Moxifloxacin 400 mg orally once daily for 14 days (grade 1D)

Alternative treatment regimens:

- Doxycycline 100 mg two times daily for 7 days followed by pristinamycin 1 g orally four times daily for 10 days (grade 2C)
- Pristinamycin 1 g orally four times daily for 10 days (grade 2C)
- Doxycycline 100 mg orally twice daily for 14 days (grade 2C)
- Minocycline 100 mg orally twice daily for 14 days (grade 2D)
- All patients should attend for a test-of-cure five weeks (and no sooner than three weeks) after the start of treatment to ensure microbiological cure (grade 1D)

1.2.3.2 UK National Guideline for the Management of Infection with *Neisseria gonorrhoeae* (2018)

This 2018 guideline was commissioned and edited by the Clinical Effectiveness Group (CEG) of BASHH[10]. The grading scheme for recommendations is similar to the one outlined in table 35 above.

The UK National Clinical Guideline has issued the recommendations below[10]:

Indications for therapy:

1. Identification of intracellular Gram-negative diplococci on microscopy
2. A positive culture for N. gonorrhoeae
3. A confirmed positive NAAT for N. gonorrhoeae
4. Sexual partner of confirmed case of gonococcal infection

Patients should be advised to abstain from sexual intercourse until seven days after they and their partner(s) have completed treatment (Grade 1D).

Treatment of uncomplicated ano-genital and pharyngeal infection in adults

- When antimicrobial susceptibility is not known prior to treatment: Ceftriaxone 1 g intramuscularly as a single dose (Grade 1C)
- When antimicrobial susceptibility is known prior to treatment: Ciprofloxacin 500 mg orally as a single dose (Grade 1A)
- The following options have all been associated with treatment failure when used as monotherapy particularly when used for pharyngeal infection, therefore it is recommended to use dual therapy with azithromycin 2 g where possible (Grade 2C).
- Cefixime 400 mg orally as a single dose plus azithromycin 2 g orally (Grade 1B)
- Gentamicin 240 mg intramuscularly as a single dose plus azithromycin 2 g orally (Grade 1A)
- Spectinomycin 2 g intramuscularly as a single dose plus azithromycin 2 g orally (Grade 1B)
- Azithromycin 2 g as a single oral dose (Grade 1B)

Treatment of complicated infections

- **Gonococcal PID:** Ceftriaxone 1 g intramuscularly as a single dose in addition to the regimen chosen to treat PID.
- **Gonococcal epididymo-orchitis**: Ceftriaxone 1 g intramuscularly as a single dose in addition to the regimen chosen to treat epididymo-orchitis.

Pregnancy and breastfeeding

Pregnant and breastfeeding individuals should not be treated with quinolone or tetracycline antimicrobials.

Pregnancy does not diminish treatment efficacy.

- Ceftriaxone 1 g intramuscularly as a single dose (Grade 1A) or
- Spectinomycin 2 g intramuscularly as a single dose (Grade 1A)
- Azithromycin 2 g as a single oral dose (Grade 1B)

1.2.3.3 United Kingdom National Guideline for the Management of Pelvic Inflammatory Disease (2019 Interim Update)

This 2019 UK National Guideline offers recommendations on the diagnostic tests, treatment regimens and health promotion principles needed for the effective management of pelvic inflammatory disease (PID) in women aged 16 years or older, covering the management of the initial presentation, as well as how to reduce

transmission, complications, and future repeat infection[19]. The grading scheme for recommendations is similar to the one outlined in table 35 above.

The UK National Clinical Guideline has issued the recommendations below[19]:

- Rest is advised for those with severe disease. (Grade 1D)
- Appropriate analgesia should be provided. (Grade 1D)
- Intravenous therapy is recommended for patients with more severe clinical disease (Grade 1D) e.g., pyrexia > 38°C, clinical signs of tubo-ovarian abscess, signs of pelvic peritonitis.
- To avoid reinfection, patients should be advised to avoid oral or genital intercourse until they, and their partner(s), have completed their treatment (Grade 1D).
- A detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partner(s) should be provided, reinforced with clear and accurate written information (Grade 1D).
- Outpatient therapy is as effective as inpatient treatment for patients with clinically mild to moderate PID. Admission for parenteral therapy, observation, further investigation and/or possible surgical intervention should be considered in the following situations (Grade 1D):
    - a surgical emergency cannot be excluded
    - lack of response to oral therapy
    - clinically severe disease
    - presence of a tubo-ovarian abscess
    - intolerance to oral therapy
    - pregnancy
- All sexually active women who are potentially fertile should be offered a pregnancy test to exclude ectopic pregnancy (Grade 1D).

Outpatient Regimens

- **First Line Therapy:** IM ceftriaxone 1g single dose followed by oral doxycycline 100mg twice daily plus metronidazole 400mg twice daily for 14 days (Grade 1A)
- **Second Line Therapy:** oral ofloxacin 400mg twice daily plus oral metronidazole 400mg twice daily for 14 days (Grade 1A) or oral moxifloxacin 400mg once daily for 14 days (Grade 1A)

- Ofloxacin, levofloxacin and moxifloxacin are effective for the treatment of C. trachomatis. Quinolones (ofloxacin, levofloxacin and moxifloxacin) can cause disabling and potentially permanent side-effects involving tendons. muscles, joints and the nervous system, and are therefore only recommended as second line therapy except for the treatment of M genitalium associated PID where no alternative therapy is available. Quinolones are also not licensed for use in patients aged under 18.
- **Alternative Regimens:** intramuscular ceftriaxone 1g immediately, followed by azithromycin 1 g/week for 2 weeks (Grade 2B)

Inpatient Regimens

- i.v. ceftriaxone 2g daily plus i.v. doxycycline 100mg twice daily (oral doxycycline may be used if tolerated) followed by oral doxycycline 100mg twice daily plus oral metronidazole 400mg twice daily for a total of 14 days (Grade 1A)
- i.v. clindamycin 900mg 3 times daily plus i.v. gentamicin (2mg/kg loading dose) followed by 1.5mg/kg 3 times daily [a single daily dose of 7mg/kg may be substituted]) followed by either oral clindamycin 450mg 4 times daily or oral doxycycline 100mg twice daily plus oral metronidazole 400mg twice daily to complete 14 days (Grade 1A)
- Intravenous therapy should be continued until 24 hours after clinical improvement and then switched to oral (Grade 2D).

Alternative regimen:

- i.v. ofloxacin 400mg BD plus i.v. metronidazole 500mg TID for 14 days (Grade 1B)
- i.v. ciprofloxacin 200mg BD plus i.v. (or oral) doxycycline 100mg BD plus i.v. metronidazole 500mg TID for 14 days (Grade 1B)

Pregnancy and breastfeeding

- There are insufficient data from clinical trials to recommend a specific regimen and empirical therapy with agents effective against gonorrhea, C. trachomatis and anaerobic infections should be considered taking into account local antibiotic sensitivity patterns (e.g. i.v. ceftriaxone, i.v. erythromycin and i.v. metronidazole switching to oral therapy following clinical response and completing 2 weeks of treatment) (Grade 2D).

Follow Up

- Review at 72 hours is recommended for those with moderate or severe symptoms or signs (Grade 2D).

- Failure to improve suggests the need for further investigation, parenteral therapy and/or surgical intervention.
- Further review, either in clinic or by phone, 2-4 weeks after therapy is recommended (Grade 1D) to ensure:
    - adequate clinical response to treatment
    - compliance with oral antibiotics
    - screening and treatment of sexual contacts
    - awareness of the significance of PID and its sequelae
    - repeat pregnancy test, if clinically indicated
- The following are recommended if the initial test for *M. genitalium* is positive:
    - treatment with moxifloxacin. This agent currently has good microbiological activity against *M. genitalium* (Grade 1D)
    - repeat testing for *M. genitalium* following treatment to ensure microbiological clearance. Treatment failure following the use of any of the recommended regimens has been reported but is least likely following treatment with moxifloxacin. The optimal time for testing after starting treatment is not known but 4 weeks is recommended based on expert opinion (Grade 1D).

Partner Notification and Treatment of Sexual Partners

- Current male partners of women with PID should be contacted and offered health advice and screening for gonorrhea and *C. trachomatis* (Grade 1D).
- Other recent sexual partners may also be offered screening - tracing of contacts within a 6 month period since onset of symptoms is recommended but this time period may be influenced by the sexual history (Grade 2D).
- Because many cases of PID are not associated with gonorrhea, *C. trachomatis* or *M. genitalium*, broad spectrum empirical therapy should also be offered to male partners e.g., doxycycline 100mg twice daily for 1 week (Grade 2D).
- Partners should be advised to avoid oral or vaginal intercourse until they and the index patient have completed their treatment course (Grade 1D).

1.2.3.4 European Guideline on the Management of Syphilis (2020)

The 2020 European guideline published by the European Academy of Dermatology and Venereology is an update of the 2014 edition[21].

Table 37. Grading the Certainty of Evidence and Strength of Recommendations of European Guidelines

Grade	Quality of evidence
A	As high-quality evidence that comes from consistent results from well-performed randomized controlled trials (RCTs) or overwhelming evidence from another source (such as well-executed observational studies with consistent strong effects and exclusion of all potential sources of bias). Grade A implies confidence that the true effect lies close to the estimate of the effect.
B	Moderate-quality evidence from randomized trials that suffers from serious flaws in conduct, inconsistency, indirectness, imprecise estimates, reporting bias or some combination of these limitations, or from other study designs with specific strengths such as observational studies with consistent effects and exclusion of the majority of the potential sources of bias
C	Low-quality evidence from controlled trials with several serious limitations or observational studies with limited evidence on effects and exclusion of most potential sources of bias.
D	Evidence is based only on case studies, expert judgement or observational studies with inconsistent effects and a potential for substantial bias, such that there can be little confidence in the effect estimate.
Level	**Strength of recommendation**
1	Strong recommendation to do (or not do) something, where benefits clearly outweigh risks (or vice versa) for most, if not all, patients. Most clinicians and patients would want to follow a strong recommendation unless there is a clear rationale for an alternative approach. A strong recommendation usually starts with the standard wording: 'We recommend …' or 'It is recommended …'
2	Weaker or conditional recommendation, where the risks and benefits are more closely balanced or are more uncertain. Alternative approaches or strategies may be reasonable depending on the individual patient's circumstances, preferences, and values. A weak or conditional

	recommendation usually starts with the standard wording: 'We suggest…' or 'It is suggested…'

The European Guideline has issued the recommendations below[21]:

Early syphilis (Primary, Secondary and Early latent, i.e., acquired <1 year previously)

- **First-line therapy option:**

  BPG 2.4 million units intramuscularly (IM), given as one injection of 2.4 million units or two separate injections of 1.2 million units in each buttock, on day 1 (1, B)

- **Second-line therapy option:**

  Procaine penicillin 600 000 units IM daily for 10–14 days, i.e., if BPG is not available (1, C)

- **Bleeding disorders:**

  Ceftriaxone 1g intravenously (IV) in a single daily dose for 10 days (1, C)

  Doxycycline 200 mg daily (either 100 mg twice daily or as a single 200 mg dose) orally for 14 days (1, C)

- **Penicillin allergy or parenteral treatment refused**

  Doxycycline 200 mg daily (either 100 mg twice daily or as a single 200 mg dose) orally for 14 days (1, C)

  Desensitization to penicillin is an option but not possible in many settings and labor intensive.

Late latent (i.e., acquired ≥ 1 year previously or of unknown duration), cardiovascular and gummatous syphilis

- **First-line therapy option:**

  BPG 2.4 million units IM, given as one injection of 2.4 million units or two separate injections of 1.2 million units in each buttock, on day 1, 8 and 15 (1, C)

- **Second-line therapy option:**

  Procaine penicillin 600 000 units IM daily for 17–21 days, i.e., if BPG is not available (1, C).

  Doxycycline 200 mg daily (either 100 mg twice daily or as a single 200 mg dose) orally for 21–28 days (2, D)

Neurosyphilis, ocular and auricular syphilis

- Regimens that achieve treponemicidal levels of an antibiotic in the CSF should be the treatment of choice: IV therapy is the best option

- First-line therapy option: Benzyl penicillin 18–24 million units IV daily, as 3–4 million units every 4 h for 10–14 days (1, C)
- Second-line therapy option If hospitalization and IV benzyl penicillin is impossible.
  Ceftriaxone 1–2 g IV in a single daily dose for 10–14 days (1, C)
  Procaine penicillin 1.2–2.4 million units IM daily AND probenecid 500 mg four times daily, both for 10–14 days (1, C)

Pregnant woman:

- **First-line option for treatment of early syphilis (i.e., acquired <1 year previously):** BPG 2.4 million units IM single dose (or 1.2 million units in each buttock) (1, B)
- **Second-line therapy option:** Procaine penicillin 600 000 units IM daily for 10–14 days, i.e., if BPG is not available (1, C).

Penicillin allergy: Desensitization to penicillin followed by the first-line regimen (1, C)

1.2.3.5 European Guideline on the Management of *Mycoplasma genitalium* Infections (2021)

This clinical guideline was also published by the European Academy of Dermatology and Venereology in 2021 (evidence grading in table 36 above)[13]. The main recommendations are summarized in table 37:

Table 38. Recommendations for the Treatment of Mycoplasma genitalium Infections

RECOMMENDATIONS	GRADE
MANAGEMENT OF PATIENTS	
Patients with M. genitalium infection should abstain from unprotected sexual contact until they and their partners have completed treatment, their symptoms have resolved, and their test of cure (TOC) is negative	1D
Patients with M. genitalium infection (and their sexual contacts) should be given verbal and written information about the infection, including details about transmission, prevention, and complications.	1D
Patients with M. genitalium infection should be screened for other STIs, including C. trachomatis, N. gonorrhoeae, syphilis, and HIV, plus T. vaginalis where appropriate	1D
M. genitalium infections during pregnancy may be treated with azithromycin or pristinamycin. Treatment may be postponed until	1D

after delivery, but the neonate should be observed for signs of infection, primarily conjunctivitis and respiratory tract infection	
INDICATIONS FOR THERAPY	
Detection of M. genitalium-specific nucleic acid in a clinical specimen	1B
Current partners of M. genitalium-positive patients should be treated with the same antimicrobial as the index patient	1B
THERAPY	
Uncomplicated M. genitalium infection in the absence of macrolide resistance mutations or resistance testing	
Azithromycin 500 mg on day one, then 250 mg od days 2-5 (oral)	1B
Josamycin 500 mg 3 times daily for 10 days (oral)	2C
Uncomplicated M. genitalium infection in the presence of macrolide resistance mutations	
Moxifloxacin 400 mg od for 7 days (oral)	1B
Second-line treatment for uncomplicated persistent M. genitalium infection after azithromycin treatment	
Moxifloxacin 400 mg od for 7 days (oral)	1B
Third-line treatment for persistent M. genitalium infection after azithromycin and moxifloxacin treatment	
Pristinamycin 1 g four times daily for 10 days (oral), 75% cure	1B
Minocycline 100 mg two times daily for 14 days (oral), 70% cure	2B
Doxycycline 100 mg two times daily for 14 days (oral), 40% cure	2B
Complicated M. genitalium infection (PID, epididymitis)	
Moxifloxacin 400 mg od for 14 days (oral)	1C
Partner notification	
Current partner(s) should always be tested and treated with the same antimicrobial as the index patient	2B
FOLLOW-UP AND TEST OF CURE	
A TOC should be considered in all patients	2C
TOC samples should be collected no earlier than three weeks after completion of treatment	1B

1.2.3.6 European Guideline for the Diagnosis and Treatment of Gonorrhea in Adults (2020)

This guideline is an updated version of the 2012 European guideline for the management of gonorrhea in adults[11]. The grading scheme adopted for the recommendations is similar to the one detailed in table 36 above.

The main recommendations are summarized below[11]:

- Patients with gonorrhea should be advised to abstain from sexual contact (or if this is not possible to consistently use barrier contraception) for 14 days (seven days if ceftriaxone monotherapy) after they and their sexual partners have completed ceftriaxone plus azithromycin dual treatment and their symptoms have resolved [2D]. This is to limit possible re-exposure in the presence of residual azithromycin.
- Patients (and their sexual partners) should be given information (verbal and written) about their infection, including details about transmission, prevention, complications, and treatment [1D].
- Patients with verified gonorrhea (and their sexual contacts) are recommended to be offered testing for other STIs, e.g. including C. trachomatis, mycoplasma genitalium (only in symptomatic patients and always including macrolide resistance testing), syphilis, HBV, HCV, and HIV [1C].

Recommended treatment for uncomplicated N. gonorrhoeae infections of the urethra, cervix and rectum in adults and adolescents when the antimicrobial susceptibility of the infection is unknown

- Ceftriaxone 1 g intramuscularly (IM) as a single dose together with azithromycin 2 g as a single oral dose [1C]
- If gastrointestinal side effects are anticipated: ceftriaxone 1 g IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6–12h later may be used to limit gastrointestinal side effects

  OR

- Ceftriaxone 1 g IM as a single dose [2C]

NOTE: Only recommended in settings where:

i. comprehensive, recent and quality-assured local in vitro ceftriaxone susceptibility testing has shown lack of ceftriaxone resistance;

ii. TOC is mandatory;

iii. the patient is considered very likely to return for TOC;

iv. doxycycline 100 mg oral dose twice daily for 7 days is administered at the same time to cover any concomitant C. trachomatis infection if C. trachomatis infection has not been excluded by NAAT.

In other settings, ceftriaxone 1 g IM monotherapy is only an alternative option if azithromycin is not available, or patient is unable to take oral medication.

Treatment when patient has history of severe hypersensitivity (e.g., anaphylaxis) to any b-lactam antimicrobial (penicillins, cephalosporins, monobactams or carbapenems

Recommended treatment:

- Spectinomycin 2 g IM as a single dose [1B] together with azithromycin 2 g as a single oral dose [1C]
- If gastrointestinal side effects are anticipated: spectinomycin 2 g IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6-12 h later may be used

Alternative treatment:

- Ciprofloxacin 500 mg as a single oral dose [1B]
- Gentamicin 240 mg IM as a single dose together with azithromycin 2 g as a single oral dose [1B]
- If gastrointestinal side effects are anticipated: gentamicin 240 mg IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6–12 h later may be used.

Treatment when administration of an intramuscular injection is contraindicated or refused

Recommended treatment:

- Cefixime 400 mg as a single oral dose together with azithromycin 2 g as a single oral dose [1B]
- If gastrointestinal side effects are anticipated: cefixime 400 mg single oral dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6-12 h later may be used

Alternative treatment:

- Ciprofloxacin 500 mg as a single oral dose [1B].

Sexual contact notification and management of sex contact(s)

- Sexual contact notification should be performed and documented by appropriately trained professionals at the time of diagnosis to prevent reinfection and reduce onwards transmission [1B]
- Sexual contacts should be contacted and offered (and encouraged to have) testing for gonorrhea (and other STIs) together with antimicrobial treatment if appropriate (i.e. if positive N. gonorrhoeae test or clinician considers contacts will not return for treatment after testing results are available) and receive counseling for gonorrhea and other STIs [1D]
- All sexual contact(s) within the preceding 3 months of onset of symptoms or diagnosis should be tested and treated if positive [2D].

1.2.3.7 European (IUSTI/WHO) International Union against sexually transmitted infections (IUSTI) World Health Organization (WHO) guideline on the management of vaginal discharge (2018)

The 2020 IUTSI/WHO Guideline[16] used a grading scheme for the recommendations similar to the one outlined in table 36 above.

The main recommendations are summarized below[16]:

Bacterial vaginosis (BV)

- Recommend 5–7 days of topical or oral metronidazole or seven days of intravaginal clindamycin as first line for uncomplicated BV in women depending on personal choice and circumstances (Grade 1, quality of evidence: Grade A).

Recommended regimens for BV:

- Metronidazole 400–500 mg orally twice daily for 5–7 days

  OR
- Intravaginal metronidazole gel (0.75%) once daily for five days

  OR
- Intravaginal clindamycin cream (2%) once daily for seven days

Alternative regimens for BV:

- Metronidazole 2 g orally in a single dose

  OR
- Tinidazole 2 g orally in a single dose

  OR

- Tinidazole 1 g orally for five days

  OR

- Clindamycin 300 mg orally twice daily for seven days

  OR

- Dequalinium chloride 10 mg vaginal tablet one daily for six days

Recurrent BV

- Recommends current best treatment for persistent and recurrent BV in women is intravaginal metronidazole (Grade 2, quality of evidence: Grade B).
- Recommends that the current best treatment for BV in pregnant women is clindamycin (Grade 2, quality of evidence: Grade C).

Management of sexual partners

- Recommends that the current advice for women diagnosed with BV is that male sexual partners do not require treatment. Female partners may be treated if they have BV (Grade 2, quality of evidence: Grade B).

1.2.3.8 European Guideline for the Management of Chancroid (2017)

The main recommendations from the 2017 European guideline for the management of chancroid[22] are summarized below.

Table 39. Grading the Certainty of Evidence and Strength of Recommendations of European Guidelines

Level	Quality of Evidence
Ia	Evidence obtained from meta-analysis of randomized controlled trial
Ib	Evidence obtained from at least one randomized controlled trial
IIa	Evidence obtained from at least one well-designed study without randomization
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental descriptive studies such as comparative studies, correlation studies and case–control studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities
Grading	**Strength of Recommendation**

A	Requires at least one randomized controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation
B	Requires availability of well-conducted clinical studies but no randomized clinical trials on the topic of recommendation
C	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.

- The antibiotics treatment should be based on local epidemiology and antibiotic susceptibility patterns.

Several antibiotic regimens have been recommended for confirmed cases of chancroid:

- First line:
    - Ceftriaxone as a single intramuscular injection of 250 mg (Ib, A) or
    - Azithromycin, as a single 1 g oral dose, (Ib, A)
- Second line:
    - Ciprofloxacin 500 mg orally twice a day for three days (Ib, B), or
    - Erythromycin orally 500 mg four times a day for seven days (Ib, B)

Adjunctive therapy

- Patients with fluctuant buboes will experience symptomatic relief if these are emptied. Needle aspiration is effective but may need to be repeated. Incision and drainage is an alternative but some authorities believe that it may lead to sinus formation. Antibiotic cover is recommended if this is done (IV, C).
- Sexual partners of patients who have chancroid should be examined and treated, regardless of whether symptoms of the disease are present, if they had sexual contact with the patient in the 10 days preceding the patient's onset of symptoms (IV, C).

1.2.3.9 European Guideline for the Management of Pelvic Inflammatory Disease (2017)

The main recommendations from the 2017 European guideline for the management of pelvic inflammatory disease[23] are summarized below (grading of evidence as table 38 above).

Information, explanation, and advice for the patient

- Patients should be advised to avoid unprotected intercourse until they, and their partner(s), have completed treatment and symptoms have resolved (Evidence level IV, C).
- A detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partner(s) should be provided, reinforced with clear and accurate written information. Appropriate information should include:
    - fertility is usually well preserved in women with first-episode PID who receive prompt appropriate antimicrobial therapy
    - the risk of impaired fertility increases significantly with each subsequent episode of PID (approximately) doubling with each new presentation
    - the risk of impaired fertility is increased in clinically more severe PID
    - chronic pelvic pain of varying severity affects around 30% of women following PID
    - PID increases the relative risk of a subsequent pregnancy being an ectopic, but the absolute risk of ectopic pregnancy remains low at around 1%
- Although laparoscopic division of hepatic adhesions has been performed in women with perihepatitis, there is insufficient clinical trial evidence to make specific recommendations for treatment beyond antibiotic therapy.
- Broad spectrum antibiotic therapy is required to cover N. gonorrhoeae, C. trachomatis and anaerobic infection. It is also desirable to include microbiological cover for other possible pathogens (e.g. M. genitalium, streptococci, staphylococci, E. coli, H. influenzae).
- The choice of an appropriate treatment regimen may be influenced by:
    - local antimicrobial sensitivity patterns
    - local epidemiology of specific infections in this setting
    - cost
    - patient preference and compliance
    - severity of disease

General measures include:

- Rest is advised for those with severe disease (Evidence level IV, C)
- If there is a possibility that the patient could be pregnant, a pregnancy test should be performed (Evidence level IV, C)
- Appropriate analgesia should be provided (Evidence level IV, C)
- Admission for parenteral therapy, observation, further investigation and/or possible surgical intervention should be considered in the following situations (Evidence level IV, C):
    - diagnostic uncertainty
    - clinical failure with oral therapy
    - severe symptoms or signs
    - presence of a tuboovarian abscess
    - inability to tolerate an oral regimen
    - pregnancy
- In inpatients the treatment response can be monitored by changes in C-reactive protein and white cell count. In severe cases and cases with failure of the initial treatment, tuboovarian abscess should be excluded by vaginal ultrasonography, CT, or MRI.
- All patients should be offered testing for Chlamydia, gonorrhea, M. genitalium, syphilis and HIV (Evidence level IV, C).
- It is likely that delaying treatment increases the risk of long-term sequelae such as ectopic pregnancy, infertility, and pelvic pain. Because of this, and the lack of definitive diagnostic criteria, a low threshold for empiric treatment of PID is recommended (Evidence level IV, C).

Recommended regimens

Choice of treatment regimen should be influenced by the following:

- Mild and moderate cases should be treated as outpatients with oral therapy (Evidence level Ib, A).
- Intravenous therapy, when given, should be continued until 24 h after clinical improvement and then switched to oral (Evidence level IV, C).
- Dosage recommendations may need to be adjusted depending on local licensing regulations and the availability of drug formulations, e.g., metronidazole may be dosed at 400 or 500 mg.

- The optimal duration of treatment is not known but most clinical trials report a response to 10–14 days of therapy.

No difference in efficacy has been demonstrated between the recommended regimens.

Outpatient regimens

- i.m. ceftriaxone 500 mg single dose followed by oral doxycycline 100 mg twice daily plus metronidazole 500 mg twice daily for 14 days (Evidence level Ia, A)
- oral ofloxacin 400 mg twice daily plus oral metronidazole 500 mg twice daily for 14 days (ofloxacin may be replaced by levofloxacin 500 mg once daily) (Evidence level Ib, A)
- oral moxifloxacin 400 mg once daily for 14 days (Evidence level Ia, A)

Inpatient regimens

- i.v./i.m. ceftriaxone 1 g once daily plus i.v. doxycycline 100 mg twice daily (oral doxycycline may be used if tolerated)

  followed by

- oral doxycycline 100 mg twice daily plus oral metronidazole 500 mg twice daily to complete 14 days (Evidence level Ia, A)
- i.v. clindamycin 900 mg three times daily plus i.m./i.v. gentamicin (3–6 mg/kg as a single daily dose with renal monitoring) followed by either
- (oral clindamycin 450 mg four times daily to complete 14 days) or (oral doxycycline 100mg twice daily plus oral metronidazole 500 mg twice daily to complete 14 days) (Evidence level Ia, A)

Alternative regimens

The evidence for alternative regimens is less robust than the regimens above:

- i.v. ofloxacin 400 mg twice daily plus i.v. metronidazole 500 mg three times daily for 14 days (Evidence level Ib, A)
- i.m. ceftriaxone 500 mg single dose plus oral azithromycin 1 g single dose followed by a second dose of oral azithromycin 1 g after one week (Evidence level Ib, A)

Partner notification

- Current partners of women with PID should be contacted and offered health advice and screening for gonorrhea and Chlamydia (and M. genitalium if the index patient is infected). Other recent sexual partners may also be offered screening – tracing of contacts within a six-month period of onset of

symptoms is recommended but this time period is not evidence based and may be influenced by the sexual history, available resources or local practice.

- Because many cases of PID are not associated with gonorrhea, Chlamydia or M. genitalium, broad spectrum empirical therapy should also be offered to male partners, e.g., doxycycline 100 mg twice daily for one week.
- Partners should be advised to avoid unprotected intercourse until they and their partner have completed the treatment course.

Section 2.0 Drug Therapy in Bacterial Genital Tract Infections

This section comprises four subsections: the first contains the newly recommended drugs, the second covers drug modifications, the third outlines the drugs to delist due to withdrawal from the market among others and the fourth tackles other drugs approved by FDA/EMA but not yet approved by SFDA.

2.1 Additions

No new drugs have been approved by the SFDA for the treatment of Bacterial Genital Tract Infections since May 2020.

2.2 Modifications

The following modifications and adjustments have been implemented since the 2020 report:

Table 40. Prescribing Edits (PE) Modifications for Bacterial Genital Tract Infections Medications

DRUGS	PE MODIFICATIONS
Azithromycin	Remove “Prior Authorization (PA)” Add “Step Therapy (ST)”: effective as alternative for treating primary, secondary syphilis, and early latent syphilis, should not be used as first-line treatment for syphilis and used with caution only when treatment with penicillin or doxycycline is not feasible. azithromycin should not be used in MSM, persons with HIV, or pregnant women, and this should be confirmed by the prescriber

Levofloxacin	Add AGE: not recommended for children < 18 years of age unless there are no suitable alternative antibiotics due to potential for musculoskeletal and joint-related side effects

2.3 Delisting

No medications have been withdrawn or are no longer recommended for the treatment of Bacterial Genital Tract Infections since May 2020.

2.4 Other Drugs

Clindamycin Phosphate (Xaciato®) vaginal gel
Xaciato® was approved by the FDA in December 2021. It is a lincosamide antibacterial indicated for the treatment of bacterial vaginosis in female patients 12 years of age and older. It is usually administered as one applicatorful (5 g of gel containing 100 mg of clindamycin) once intravaginally as a single dose at any time of the day[24].

Section 3.0 Key Recommendations Synthesis

- **Prevention of STIs:**
    - HPV vaccination is recommended up to age 26 for those not previously vaccinated at ages 11 or 12.
    - Administer the HBV vaccination series to all adolescents and young adults who missed it during childhood.
    - Offer the HAV vaccination series to adolescents and young adults, especially those who did not receive it in childhood[6].
- Treatment for **chancroid** include azithromycin, ceftriaxone, ciprofloxacin and erythromycin base.
    - Azithromycin and ceftriaxone offer the advantage of single-dose therapy.
    - Ciprofloxacin presents a low risk to the fetus during pregnancy but has potential for toxicity during breastfeeding[6, 7]
- **Granuloma Inguinale (Donovanosis):** it is recommended to give azithromycin as a first-line therapy.
    - Alternative regimens are doxycycline, erythromycin base and trimethoprim-sulfamethoxazole.
    - Pregnant and lactating women with granuloma inguinale should be treated with a macrolide regimen (erythromycin or azithromycin) rather than doxycycline (associated with teeth discoloration[6].
- Recommended treatment regimens for primary and secondary syphilis consists of benzathine penicillin G given IM in a single dose as opposed to **three doses of Benzathin G at 1-week interval from each other for late latent syphilis and tertiary syphilis.** This drug is used for both children and adults with corresponding doses. In case of pregnancy, pregnant women with primary or secondary syphilis who are allergic to penicillin should be desensitized and treated with penicillin G[6, 7].
- Recommended regiment for **nongonococcal urethritis** consists of doxycycline with alternative being azithromycin. Usually, it is always considered to check for compliance with medication whenever a patient presents with recurrent urethritis because it could be the cause of mistreatment. Once this has been ruled out, alternative treatment options can be considered[6].
- Presumptive treatment for **cervicitis** caused by Chlamydia and Gonorrhea is recommended for women at increased risk (e.g., those under 25, those with a

new or high-risk sex partner, or if follow-up isn't possible or testing isn't available). In case treatment for cervicitis is considered, options include doxycycline as first line and azithromycin as an alternative treatment[6].

  - For women at lower risk for STIs, deferring treatment until diagnostic test results are available is an option.
  - If treatment is deferred and Chlamydia and Gonorrhea tests are negative, a follow-up visit to check cervicitis resolution can be considered[6].

- **Chlamydial infections** should be treated on the spot to prevent adverse reproductive health complications and continued sexual transmission. It is also essential to treat sexual partners and pregnant women to prevent any further spread of the infection. Treatment options for adults include doxycycline and alternatives could be azithromycin and levofloxacin. Doxycycline is contraindicated during the second and third trimesters of pregnancy because of the risk for tooth discoloration. Hence, pregnant women should be treated with azithromycin preferably[6].
- **Chlamydial infections** for neonates and infants should be treated with erythromycin base or ethyl succinate. For children <45 kg: Erythromycin base or ethyl succinate are considered. For children ≥45 kg, consider azithromycin or doxycycline treatment[6].
- For **gonococcal infections** of the cervix, urethra or rectum among adolescents and adults, ceftriaxone if the preferred regimen. In case ceftriaxone is not available, gentamicin plus azithromycin can be used or cefixime.
  - Provide immediate treatment for individuals with confirmed urethral discharge to address N. gonorrhoeae and C. trachomatis infections on the same day.
  - When dealing with patients suspected of treatment failure for certain infections, the initial treatment regimen (ceftriaxone 500 mg IM) should be administered again, with the inclusion of doxycycline if chlamydia infection is also suspected. This is because reinfections are more common than actual treatment failures.
  - Pregnant women should be treated with ceftriaxone[6, 7, 10, 11].
- Two-stage therapy approaches, ideally using resistance-guided therapy, are recommended for treatment of **Mycoplasma Genitalium.** If patients are macrolide sensitive, recommend doxycycline therapy followed by azithromycin. In case patients are macrolide resistant, doxycycline therapy followed by moxifloxacin is recommended. Third-line treatment for persistent

M. genitalium infection after azithromycin and moxifloxacin treatment include pristinamycin and minocycline[6].

- Treatment for **BV** is recommended for women with symptoms. Recommended regimens include metronidazole oral and intravaginal as well as clindamycin intravaginal. Alternatives to those regimens are clindamycin oral, oral secnidazole and oral tinidazole. Suggest treating for bacterial vaginosis if vaginal discharge is present (for example, tenacious or thin) or based on the results of microscopy, if available [6, 7, 15, 16].
- The use of probiotics as an adjunctive or replacement therapy in women with **BV** is not currently recommended. The use of high-dose vitamin D supplementation among symptomatic women with BV as was not associated with a decrease in BV recurrence[14].
- Physicians should explain potential adverse effects with oral metronidazole use for **BV,** including a possible disulfiram-like reaction with alcohol consumption or gastrointestinal symptoms[15,].
- **PID** treatment regimens should provide empiric, broad-spectrum coverage of likely pathogens. All regimens used to treat PID should also be effective against *N. gonorrhoeae* and *C. trachomatis* because negative endocervical screening for these organisms does not rule out upper genital tract infection.

Recommended parenteral treatment regimens include:

  - Ceftriaxone plus doxycycline plus metronidazole
  - Cefotetan plus doxycycline
  - Cefoxitin plus doxycycline

Alternative parenteral regimens include:

  - Ampicillin-sulbactam plus doxycycline
  - Clindamycin plus gentamicin

Recommended IM/oral treatment regimens include:

  - Ceftriaxone plus doxycycline plus metronidazole
  - Cefoxitin and probenecid plus doxycycline with metronidazole
  - Other parenteral third-generation cephalosporin (ceftizoxime or cefotaxime) plus doxycycline with metronidazole[6, 17, 18, 19].

- For **acute epididymitis** most likely caused by chlamydia or gonorrhea: Ceftriaxone IM in a single dose plus doxycycline. For acute epididymitis most likely caused by chlamydia, gonorrhea, or enteric organisms (men who practice insertive anal sex): Ceftriaxone IM in a single dose plus levofloxacin.

For acute epididymitis most likely caused by enteric organisms only: Levofloxacin monotherapy[6].

- Treating sexual partners is essential to prevent the spread of chancroid, urethritis, cervicitis, chlamydial infections, gonococcal infections, Mycoplasma Genitalium, ensure proper care, and reduce the risk of reinfection. It is a crucial aspect of comprehensive disease management and public health. For BV, treatment of sexual partner is not recommended. For PID, the most recent sexual partner (<60 days) should be treated[6].

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Bacterial Genital Tract Infections report** and aims to provide recommendations to aid in the management of Bacterial Genital Tract Infections. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with Bacterial Genital Tract Infections. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

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Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

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. Bacterial Genital Tract Infections Scope

<table>
<tr><th>Section</th><th>Rationale/Updates</th></tr>
<tr><td>Section 1.1
CDC STI treatment guidelines (2021)[6]</td><td>
Missing recommendations:
Primary prevention:
Primary prevention and anticipatory guidance for recognizing symptoms and behaviors associated with STIs are strategies that should be incorporated into all types of health care visits for adolescents and young adults. The following recommendations for primary prevention of STIs (i.e., vaccination and counseling) are based on published clinical guidelines for sexually active adolescents and young adults from federal agencies and medical professional organizations.
o HPV vaccination is recommended through age 26 years for those not vaccinated previously at the routine age of 11 or 12 years
o The HBV vaccination series is recommended for all adolescents and young adults who have not previously received the universal HBV vaccine series during childhood (12).
o The HAV vaccination series should be offered to adolescents and young adults as well as those who have not previously received the universal HAV vaccine series during childhood
o Medical providers who care for adolescents and young adults should integrate sexuality education into clinical practice. Health care providers should counsel adolescents about the sexual behaviors that are associated with risk for acquiring STIs and should educate patients regarding evidence-based prevention strategies, which includes a discussion about abstinence and other risk-reduction behaviors (e.g., consistent and correct condom use and reduction in the number of sex partners including concurrent partners). Interactive counseling approaches (e.g., patient-centered counseling and motivational interviewing) are effective STI and HIV prevention strategies and are recommended by USPSTF. Educational materials (e.g., handouts, pamphlets, and videos) can reinforce office-based educational efforts.

Chancroid:
<table>
<tr><th>Recommended Regimens for Chancroid</th></tr>
<tr><td>Azithromycin 1 g orally in a single dose</td></tr>
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or
Ceftriaxone 250 mg IM in a single dose
or
Ciprofloxacin 500 mg orally 2 times/day for 3 days
or
Erythromycin base 500 mg orally 3 times/day for 7 days

- Azithromycin and ceftriaxone offer the advantage of single-dose therapy. Worldwide, several isolates with intermediate resistance to either ciprofloxacin or erythromycin have been reported. However, because cultures are not routinely performed, and chancroid is uncommon, data are limited regarding prevalence of *H. ducreyi* antimicrobial resistance.
- Patients should be reexamined 3–7 days after therapy initiation. If treatment is successful, ulcers usually improve symptomatically within 3 days and objectively within 7 days after therapy. If no clinical improvement is evident, the clinician should consider whether the diagnosis is correct, another STI is present, the patient has HIV infection, the treatment was not used as instructed, or the *H. ducreyi* strain causing the infection is resistant to the prescribed antimicrobial.
- The time required for complete healing depends on the size of the ulcer; large ulcers might require >2 weeks. In addition, healing can be slower for uncircumcised men who have ulcers under the foreskin. Clinical resolution of fluctuant lymphadenopathy is slower than that of ulcers and might require needle aspiration or incision and drainage, despite otherwise successful therapy.
- Regardless of whether disease symptoms are present, sex partners of patients with chancroid should be examined and treated if they had sexual contact with the patient during the 10 days preceding the patient's symptom onset.
- Data indicate ciprofloxacin presents a low risk to the fetus during pregnancy but has potential for toxicity during breastfeeding. Alternative drugs should be used if the patient

is pregnant or lactating. No adverse effects of chancroid on pregnancy outcome have been reported.

Granuloma Inguinale (Donovanosis)

- Multiple antimicrobial regimens have been effective; however, only a limited number of controlled trials have been published.
- Treatment has been reported to halt progression of lesions, and healing typically proceeds inward from the ulcer margins.
- Prolonged therapy is usually required to permit granulation and reepithelialization of the ulcers. Relapse can occur 6–18 months after apparently effective therapy.

Recommended Regimen for Granuloma Inguinale (Donovanosis)
Azithromycin 1 g orally once/week or 500 mg daily for >3 weeks and until all lesions have completely healed
Alternative Regimens
Doxycycline 100 mg orally 2 times/day for at least 3 weeks and until all lesions have completely healed
or
Erythromycin base 500 mg orally 4 times/day for >3 weeks and until all lesions have completely healed
or
Trimethoprim-sulfamethoxazole one double-strength (160 mg/800 mg) tablet orally 2 time/day for >3 weeks and until all lesions have completely healed

- The addition of another antibiotic to these regimens can be considered if improvement is not evident within the first few days of therapy.
- Persons who have had sexual contact with a patient who has granuloma inguinale within the 60 days before onset of the patient's symptoms should be examined and offered therapy. However, the value of empiric therapy in the absence of clinical signs and

symptoms has not been established.

- Use of doxycycline in pregnancy might be associated with discoloration of teeth; however, the risk is not well defined. Doxycycline is compatible with breastfeeding. Sulfonamides can be associated with neonatal kernicterus among those with glucose-6-phospate dehydrogenase deficiency and should be avoided during the third trimester and while breastfeeding. For these reasons, pregnant and lactating women with granuloma inguinale should be treated with a macrolide regimen (erythromycin or azithromycin).

Syphilis

- Parenteral penicillin G has been used effectively for achieving clinical resolution (i.e., the healing of lesions and prevention of sexual transmission) and for preventing late sequelae. However, no comparative trials have been conducted to guide selection of an optimal penicillin regimen. Substantially fewer data are available for nonpenicillin regimens.

Recommended Regimen for Primary and Secondary Syphilis*
Among Adults

Benzathine penicillin G 2.4 million units IM in a single dose

* Recommendations for treating syphilis among persons with HIV infection and pregnant women are discussed elsewhere in this report (see Syphilis Among Persons with HIV Infection; Syphilis During Pregnancy).

Available data demonstrate that use of additional doses of benzathine penicillin G, amoxicillin, or other antibiotics do not enhance efficacy of this recommended regimen when used to treat primary and secondary syphilis, regardless of HIV status (*591–593*).

Recommended Regimen for Syphilis Among Infants and Children

Benzathine penicillin G 50,000 units/kg body weight IM, up to the adult dose of 2.4 million units in a single dose

- Infants and children aged ≥1 month who receive a syphilis diagnosis should have birth and maternal medical records reviewed to assess whether they have congenital or acquired syphilis (see Congenital Syphilis). Infants and children aged ≥1 month with primary and

	secondary syphilis should be managed by a pediatric infectious disease specialist and evaluated for sexual abuse (e.g., through consultation with child protective services) • Clinical and serologic evaluation should be performed at 6 and 12 months after treatment; more frequent evaluation might be prudent if opportunity for follow-up is uncertain or if repeat infection is a clinical concern • Pregnant women with primary or secondary syphilis who are allergic to penicillin should be desensitized and treated with penicillin G. Skin testing or oral graded penicillin dose challenge might be helpful in identifying women at risk for acute allergic reactions • Data to support use of alternatives to penicillin in treating primary and secondary syphilis are limited. However, multiple therapies might be effective for nonpregnant persons with penicillin allergy who have primary or secondary syphilis. • Doxycycline (100 mg orally 2 times/day for 14 days) (*600*,*601*) and tetracycline (500 mg orally 4 times/day for 14 days) have been used for years and can be effective. Compliance is likely to be better with doxycycline than tetracycline because tetracycline can cause more gastrointestinal side effects and requires more frequent dosing. • Limited clinical studies, along with biologic and pharmacologic evidence, indicate that ceftriaxone (1 g daily either IM or IV for 10 days) is effective for treating primary and secondary syphilis; however, the optimal dose and duration of ceftriaxone therapy have not been defined. • Azithromycin as a single 2-g oral dose has been effective for treating primary and secondary syphilis among certain populations. However, because of *T. pallidum* chromosomal mutations associated with azithromycin and other macrolide resistance and documented treatment failures in multiple U.S. geographic areas, azithromycin should not be used as treatment for syphilis. Thorough clinical and serologic follow-up of persons receiving any alternative therapy is essential. • Persons with a penicillin allergy whose compliance with therapy or follow-up cannot be ensured should be desensitized and treated with benzathine penicillin G. Skin testing for penicillin allergy might be useful in circumstances in which the reagents and expertise are available for performing the test adequately

	Because latent syphilis is not transmitted sexually, the objective of treating persons in this disease stage is to prevent medical complications of syphilis. Latent syphilis can also be vertically transmitted to a fetus; therefore, the goal of treating a pregnant woman is to prevent congenital syphilis. Although clinical experience supports the effectiveness of penicillin in achieving this goal, limited evidence is available for guiding choice of specific regimens or duration. Available data demonstrate that additional doses of benzathine penicillin G, amoxicillin, or other antibiotics in early latent syphilis do not enhance efficacy, regardless of HIV status. **Recommended Regimens for Latent Syphilis* Among Adults** **Early latent syphilis: Benzathine penicillin G** 2.4 million units IM in a single dose **Late latent syphilis: Benzathine penicillin G** 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals * Recommendations for treating syphilis in persons with HIV and pregnant women are discussed elsewhere in this report (see Syphilis Among Persons with HIV Infection; Syphilis During Pregnancy). Tertiary syphilis refers to gummas, cardiovascular syphilis, psychiatric manifestations (e.g., memory loss or personality changes), or late neurosyphilis. Guidelines for all forms of neurosyphilis (e.g., early or late neurosyphilis) are discussed elsewhere in these recommendations (see Neurosyphilis, Ocular Syphilis, and Otosyphilis). Persons with gummas and cardiovascular syphilis who are not allergic to penicillin and have no evidence of neurosyphilis by clinical and CSF examination should be treated with the following regimen. **Recommended Regimen for Tertiary Syphilis Among Adults** **Tertiary syphilis with normal CSF examination: Benzathine penicillin G** 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals **Urethritis** • Ideally, treatment should be pathogen based; however, diagnostic information might not

	be immediately available. Presumptive treatment should be initiated at NGU diagnosis. • Doxycycline is highly effective for chlamydial urethral infections and is also effective for chlamydial infections of the rectum; it also has some activity against *M. genitalium*. In contrast, reports have increased of azithromycin treatment failures for chlamydial infection, and the incidence of macrolide resistance in *M. genitalium* also has been rapidly rising. Pharmacokinetic data indicate that changing azithromycin dosing from a single-dose strategy to a multiday strategy might protect against inducing resistance in *M. genitalium* infections **Recommended Regimen for Nongonococcal Urethritis** **Doxycycline** 100 mg orally 2 times/day for 7 days **Alternative Regimens** **Azithromycin** 1 g orally in a single dose *or* **Azithromycin** 500 mg orally in a single dose; then 250 mg orally daily for 4 days • All sex partners of men with NGU within the preceding 60 days should be referred for evaluation and testing and presumptive treatment with a drug regimen effective against chlamydia. All partners should be evaluated and treated according to the management section for their respective pathogen; EPT could be an alternate approach if a partner is unable to access timely care. To avoid reinfection, sex partners should abstain from sexual intercourse until they and their partners are treated. • The objective diagnosis of persistent or recurrent NGU • should be made before considering additional antimicrobial therapy. Symptomatic recurrent or persistent urethritis might be caused by treatment failure or reinfection after successful treatment. • The initial step in recurrent urethritis is assessing compliance with treatment or potential reexposure to an untreated sex partner. If the patient did not comply with the treatment

	regimen or was reexposed to an untreated partner, retreatment with the initial regimen can be considered. If therapy was appropriately completed and no reexposure occurred, therapy is dependent on the initial treatment regimen. Ideally, diagnostic testing among men with recurrent or persistent symptoms, including those with gonorrhea, chlamydia, *M. genitalium*, and trichomoniasis, can be used to guide further management decisions. • *T. vaginalis* is also known to cause urethritis among men who have sex with women. In areas where *T. vaginalis* is prevalent, men who have sex with women with persistent or recurrent urethritis should be tested for *T. vaginalis* and presumptively treated with metronidazole 2 g orally in a single dose or tinidazole 2 g orally in a single dose; their partners should be referred for evaluation and treatment, if needed. • If *T. vaginalis* is unlikely (MSM with NGU or negative *T. vaginalis* NAAT), men with recurrent NGU should be tested for *M. genitalium* by using an FDA-cleared NAAT. Treatment for *M. genitalium* includes a two-stage approach, ideally using resistance-guided therapy. If *M. genitalium* resistance testing is available it should be performed, and the results should be used to guide therapy (see *Mycoplasma genitalium*). If *M. genitalium* resistance testing is not available, doxycycline 100 mg orally 2 times/day for 7 days followed by moxifloxacin 400 mg orally once daily for 7 days should be used. The rationale for this approach is that although not curative, doxycycline decreases the *M. genitalium* bacterial load, thereby increasing likelihood of moxifloxacin success. Higher doses of azithromycin have not been effective for *M. genitalium* after azithromycin treatment failures. Men with persistent or recurrent NGU after treatment for *M. genitalium* or *T. vaginalis* should be referred to an infectious disease or urology specialist. **Cervicitis** • Multiple factors should affect the decision to provide presumptive therapy for cervicitis. Presumptive treatment with antimicrobials for *C. trachomatis* and *N. gonorrhoeae* should be provided for women at increased risk (e.g., those aged <25 years and women with a new sex partner, a sex partner with concurrent partners, or a sex partner who has an STI), if follow-up cannot be ensured, or if testing with NAAT is not possible. Trichomoniasis and BV should be treated if detected.

	• For women at lower risk for STIs, deferring treatment until results of diagnostic tests are available is an option. If treatment is deferred and *C. trachomatis* and *N. gonorrhoeae* NAATs are negative, a follow-up visit to determine whether the cervicitis has resolved can be considered. **Recommended Regimen for Cervicitis*** **Doxycycline** 100 mg orally 2 times/day for 7 days * Consider concurrent treatment for gonococcal infection if the patient is at risk for gonorrhea or lives in a community where the prevalence of gonorrhea is high (see Gonococcal Infections). **Alternative Regimen** **Azithromycin** 1 g orally in a single dose • Management of sex partners of women treated for cervicitis should be tailored for the specific infection identified or suspected. All sex partners during the previous 60 days should be referred for evaluation, testing, and presumptive treatment if chlamydia, gonorrhea, or trichomoniasis was identified. • EPT and other effective partner referral strategies are alternative approaches for treating male partners of women who have chlamydial or gonococcal infection. To avoid reinfection, sex partners should abstain from sexual intercourse until they and their partners are treated. • Diagnosis and treatment of cervicitis for pregnant women does not differ from that for women who are not pregnant • Among women with persistent cervicitis who were previously treated with doxycycline or azithromycin, testing for *M. genitalium* can be considered and treatment initiated on the basis of results of diagnostic testing. For women with persistent symptoms that are clearly attributable to cervicitis, referral to a gynecologic specialist can be considered for evaluation of noninfectious causes **Chlamydial Infection Among Adolescents and Adults** Treating persons with *C. trachomatis* prevents adverse reproductive health complications and

	continued sexual transmission. Furthermore, treating their sex partners can prevent reinfection and infection of other partners. Treating pregnant women usually prevents transmission of *C. trachomatis* to neonates during birth. Treatment should be provided promptly for all persons with chlamydial infection; treatment delays have been associated with complications (e.g., PID) in a limited proportion of women (*810*). **Recommended Regimen for Chlamydial Infection Among Adolescents and Adults** **Doxycycline** 100 mg orally 2 times/day for 7 days **Alternative Regimens** **Azithromycin** 1 g orally in a single dose *or* **Levofloxacin** 500 mg orally once daily for 7 days • To minimize disease transmission to sex partners, persons treated for chlamydia should be instructed to abstain from sexual intercourse for 7 days after single-dose therapy or until completion of a 7-day regimen and resolution of symptoms if present. To minimize risk for reinfection, patients also should be instructed to abstain from sexual intercourse until all of their sex partners have been treated • Sex partners should be referred for evaluation, testing, and presumptive treatment if they had sexual contact with the partner during the 60 days preceding the patient's onset of symptoms or chlamydia diagnosis. Although the exposure intervals defining identification of sex partners at risk are based on limited data, the most recent sex partner should be evaluated and treated, even if the time of the last sexual contact was >60 days before symptom onset or diagnosis. • Clinical experience and published studies indicate that azithromycin is safe and effective during pregnancy. • Doxycycline is contraindicated during the second and third trimesters of pregnancy because of risk for tooth discoloration. Human data reveal that levofloxacin presents a low risk to the fetus during pregnancy but has potential for toxicity during breastfeeding;

	however, data from animal studies increase concerns regarding cartilage damage to neonates **Recommended Regimen for Chlamydial Infection During Pregnancy** **Azithromycin** 1 g orally in a single dose **Alternative Regimen** **Amoxicillin** 500 mg orally 3 times/day for 7 days **Chlamydial Infection Among Neonates** **Recommended Regimen for Chlamydial Infection Among Neonates** **Erythromycin base or ethyl succinate** 50 mg/kg body weight/day orally, divided into 4 doses daily for 14 days* * An association between oral erythromycin and azithromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported among infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for IHPS signs and symptoms. • Although data regarding use of azithromycin for treating neonatal chlamydial infection are limited, available data demonstrate that a short therapy course might be effective. • Topical antibiotic therapy alone is inadequate for treating ophthalmia neonatorum caused by chlamydia and is unnecessary when systemic treatment is administered. • Mothers of infants who have ophthalmia caused by chlamydia and the sex partners of these women should be evaluated and presumptively treated for chlamydia **Chlamydial Infection Among Infants and Children** **Recommended Regimens for Chlamydial Infection Among Infants and Children**

	For infants and children weighing <45 kg: Erythromycin base or ethyl succinate 50 mg/kg body weight/day orally divided into 4 doses daily for 14 days Data are limited regarding the effectiveness and optimal dose of azithromycin for treating chlamydial infection among infants and children weighing <45 kg. **For children weighing ≥45 kg but aged <8 years: Azithromycin** 1 g orally in a single dose **For children aged ≥8 years: Azithromycin** 1 g orally in a single dose *or* **Doxycycline** 100 mg orally 2 times/day for 7 days Gonococcal Infection Among Adolescents and Adults **Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum** **Recommended Regimen for Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum Among Adults and Adolescents** **Ceftriaxone** 500 mg* IM in a single dose for persons weighing <150 kg If chlamydial infection has not been excluded, treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days. * For persons weighing ≥150 kg, 1 g ceftriaxone should be administered. **Alternative Regimens if Ceftriaxone Is Not Available** **Gentamicin** 240 mg IM in a single dose *plus* **Azithromycin** 2 g orally in a single dose *or*

	Cefixime* 800 mg orally in a single dose * If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days. • Recent sex partners (i.e., persons having sexual contact with the infected patient <60 days preceding onset of symptoms or gonorrhea diagnosis) should be referred for evaluation, testing, and presumptive treatment. If the patient's last potential sexual exposure was >60 days before onset of symptoms or diagnosis, the most recent sex partner should be treated • Treatment of the sexual partner with cefixime 800 mg as a single dose is recommended, provided that concurrent chlamydial infection has been excluded. If a chlamydia test result has not been documented, the partner may be treated with a single dose of oral cefixime 800 mg plus oral doxycycline 100 mg 2 times/day for 7 days. • If adherence with multiday dosing is a considerable concern, azithromycin 1 g can be considered but has lower treatment efficacy among persons with rectal chlamydia • Patients with suspected treatment failures should first be retreated routinely with the initial regimen used (ceftriaxone 500 mg IM), with the addition of doxycycline if chlamydia infection exists, because reinfections are more likely than actual treatment failures. However, in situations with a higher likelihood of treatment failure than reinfection, relevant clinical specimens should be obtained for culture (preferably with simultaneous NAAT) and antimicrobial susceptibility testing before retreatment. • Dual treatment with single doses of IM gentamicin 240 mg plus oral azithromycin 2 g can be considered, particularly when isolates are identified as having elevated cephalosporin MICs. • Persons with suspected treatment failure after treatment with the alternative regimen (cefixime or gentamicin) should be treated with ceftriaxone 500 mg as a single IM dose or as a single dose with or without an antichlamydial agent on the basis of chlamydia infection status. • Pregnant women infected with *N. gonorrhoeae* should be treated with ceftriaxone 500 mg in a single IM dose plus treatment for chlamydia if infection has not been excluded. When

	cephalosporin allergy or other considerations preclude treatment with this regimen, consultation with an infectious disease specialist or an STD clinical expert is recommended. Gentamicin use is cautioned during pregnancy because of risk for neonatal birth defects, nephrotoxicity, or ototoxicity Gonococcal Infection Among Infants and Children Recommended Regimen for Uncomplicated Gonococcal Vulvovaginitis, Cervicitis, Urethritis, Pharyngitis, or Proctitis Among Infants and Children Weighing ≤45 kg Ceftriaxone 25–50 mg/kg body weight IV or IM in a single dose, not to exceed 250 mg IM Recommended Regimen for Uncomplicated Gonococcal Vulvovaginitis, Cervicitis, Urethritis, Pharyngitis, or Proctitis Among Children Weighing >45 kg Treat with the regimen recommended for adults (see Gonococcal Infections Recommended Regimen for Bacteremia or Arthritis Among Children Weighing ≤45 kg Ceftriaxone 50 mg/kg body weight (maximum dose: 2 g) IM or IV in a single dose daily every 24 hours for 7 days Recommended Regimen for Bacteremia or Arthritis Among Children Weighing >45 kg Ceftriaxone 1 g IM or IV in a single dose daily every 24 hours for 7 days **Mycoplasma genitalium** • *M. genitalium* lacks a cell wall, and thus antibiotics targeting cell-wall biosynthesis (e.g., ß-lactams including penicillins and cephalosporins) are ineffective against this organism. Because of the high rates of macrolide resistance with treatment failures and efficient selection of additional resistance, a 1-g dose of azithromycin should not be used.

	• Two-stage therapy approaches, ideally using resistance-guided therapy, are recommended for treatment. Resistance-guided therapy has demonstrated cure rates of >90% and should be used whenever possible; however, it requires access to macrolide-resistance testing. • As part of this approach, doxycycline is provided as initial empiric therapy, which reduces the organism load and facilitates organism clearance, followed by macrolide-sensitive *M. genitalium* infections treated with high-dose azithromycin; macrolide-resistant infections are treated with moxifloxacin. **Recommended Regimens if *M. genitalium* Resistance Testing Is Available** **If macrolide sensitive: Doxycycline** 100 mg orally 2 times/day for 7 days, followed by **azithromycin** 1 g orally initial dose, followed by 500 mg orally daily for 3 additional days (2.5 g total) **If macrolide resistant: Doxycycline** 100 mg orally 2 times/day for 7 days followed by **moxifloxacin** 400 mg orally once daily for 7 days **Recommended Regimen if *M. genitalium* Resistance Testing Is Not Available** **If *M. genitalium* is detected by an FDA-cleared NAAT:** **Doxycycline** 100 mg orally 2 times/day for 7 days, followed by **moxifloxacin** 400 mg orally once daily for 7 days • Although the majority of *M. genitalium* strains are sensitive to moxifloxacin, resistance has been reported, and adverse side effects and cost should be considered with this regimen. In settings without access to resistance testing and when moxifloxacin cannot be used, an alternative regimen can be considered, based on limited data: doxycycline 100 mg orally 2 times/day for 7 days, followed by azithromycin (1 g orally on day 1 followed by 500 mg once daily for 3 days) and a test of cure 21 days after completion of therapy. • Because of the high prevalence of macrolide resistance and high likelihood of treatment failure, this regimen should be used only when a test of cure is possible, and no other alternatives exist. If symptomatic treatment failure or a positive test of cure occurs after this regimen, expert consultation is recommended.

	• Data are limited regarding use of minocycline in instances of treatment failure. • Sex partners of patients with symptomatic *M. genitalium* infection can be tested, and those with a positive test can be treated to possibly reduce the risk for reinfection. If testing the partner is not possible, the antimicrobial regimen that was provided to the patient can be provided **Bacterial Vaginosis** • Treatment for BV is recommended for women with symptoms. Established benefits of therapy among nonpregnant women are to relieve vaginal symptoms and signs of infection. Other potential benefits of treatment include reduction in the risk for acquiring *C. trachomatis, N. gonorrhoeae*, *T. vaginalis*, *M. genitalium*, HIV, HPV, and HSV-2. No data are available that directly compare the efficacy of oral and topical medications for treating BV. **Recommended Regimens for Bacterial Vaginosis** **Metronidazole** 500 mg orally 2 times/day for 7 days *or* **Metronidazole gel 0.75%** one full applicator (5 g) intravaginally, once daily for 5 days *or* **Clindamycin cream 2%** one full applicator (5 g) intravaginally at bedtime for 7 days **Alternative Regimens** **Clindamycin** 300 mg orally 2 times/day for 7 days *or* **Clindamycin ovules** 100 mg intravaginally once at bedtime for 3 days* *or* **Secnidazole** 2 g oral granules in a single dose† *or*

	Tinidazole 2 g orally once daily for 2 days *or* **Tinidazole** 1 g orally once daily for 5 days • Metronidazole does not inhibit acetaldehyde dehydrogenase, as occurs with disulfiram. Ethanol alone or ethanol-independent side effects of metronidazole might explain the suspicion of disulfiram-like effects. Thus, refraining from alcohol use while taking metronidazole (or tinidazole) is unnecessary. Clindamycin cream is oil based and might weaken latex condoms and diaphragms for 5 days after use (refer to clindamycin product labeling for additional information). • Women should be advised to refrain from sexual activity or to use condoms consistently and correctly during the BV treatment regimen. Douching might increase the risk for relapse, and no data support use of douching for treatment or symptom relief. • Data from earlier clinical trials indicate that a woman's response to therapy and the likelihood of relapse or recurrence are not affected by treatment of her sex partner. Therefore, routine treatment of sex partners is not recommended. • BV treatment is recommended for all symptomatic pregnant women because symptomatic BV has been associated with adverse pregnancy outcomes, including premature rupture of membranes, preterm birth, intra-amniotic infection, and postpartum endometritis. Studies have been undertaken to determine the efficacy of BV treatment among this population, including two trials demonstrating that oral metronidazole was efficacious during pregnancy by using the 250 mg 3 times/day regimen; however, oral metronidazole administered as a 500 mg 2 times/day regimen can also be used. One trial involving a limited number of participants revealed treatment with oral metronidazole 500 mg 2 times/day for 7 days to be equally effective as metronidazole gel 0.75% for 5 days, with cure rates of 70% by using Amsel criteria to define cure (*1039*). Another trial demonstrated a cure rate of 85% by using Gram-stain criteria after treatment with oral clindamycin 300 mg 2 times/day for 7 days

	Pelvic Inflammatory Disease • PID treatment regimens should provide empiric, broad-spectrum coverage of likely pathogens. • Multiple parenteral and oral antimicrobial regimens have been effective in achieving clinical and microbiologic cure in randomized clinical trials with short-term follow-up. However, only a limited number of studies have assessed and compared these regimens with regard to infection elimination in the endometrium and fallopian tubes or determined the incidence of long-term complications (e.g., tubal infertility and ectopic pregnancy) after antimicrobial regimens. • The optimal treatment regimen and long-term outcome of early treatment of women with subclinical PID are unknown. All regimens used to treat PID should also be effective against *N. gonorrhoeae* and *C. trachomatis* because negative endocervical screening for these organisms does not rule out upper genital tract infection. • Anaerobic bacteria have been isolated from the upper genital tract of women who have PID, and data from in vitro studies have revealed that some anaerobes (e.g., *Bacteroides fragilis*) can cause tubal and epithelial destruction. BV is often present among women who have PID • Addition of metronidazole to IM or oral PID regimens more effectively eradicates anaerobic organisms from the upper genital tract. Until treatment regimens that do not cover anaerobic microbes have been demonstrated to prevent long-term sequelae (e.g., infertility and ectopic pregnancy) as successfully as the regimens that are effective against these microbes, using regimens with anaerobic activity should be considered. Treatment should be initiated as soon as the presumptive diagnosis has been made because prevention of long-term sequelae is dependent on early administration of recommended antimicrobials. For women with PID of mild or moderate clinical severity, parenteral and oral regimens appear to have similar efficacy. The decision of whether hospitalization is necessary should be based on provider judgment and whether the woman meets any of the following criteria: ▪ Surgical emergencies (e.g., appendicitis) cannot be excluded

	▪ Tubo-ovarian abscess ▪ Pregnancy ▪ Severe illness, nausea and vomiting, or oral temperature >38.5°C (101°F) ▪ Unable to follow or tolerate an outpatient oral regimen ▪ No clinical response to oral antimicrobial therapy No evidence is available to indicate that adolescents have improved outcomes from hospitalization for treatment of PID, and the clinical response to outpatient treatment is similar among younger and older women. The decision to hospitalize adolescents with acute PID should be based on the same criteria used for older women. **Recommended Parenteral Regimens for Pelvic Inflammatory Disease** **Ceftriaxone** 1 g by every 24 hours *plus* **Doxycycline** 100 mg orally or IV every 12 hours *plus* **Metronidazole** 500 mg orally or IV every 12 hours *or* **Cefotetan** 2 g IV every 12 hours *plus* **Doxycycline** 100 mg orally or IV every 12 hours *or* **Cefoxitin** 2 g IV every 6 hours *plus* **Doxycycline** 100 mg orally or IV every 12 hours • Because of the pain associated with IV infusion, doxycycline should be administered orally when possible. Oral and IV administration of doxycycline and metronidazole provide similar bioavailability. Oral metronidazole is well absorbed and can be considered instead of IV for

	women without severe illness or tubo-ovarian abscess when possible. • After clinical improvement with parenteral therapy, transition to oral therapy with doxycycline 100 mg 2 times/day and metronidazole 500 mg 2 times/day is recommended to complete 14 days of antimicrobial therapy. **Alternative Parenteral Regimens** **Ampicillin-sulbactam** 3 g IV every 6 hours *plus* **Doxycycline** 100 mg orally or IV every 12 hours *or* **Clindamycin** 900 mg IV every 8 hours *plus* **Gentamicin** loading dose IV or IM (2 mg/kg body weight), followed by a maintenance dose (1.5 mg/kg body weight) every 8 hours; single daily dosing (3–5 mg/kg body weight) can be substituted **Recommended Intramuscular or Oral Regimens for Pelvic Inflammatory Disease** **Ceftriaxone** 500 mg* IM in a single dose *plus* **Doxycycline** 100 mg orally 2 times/day for 14 days with **metronidazole** 500 mg orally 2 times/day for 14 days *or* **Cefoxitin** 2 g IM in a single dose and **probenecid** 1 g orally administered concurrently in a single dose *plus* **Doxycycline** 100 mg orally 2 times/day for 14 days with **metronidazole** 500 mg orally 2 times/day for 14 days *or*

	Other parenteral third-generation cephalosporin (e.g., ceftizoxime or cefotaxime) *plus* **Doxycycline** 100 mg orally 2 times/day for 14 days with **metronidazole** 500 mg orally 2 times/day for 14 days * For persons weighing ≥150 kg, 1 g of ceftriaxone should be administered • Persons who have had sexual contact with a partner with PID during the 60 days preceding symptom onset should be evaluated, tested, and presumptively treated for chlamydia and gonorrhea, regardless of the PID etiology or pathogens isolated. If the last sexual intercourse was >60 days before symptom onset or diagnosis, the most recent sex partner should be treated • Pregnant women suspected of having PID are at high risk for maternal morbidity and preterm delivery. These women should be hospitalized and treated with IV antimicrobials in consultation with an infectious disease specialist. **Epididymitis** • To prevent complications and transmission of STIs, presumptive therapy for all sexually active men is indicated at the time of the visit before all laboratory test results are available. • Selection of presumptive therapy is based on risk for chlamydial and gonococcal infections or enteric organisms. Treatment goals for acute epididymitis are 1) microbiologic infection cure, 2) improvement of signs and symptoms, 3) prevention of transmission of chlamydia and gonorrhea to others, and 4) decreased potential for chlamydial or gonococcal epididymitis complications (e.g., infertility or chronic pain). • Although the majority of men with acute epididymitis can be treated on an outpatient basis, referral to a specialist and hospitalization should be considered when severe pain or fever indicates other diagnoses (e.g., torsion, testicular infarction, abscess, or necrotizing fasciitis) or when men are unable to comply with an antimicrobial regimen. Age, history of diabetes, fever, and elevated C-reactive protein can indicate more severe disease requiring hospitalization.

	Recommended Regimens for Epididymitis **For acute epididymitis most likely caused by chlamydia or gonorrhea: Ceftriaxone** 500 mg* IM in a single dose *plus* **Doxycycline** 100 mg orally 2 times/day for 10 days **For acute epididymitis most likely caused by chlamydia, gonorrhea, or enteric organisms (men who practice insertive anal sex): Ceftriaxone** 500 mg* IM in a single dose *plus* **Levofloxacin** 500 mg orally once daily for 10 days **For acute epididymitis most likely caused by enteric organisms only: Levofloxacin** 500 mg orally once daily for 10 days * For persons weighing ≥150 kg, 1 g of ceftriaxone should be administered o Levofloxacin monotherapy should be considered if the infection is most likely caused by enteric organisms only, and gonorrhea has been ruled out by Gram, MB, or GV stain. This includes men who have undergone prostate biopsy, vasectomy, and other urinary tract instrumentation procedures. o Treatment should be guided by bacterial cultures and antimicrobial susceptibilities. As an adjunct to therapy, bed rest, scrotal elevation, and nonsteroidal anti-inflammatory drugs are recommended until fever and local inflammation have subsided. Complete resolution of discomfort might not occur for a few weeks after completion of the antibiotic regimen o Men who have acute epididymitis confirmed or suspected to be caused by *N. gonorrhoeae* or *C. trachomatis* should be advised to abstain from sexual intercourse until they and their partners have been treated and symptoms have resolved. All men with acute epididymitis should be tested for HIV and syphilis o Men who have acute sexually transmitted epididymitis confirmed or suspected to be caused by *N. gonorrhoeae* or *C. trachomatis* should be instructed to refer all sex partners

	during the previous 60 days before symptom onset for evaluation, testing, and presumptive treatment (see Chlamydial Infections; Gonococcal Infections). If the last sexual intercourse was >60 days before onset of symptoms or diagnosis, the most recent sex partner should be evaluated and treated. Arrangements should be made to link sex partners to care. EPT is an effective strategy for treating sex partners of men who have or are suspected of having chlamydia or gonorrhea for whom linkage to care is anticipated to be delayed. Partners should be instructed to abstain from sexual intercourse until they and their sex partners are treated and symptoms have resolved.
Addition of a new section: WHO Guidelines for the management of symptomatic sexually transmitted infections **(2021)**[7]	**Urethral discharge management** ***Settings with quality-assured molecular testing in a laboratory with a fully operational quality management system and results available on the same day of the visit*** • For people with symptom of urethral discharge from the penis, management is recommended to be based on the results of quality-assured molecular assays. However, in settings with limited or no molecular tests or laboratory capacity, WHO recommends syndromic treatment to ensure treatment on the same day of the visit. (Strong recommendation; moderate certainty evidence) • Treat according to the test results on the same day. If urethral discharge is present but tests are negative, treat for nongonococcal and non-chlamydial urethritis (such as Mycoplasma genitalium or Trichomonas vaginalis). (Strong recommendation; moderate certainty evidence) • When treatment based on molecular assays is not feasible on the same day of the visit, WHO recommends syndromic treatment of infection with N. gonorrhoeae and C. trachomatis and using the test results to support managing the partner when tests areavailable. (Strong recommendation; moderate certainty evidence) • Treat people with recurrent or persistent urethral discharge based on a repeat molecular assay (such as NAAT) after 21 days, testing for N. gonorrhoeae, C. trachomatis as well as M. genitalium and T. vaginalis and testing for antimicrobial-resistant N. gonorrhoeae. (Strong recommendation; moderate certainty evidence)

Settings in which same-day treatment is not feasible with molecular testing or with limited or no molecular testing

- Treat people who have urethral discharge confirmed on examination for N. gonorrhoeae and C. trachomatis to ensure same-day treatment. (Conditional recommendation; low-certainty evidence)
- Treat people with recurrent or persistent urethral discharge for treatment failure based on WHO guidelines and review. (Conditional recommendation; low-certainty evidence)

Therapy for uncomplicated *Neisseria gonorrhoeae (24)*

Plus

Therapy for *Chlamydia trachomatis (25)*

Infections covered	**First-line options**	**Effective substitutes**
In settings in which local antimicrobial resistance data are not available, the WHO STI guideline suggests dual therapy for gonorrhea.		
*N. gonorrhoeae*a	**Ceftriaxone 250 mg**, intramuscularly, single dose *Plus* **Azithromycin 1 gram**, orally, single dose	**Cefixime 400 mg**, orally, single dose *Plus* **Azithromycin 1 gram**, orally, single dose
C. trachomatis	**Doxycycline 100 mg**, orally, twice daily for seven days (to be given only if gonorrhea therapy	**Azithromycin 1 gram**, orally, single dose *or* **Erythromycin 500 mg**, orally, 4 times a day for 7 days

		did not include azithromycin)	*or* **Ofloxacin 200–400 mg**, orally, twice a day for 7 days. (to be given only if gonorrhea therapy did not include azithromycin)
	In settings in which local antimicrobial resistance data reliably confirm the susceptibility of *N. gonorrhoeae* to the antimicrobial agent, singe therapy may be given.		
	N. gonorrhoeae	**Ceftriaxone 250 mg**, intramuscularly, single dose	**Cefixime 400 mg**, orally, single dose *or* **Spectinomycin 2 grams**, intramuscularly, single dose (availability makes this antibiotic impractical)
	Additional therapeutic options for recurrent or persistent infections		
	T. vaginalis	**Metronidazole 2 grams**, orally, single doses	**Metronidazole 400 or 500 mg**, twice daily for 7 days
	M. genitalium	**Azithromycin 500 mg**, orally on day 1, 250 mg daily on days 2–5	
	Vaginal discharge management • For people with symptom of vaginal discharge, WHO recommends treatment for N. gonorrhoeae and/or C. trachomatis and/or T. vaginalis on the same visit. WHO suggests		

	treatment based on the results of quality-assured molecular assays for N. gonorrhoeae and/or C. trachomatis and/or T. vaginalis. In settings in which treatment based on the results of molecular assay in the same visit is not feasible or that have limited or no molecular testing, WHO suggests treatment based on testing with quality-assured rapid point-of-care tests or on syndromic treatment. (Strong recommendation; Moderate certainty evidence) ***Settings in which treatment is based on quality-assured molecular assays in a laboratory with a fully operational quality management system and results available on the same day of the visit*** • Recommends treating N. gonorrhoeae and/or C. trachomatis and/or T. vaginalis based on the results of quality-assured molecular assays on a self-collected, or clinician-collected, vaginal swab or on a urine specimen. (Strong recommendation; Moderate certainty evidence) • Suggest treating for bacterial vaginosis if vaginal discharge is present (for example, tenacious or thin) or based on the results of microscopy, if available. (Strong recommendation; Moderate certainty evidence) • Suggest treating for candidiasis, where indicated by type of discharge (such as curd-like with vaginal itching) or by the results of microscopy, if available. (Strong recommendation; Moderate certainty evidence) Settings in which same-day treatment is not feasible with molecular testing or with limited or no molecular testing • Suggests treating based on a quality-assured rapid test with a minimum sensitivity of 80% and specificity of 90%, if available, to confirm or exclude infection with N. gonorrhoeae and C. trachomatis • If the availability of a low-cost rapid test or molecular assay is limited, WHO suggests performing a speculum examination and treating for N. gonorrhoeae and C. trachomatis if there is evidence of cervicitis and performing a low-cost rapid test or molecular assay for people with a negative speculum examination who are at high risk of infection with N. gonorrhoeae and C. trachomatis and treating based on the test results

- If a rapid test is not available, WHO suggests treating people who have signs of cervicitis on speculum examination for infection with N. gonorrhoeae and C. trachomatis
- If a rapid test is not available and a speculum examination is not feasible or acceptable, WHO suggests treating people for N. gonorrhoeae and C. trachomatis, all people at high risk of STIs and all people who have vaginal discharge on genital examination
- suggests treating people for bacterial vaginosis and T. vaginalis if vaginal discharge is present or based on the results of microscopy, if available.
- suggests treating people for candidiasis, where indicated by type of discharge (such as curd-like with vaginal itching) or by the results of microscopy, if available.

(Conditional recommendation; low-certainty evidence for all of the above)

Therapy for bacterial vaginosis and trichomoniasis

Infections covered	**First-line options**	**Effective substitutes**	**Note: In pregnancy, metronidazole should, ideally, be avoided in the first trimester**
Bacterial vaginosis	**Metronidazole 400 mg or 500 mg,** orally, twice daily for 7 days	**Clindamycin 300 mg,** orally, twice daily for 7 days *or* **Metronidazole 2 grams,** orally, single dose	**Metronidazole 200 mg or 250 mg,** orally, 3 times a day for 7 days *or* **Metronidazole gel** 0.75%, one full applicator (5 grams)

				intravaginally, twice a day for 7 days *or* **Clindamycin 300 mg,** orally, twice daily for 7 days
	T. vaginalis	**Metronidazole 2 grams,** orally, in a single dose *or* **Metronidazole 400 mg or 500 mg,** orally, twice daily for 7 days	**Tinidazole 2 grams orally,** single dose *or* **Tinidazole 500 mg orally,** twice daily for 5 days	**Metronidazole 200 mg or 250 mg,** orally, 3 times a day for 7 days *or* **Metronidazole gel** 0.75%, one full applicator (5 grams) intravaginally, twice a day for 7 days
	Therapy for uncomplicated *N. gonorrhoeae (24)* *Plus* Therapy for *C. trachomatis (25)*			
	Infections covered	**First-line options**	**Effective substitutes**	**Options for pregnant women or**

				during breastfeeding
	In settings in which local antimicrobial resistance data are not available, the WHO STI guidelines suggest dual therapy for gonorrhea.			
	N. gonorrhoeae a	**Ceftriaxone 250 mg,** intramuscularly, single dose *plus* **Azithromycin 1 gram,** orally, single dose	Cefixime 400 mg, orally, single dose *plus* Azithromycin 1 gram, orally, single dose	**Ceftriaxone 250 mg,** intramuscularly, single dose *plus* **Azithromycin 1 gram,** orally, single dose *or* **Cefixime 400 mg,** orally, single dose *plus* **Azithromycin 1 gram,** orally, single dose
	C. trachomatis	**Doxycycline 100 mg,** orally, twice daily for 7 days (to be given only if gonorrhea therapy did not	**Azithromycin 1 gram,** orally, single dose *or* **Erythromycin 500 mg,** orally, 4 times	**Erythromycin 500 mg,** orally, 4 times a day for 7 days *or* **Azithromycin 1 gram,** orally, single dose

		include azithromycin)	a day for 7 days *or* **Ofloxacin 200–400 mg,** orally, twice daily for 7 days (to be given only if gonorrhea therapy did not include azithromycin)	(to be given only if gonorrhea therapy did not include azithromycin)
	M. genitalium	**Azithromycin 500 gram,** orally day 1, 250 mg daily, days 2–5 (absence of macrolide resistance)	**Azithromycin 500 gram,** orally, day 1, 250 mg daily, days 2–5 (absence of macrolide resistance)	
	Management of lower abdominal pain among women • For sexually active women with symptom of lower abdominal pain, suggest assessing for pelvic inflammatory disease and treating syndromically. (Conditional recommendation; low-certainty evidence for all of the above) • For sexually active women with lower abdominal pain with either of the following features on clinical examination (bimanual palpation): · cervical motion tenderness; or			

	• lower abdominal tenderness: WHO suggests the following. • Treat for pelvic inflammatory disease on the same visit. • Test for infection with N. gonorrhoeae and C. trachomatis and, if available, M. genitalium, to support partner management when tests are available. • Schedule follow-up assessment three days later to assess for clinical improvement, and if the woman has not improved, refer for further assessment. Conditional recommendation; moderate-certainty evidence for all of the above) Therapy for uncomplicated *N. gonorrhoeae (24)* *plus* Therapy for *C. trachomatis (25)* *plus* Therapy for anaerobic infections

Infections covered	**First-line options**	**Effective substitutes**
In settings in which local antimicrobial resistance data are not available, the WHO STI guidelines suggest dual therapy for gonorrhea.		
N. gonorrhoeae	**Ceftriaxone 250 mg,** intramuscularly, single dose *plus* **Azithromycin 1 gram,** orally, single dose	**Cefixime 400 mg,** orally, single dose *plus* **Azithromycin 1 gram,** orally, single dose

	C. trachomatis	**Doxycycline 100 mg,** orally, twice daily for 14 days	**Erythromycin 500 mg,** four times daily for 14 days (to be given only if gonorrhea therapy did not include azithromycin)
	In settings in which local antimicrobial resistance data reliably confirm the susceptibility of *N. gonorrhoeae* to the antimicrobial agent, singe therapy may be given as below.		
	N. gonorrhoeae	**Ceftriaxone 250 mg,** intramuscularly, single dose	**Cefixime 400 mg,** orally, single dose
	The treatment for anaerobes must be included in either treatment option above.		
	Anaerobes	**Metronidazole 400 mg or 500 mg**, orally, twice daily for 14 days	
	Management of genital ulcer disease, including anorectal ulcers • For people who present with genital ulcers (including anorectal ulcers), WHO recommends treatment based on quality-assured molecular assays of the ulcer. However, in settings with limited or no molecular tests or laboratory capacity, WHO recommends syndromic treatment to ensure treatment on the same day of the visit. (Strong recommendation; moderate certainty evidence) ***Settings with quality-assured molecular testing in a laboratory with a fully operational quality management system and results available on the same day of the visit*** • For people with confirmed anogenital ulcers, WHO recommends the following. 1. Perform molecular assays (NAAT) from anogenital lesions to confirm or exclude herpes simplex virus and Treponema pallidum		

	(syphilis). 2. Perform molecular assays from anogenital lesions to confirm lymphogranuloma venereum in geographical settings and/or populations iin which cases are reported or emerging. 3. Perform serological tests for syphilis, with appropriate interpretation for management depending on the test or tests used. 4. Treat for syphilis and/or herpes simplex virus according to the results available on the same day of the visit or treat syndromically and revise management according to the results when available. 5. Treat for lymphogranuloma venereum when the results are positive. 6. Treat for chancroid only in geographical settings where cases (Strong recommendation; moderate certainty evidence) ***Settings in which same-day treatment is not feasible with molecular testing or with limited or no molecular testing*** For people with confirmed anogenital ulcers, WHO suggests the following. 1. Treat syndromically for syphilis and herpes simplex virus on the same day. 2. Treat for herpes simplex virus if the ulcer is recurrent or vesicular, and treat for syphilis if the person has no history of recent treatment for syphilis (in the past three months). 3. Treat for chancroid only in geographical settings where cases are reported or emerging. (Conditional recommendation; moderate certainty evidence)

	Infections covered	**First-line options**	**Effective substitutes**	**For pregnant and breastfeeding women and people younger than 16 years**
	Syphilis (early) (treatment for primary, secondary and early latent [less than two years since infection] syphilis)	**Benzathine penicillin 2.4 million units,** intramuscularly in a single dose	**Doxycycline 100 mg,** orally, twice a day for 14 days *or* **Erythromycin 500 mg,** 4 times a day for 14 days	**Benzathine penicillin 2.4 million units**, intramuscularly in a single dose *or* **Erythromycin 500 mg,** orally, 4 times a day for 14 daysb
	Syphilis (late) (treatment for late latent and tertiary syphilis)	**Benzathine penicillin 2.4 million units** by intramuscular injection, once weekly for 3 consecutive weeks	**Procaine penicillin 1.2 million units** by intramuscular injection, once daily for 20 consecutive days *or*	**Erythromycin 500mg** orally, 4 times a day for 30 daysb

	Doxycycline **100 mg,** orally, twice daily for 30 days

Management of anorectal discharge

- For people with symptom of anorectal discharge and report receptive anal sex, WHO recommends management based on the results of quality-assured molecular assays. However, in settings with limited or no molecular tests or laboratory capacity, WHO recommends syndromic treatment to ensure treatment on the same day of the visit (Strong recommendation; moderate certainty evidence)

Settings with quality-assured molecular testing in a laboratory with a fully operational quality management system and results available on the same day of the visit

WHO recommends the following.

- Perform molecular assays (NAAT) using a self-collected or clinician-collected anorectal swab to confirm or exclude infection with N. gonorrhoeae and/or C. trachomatis and treat the individual infections detected.
- Treat, additionally, for herpes simplex virus if there is anorectal pain.
- Follow the genital ulcer guidelines if ulceration is present. (Strong recommendation; moderate certainty evidence)

Settings in which same-day treatment is not feasible with molecular testing or with limited or no molecular testing

WHO suggests the following.

- Treat for N. gonorrhoeae and C. trachomatis if discharge is present.
- Treat, additionally, for herpes simplex virus if there is anorectal pain. (Conditional recommendation; moderate certainty evidence)

Recommended treatment regimens for anorectal infections

Infections covered	**First-line options**	**Effective substitutes**

	N. gonorrhoeae *(24)*	**Ceftriaxone 250 mg,** intramuscularly, single dose *plus* **Azithromycin 1 gram,** orally, single dose	**Cefixime 400 mg,** orally, single dose *plus* **Azithromycin 1 gram,** orally, single dose
	C. trachomatis *(25)*	**Doxycycline 100 mg** orally, twice daily, for 7 days *or* **Doxycycline for 21 days** (to cover rectal lymphogranuloma venereum) if suspected or confirmed on NAAT (to be given only if dual therapy did not include azithromycin)	**Erythromycin 500 mg,** orally, 4 times a day for 14 days (to be given only if dual therapy did not include azithromycin)
	Syphilis *(26)* (if ulcer present)	**Benzathine penicillin 2.4 million units** intramuscularly, single dose People with a positive syphilis test and no ulcer: administer the same dose at weekly intervals for a total of three doses	**Doxycycline 100 mg** orally, twice daily for 14 days **Erythromycin 500 mg** 4 times a day, orally, for 14 days Extend treatment to 30 days if syphilis serology is positive

	Genital herpes *(27)*	**Recurrent infection:** **Acyclovir 400 mg,** orally, 3 times a day for 5 days *or* **Acyclovir 800 mg,** orally, 3 times a day for 2 days *or* **Acyclovir 800 mg,** orally, 2 times a day for 5 days	**Recurrent infection:** **Valaciclovir 500 mg,** twice daily for 3 days
		Primary genital herpes: **Acyclovir 400 mg,** orally, 3 times a day for 10 days *or* **Acyclovir 200 mg,** 5 times a day for 10 days	**Primary genital herpes:** **Valaciclovir 500 mg,** orally, twice daily for 10 days
		Suppressive therapy for recurrent herpes **Acyclovir 400 mg,** orally, twice daily *or* **Valaciclovir 500 mg,** once daily	Suppressive therapy for recurrences Famciclovir 250 mg, orally, twice daily (Famciclovir 500 mg, twice daily for people living with HIV or immunocompromised

	For duration, see the genital ulcer disease section
Addition of a new section AAFP; Vaginitis: Diagnosis and Treatment **(2018)**[15]	First-line and alternative treatment regimens for vaginitis are presented in Table 4 with suggestions for recurrent infection, treatment during pregnancy, and treatment of sex partners. **BACTERIAL VAGINOSIS** Treatment of bacterial vaginosis is recommended for resolving symptoms, as well as reducing the risk of Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis, human immunodeficiency virus (HIV), and herpes simplex virus type 2 infections. Shifts in vaginal flora have been associated with increased risk of these infections, leading researchers to conclude that treatment of bacterial vaginosis may decrease susceptibility to these infections. First-line therapy includes seven-day courses of oral metronidazole (Flagyl), intravaginal metronidazole (Metrogel), or intravaginal clindamycin.9 No significant difference in effectiveness has been demonstrated among these regimens. Patient preference should be considered when choosing an agent. Physicians should explain potential adverse effects with each regimen, including a possible disulfiram-like reaction with alcohol consumption or gastrointestinal symptoms in persons taking oral metronidazole, or possible weakening of latex condoms with the use of topical therapies containing oil-based preparations. The U.S. Food and Drug Administration recently approved a single-dose oral therapy for bacterial vaginosis, secnidazole (Solosec), which will be available in 2018. A randomized controlled trial demonstrated similar effectiveness and outcomes compared with metronidazole for the treatment of bacterial vaginosis. The dosing involves one-time oral administration of a 2-g packet of granules mixed into applesauce, yogurt, or pudding. A primary adverse effect of this regimen is vulvovaginal candidiasis. Data are insufficient on the safety of secnidazole use in pregnancy, and use is not recommended with breastfeeding. **Bacterial Vaginosis in Pregnancy.** In the past, treatment for bacterial vaginosis during pregnancy was recommended to prevent preterm births. Further review of the evidence has demonstrated that antibiotic treatment does not prevent preterm birth for women with symptomatic or asymptomatic bacterial vaginosis.

Although a previous meta-analysis demonstrated a possible reduction in preterm labor with treatment of bacterial vaginosis, particularly in early pregnancy (before 20 weeks' gestation), a more recent meta-analysis of 21 studies found that antibiotic treatment—regardless of route of administration (oral or topical), the timing in pregnancy, or history of preterm labor in previous pregnancies—does not prevent preterm birth for women with symptomatic or asymptomatic bacterial vaginosis.45 Two studies cited in this meta-analysis that included the presence of abnormal vaginal flora as well as bacterial vaginosis showed a possible reduction in preterm labor before 37 weeks' gestation with treatment; therefore, further investigation may provide more information about the role of abnormal bacterial flora and its treatment in pregnancy. Regardless, treatment of bacterial vaginosis is generally recommended for symptomatic relief, and adverse effects of metronidazole in pregnancy have not been demonstrated.

Clinical recommendation	**Evidence rating**
Symptoms alone cannot differentiate between the causes of vaginitis. Office-based or laboratory testing should be used with the history and physical examination findings to make the diagnosis.	**C**
Do not obtain culture for the diagnosis of bacterial vaginosis because it represents a polymicrobial infection.	**C**
Nucleic acid amplification testing is recommended for the diagnosis of trichomoniasis in symptomatic or high-risk women.	**C**
Treatment of bacterial vaginosis during pregnancy improves symptoms but does not reduce the risk of preterm birth.	**A**
In nonpregnant women, oral and vaginal treatment options for uncomplicated vulvovaginal candidiasis have similar clinical cure rates.	**B**

<table>
<tr><td></td><td colspan="5">Regimens for the Most Common Causes of Vaginitis</td></tr>
<tr><td></td><td>Initial regimens</td><td>Alternative regimens</td><td>Pregnancy</td><td>Recurrence</td><td>Treatment of sex partners</td></tr>
<tr><td></td><td colspan="5">Bacterial vaginosis</td></tr>
<tr><td></td><td>Metronidazole (Flagyl), 500 mg orally twice daily for seven days*
or
Metronidazole 0.75% gel (Metrogel), one full appli-cator (5 g) intravaginally daily for five days
or
Clindamycin 2% cream, one full applicator (5 g) intravaginally at bedtime for seven days†</td><td>Tinidazole (Tindamax), 2 g orally once daily for two days
or
Tinidazole, 1 g orally once daily for five days
or
Clindamycin, 300 mg orally twice daily for seven days
or
Clindamycin (Cleocin Ovules), 100 mg intra-vaginally at bedtime for three days</td><td>Metronidazole, 500 mg orally twice daily for seven days</td><td>First recurrence: Retrial of same regimen
or
Trial of alternative initial regimen
Multiple recurrences: Metronidazol e 0.75% gel, intravaginally twice weekly for four to six months</td><td>Routine treatment of sex partners is not recommende d</td></tr>
<tr><td>Addition of a</td><td colspan="5">• The diagnosis of PID should be made clinically in the absence of other obvious causes in an</td></tr>
</table>

new section: AAFP Pelvic Inflammatory Disease: Diagnosis, Management, and Prevention (2019)[17]	at-risk woman with unexplained pelvic pain and cervical motion, uterine, or adnexal tenderness (grade C). • Empiric antibiotic treatment should be offered at the time of presentation to patients with PID symptoms (grade C). • Women with mild to moderate PID may be treated in an outpatient setting without increased risk of sequelae (grade B). • Patient-delivered or expedited partner therapy for STIs should be offered where legal to decrease rates of reinfection (Grade B). • Annual screening for chlamydia and gonorrhea is recommended in all sexually active women younger than 25 years and any women who are at increased risk of STIs (grade B). **Inpatient Treatment Regimens for Pelvic Inflammatory Disease** **Recommended regimens** Cefotetan (Cefotan), 2 g IV every 12 hours *plus* Doxycycline, 100 mg orally or IV every 12 hours *OR* Cefoxitin, 2 g IV every six hours *plus* Doxycycline, 100 mg orally or IV every 12 hours *OR* Clindamycin, 900 mg IV every eight hours *plus* Gentamicin, loading dose of 2 mg per kg IV or IM, followed by a maintenance dosage of 1.5 mg per kg every eight hours. Single daily dosing of 3 to 5 mg per kg can be substituted **Alternative regimen**

	Ampicillin/sulbactam (Unasyn), 3 g IV every six hours *plus* Doxycycline, 100 mg orally or IV every 12 hours IM = intramuscularly; IV = intravenously **Outpatient Treatment Regimens for Pelvic Inflammatory Disease** Ceftriaxone (Rocephin), 250 mg* IM in a single dose *plus* Doxycycline, 100 mg orally twice a day for 14 days *with† or without* Metronidazole (Flagyl), 500 mg orally twice a day for 14 days *OR* Cefoxitin, 2 g IM, and probenecid, 1 g orally, administered concurrently in a single dose *plus* Doxycycline, 100 mg orally twice a day for 14 days *with† or without* Metronidazole, 500 mg orally twice a day for 14 days *OR* Other parenteral cephalosporins: ceftizoxime (Cefizox) or cefotaxime (Claforan) *plus* Doxycycline, 100 mg orally twice a day for 14 days *with† or without* Metronidazole, 500 mg orally twice a day for 14 days CDC = Centers for Disease Control and Prevention; IM = intramuscularly.

Addition of a new section: British Association for Sexual Health and HIV national guideline for the management of infection with Mycoplasma genitalium **(2018)**[12]	**Treatment regimens for uncomplicated infection:** • Doxycycline 100 mg two times daily for 7 days followed by azithromycin 1 g orally as a single dose then 500 mg orally once daily for 2 days (grade 1D) • Moxifloxacin 400 mg orally once daily for 10 days (grade 1B) **Treatment regimens for complicated infection (PID, epididymo-orchitis):** • Moxifloxacin 400 mg orally once daily for 14 days (grade 1D) **Alternative treatment regimens:** • Doxycycline 100 mg two times daily for 7 days followed by pristinamycin 1 g orally four times daily for 10 days (grade 2C) • Pristinamycin 1 g orally four times daily for 10 days (grade 2C) • Doxycycline 100 mg orally twice daily for 14 days (grade 2C) • Minocycline 100 mg orally twice daily for 14 days (grade 2D) • All patients should attend for a test-of-cure five weeks (and no sooner than three weeks) after the start of treatment to ensure microbiological cure (grade 1D)
Addition of a new section: UK national guideline for the management of infection with Neisseria gonorrhoeae **(2018)**[10]	**Indications for therapy:** 1. Identification of intracellular Gram-negative diplococci on microscopy 2. A positive culture for N. gonorrhoeae 3. A confirmed positive NAAT for N. gonorrhoeae 4. Sexual partner of confirmed case of gonococcal infection (See section below on Sexual Partners) o Patients should be advised to abstain from sexual intercourse until seven days after they and their partner(s) have completed treatment (Grade 1D). **Treatment of uncomplicated ano-genital and pharyngeal infection in adults** • When antimicrobial susceptibility is not known prior to treatment: Ceftriaxone 1 g intramuscularly as a single dose (Grade 1C)

	• When antimicrobial susceptibility is known prior to treatment: Ciprofloxacin 500 mg orally as a single dose (Grade 1A) • The following options have all been associated with treatment failure when used as monotherapy particularly when used for pharyngeal infection,76–79 therefore it is recommended to use dual therapy with azithromycin 2 g where possible (Grade 2C). • Cefixime 400 mg orally as a single dose plus azithromycin 2 g orally (Grade 1B) • Gentamicin 240 mg intramuscularly as a single dose plus azithromycin 2 g orally (Grade 1A) • Spectinomycin 2 g intramuscularly as a single dose plus azithromycin 2 g orally (Grade 1B) • Azithromycin 2 g as a single oral dose (Grade 1B) **Treatment of complicated infections** • **Gonococcal PID:** Ceftriaxone 1 g intramuscularly as a single dose in addition to the regimen chosen to treat PID • **Gonococcal epididymo-orchitis**: Ceftriaxone 1 g intramuscularly as a single dose in addition to the regimen chosen to treat epididymo-orchitis **Pregnancy and breastfeeding** Pregnant and breastfeeding individuals should not be treated with quinolone or tetracycline antimicrobials. Pregnancy does not diminish treatment efficacy. • Ceftriaxone 1 g intramuscularly as a single dose (Grade 1A) or • Spectinomycin 2 g intramuscularly as a single dose (Grade 1A) • Azithromycin 2 g as a single oral dose (Grade 1B)
Addition of a new section: United Kingdom National Guideline for the	• Rest is advised for those with severe disease. (Grade 1D) • Appropriate analgesia should be provided. (Grade 1D) • Intravenous therapy is recommended for patients with more severe clinical disease (Grade 1D) e.g. pyrexia > 38oC, clinical signs of tubo-ovarian abscess, signs of pelvic peritonitis. • To avoid reinfection, patients should be advised to avoid oral or genital intercourse until they, and their partner(s), have completed their treatment (Grade 1D). • A detailed explanation of their condition with particular emphasis on the long term

Management of Pelvic Inflammatory Disease **(2019 Interim Update)**[19]	implications for the health of themselves and their partner(s) should be provided, reinforced with clear and accurate written information (Grade 1D). • Outpatient therapy is as effective as inpatient treatment for patients with clinically mild to moderate PID. Admission for parenteral therapy, observation, further investigation and/or possible surgical intervention should be considered in the following situations (Grade 1D): · a surgical emergency cannot be excluded · lack of response to oral therapy · clinically severe disease · presence of a tubo-ovarian abscess · intolerance to oral therapy · pregnancy • All sexually active women who are potentially fertile should be offered a pregnancy test to exclude ectopic pregnancy (Grade 1D). **Outpatient Regimens** • **First Line Therapy:** IM ceftriaxone 1g single dose followed by oral doxycycline 100mg twice daily plus metronidazole 400mg twice daily for 14 days (Grade 1A) • **Second Line Therapy:** oral ofloxacin 400mg twice daily plus oral metronidazole 400mg twice daily for 14 days (Grade 1A) or oral moxifloxacin 400mg once daily for 14 days (Grade 1A) • Ofloxacin, levofloxacin and moxifloxacin are effective for the treatment of C. trachomatis. Quinolones (ofloxacin, levofloxacin and moxifloxacin) can cause disabling and potentially permanent side-effects involving tendons. muscles, joints and the nervous system, and are therefore only recommended as second line therapy except for the treatment of M genitalium associated PID where no alternative therapy is available. Quinolones are also not licensed for use in patients aged under 18. • **Alternative Regimens:** intramuscular ceftriaxone 1g immediately, followed by azithromycin 1 g/week for 2 weeks (Grade 2B) **Inpatient Regimens** • i.v. ceftriaxone 2g daily plus i.v. doxycycline 100mg twice daily (oral doxycycline may be

	used if tolerated) followed by oral doxycycline 100mg twice daily plus oral metronidazole 400mg twice daily for a total of 14 days (Grade 1A) • i.v. clindamycin 900mg 3 times daily plus i.v. gentamicin (2mg/kg loading dose) followed by 1.5mg/kg 3 times daily [a single daily dose of 7mg/kg may be substituted]) followed by either oral clindamycin 450mg 4 times daily or oral doxycycline 100mg twice daily plus oral metronidazole 400mg twice daily to complete 14 days (Grade 1A) • Intravenous therapy should be continued until 24 hours after clinical improvement and then switched to oral (Grade 2D). **Alternative regimen:** • i.v. ofloxacin 400mg BD plus i.v. metronidazole 500mg TID for 14 days (Grade 1B) • i.v. ciprofloxacin 200mg BD plus i.v. (or oral) doxycycline 100mg BD plus i.v. metronidazole 500mg TID for 14 days (Grade 1B) **Pregnancy and breastfeeding** • There are insufficient data from clinical trials to recommend a specific regimen and empirical therapy with agents effective against gonorrhea, C. trachomatis and anaerobic infections should be considered taking into account local antibiotic sensitivity patterns (e.g. i.v. ceftriaxone, i.v. erythromycin and i.v. metronidazole switching to oral therapy following clinical response and completing 2 weeks of treatment) (Grade 2D). **Follow Up** • Review at 72 hours is recommended for those with moderate or severe symptoms or signs (Grade 2D). • Failure to improve suggests the need for further investigation, parenteral therapy and/or surgical intervention. • Further review, either in clinic or by phone, 2-4 weeks after therapy is recommended (Grade 1D) to ensure: · adequate clinical response to treatment · compliance with oral antibiotics · screening and treatment of sexual contacts · awareness of the significance of PID and its sequelae

	• repeat pregnancy test, if clinically indicated • The following are recommended if the initial test for *M. genitalium* is positive: • treatment with moxifloxacin. This agent currently has good microbiological activity against *M. genitalium* (Grade 1D) • repeat testing for *M. genitalium* following treatment to ensure microbiological clearance. Treatment failure following the use of any of the recommended regimens has been reported but is least likely following treatment with moxifloxacin. The optimal time for testing after starting treatment is not known but 4 weeks is recommended based on expert opinion (Grade 1D). **Partner Notification and Treatment of Sexual Partners** • Current male partners of women with PID should be contacted and offered health advice and screening for gonorrhea and *C. trachomatis* (Grade 1D). • Other recent sexual partners may also be offered screening - tracing of contacts within a 6 month period since onset of symptoms is recommended but this time period may be influenced by the sexual history (Grade 2D). • Because many cases of PID are not associated with gonorrhea, *C. trachomatis* or *M. genitalium*, broad spectrum empirical therapy should also be offered to male partners e.g. doxycycline 100mg twice daily for 1 week (Grade 2D). • Partners should be advised to avoid oral or vaginal intercourse until they and the index patient have completed their treatment course (Grade 1D).
Addition of a new section: European guideline on the management of syphilis **(2020)**[21]	**Table 1** **Early syphilis (Primary, Secondary and Early latent, i.e. acquired <1 year previously)** • **First-line therapy option:** BPG 2.4 million units intramuscularly (IM), given as one injection of 2.4 million units or two separate injections of 1.2 million units in each buttock, on day 1 (1, B) • **Second-line therapy option:** Procaine penicillin 600 000 units IM daily for 10–14 days, i.e. if BPG is not available (1, C) • **Bleeding disorders:**

	Ceftriaxone 1g intravenously (IV) in a single daily dose for 10 days (1, C) Doxycycline 200 mg daily (either 100 mg twice daily or as a single 200 mg dose) orally for 14 days (1, C) • **Penicillin allergy or parenteral treatment refused** · Doxycycline 200 mg daily (either 100 mg twice daily or as a single 200 mg dose) orally for 14 days (1, C) · Desensitization to penicillin is an option but not possible in many settings and labour intensive. **Late latent (i.e. acquired ≥1 year previously or of unknown duration), cardiovascular and gummatous syphilis** • **First-line therapy option:** BPG 2.4 million units IM, given as one injection of 2.4 million units or two separate injections of 1.2 million units in each buttock, on day 1, 8 and 15 (1, C) • **Second-line therapy option:** -Procaine penicillin 600 000 units IM daily for 17–21 days, i.e. if BPG is not available (1, C). -Doxycycline 200 mg daily (either 100 mg twice daily or as a single 200 mg dose) orally for 21–28 days (2, D) **Pregnant woman:** • **First-line option for treatment of early syphilis (i.e. acquired <1 year previously):** BPG 2.4 million units IM single dose (or 1.2 million units in each buttock) (1, B) • **Second-line therapy option:** Procaine penicillin 600 000 units IM daily for 10–14 days,i.e. if BPG is not available (1, C). **Penicillin allergy:** Desensitization to penicillin followed by the first-line regimen (1, C)
Addition of a new section: European guideline for the diagnosis and treatment of gonorrhea in adults **(2020)**[11]	• Patients with gonorrhea should be advised to abstain from sexual contact (or if this is not possible to consistently use barrier contraception) for 14 days (seven days if ceftriaxone monotherapy) after they and their sexual partners have completed ceftriaxone plus azithromycin dual treatment and their symptoms have resolved [2D]. This is to limit possible re-exposure in the presence of residual azithromycin. • Patients (and their sexual partners) should be given information (verbal and written) about their infection, including details about transmission, prevention, complications, and treatment [1D].

	• Patients with verified gonorrhea (and their sexual contacts) are recommended to be offered testing for other STIs, e.g. including C. trachomatis, mycoplasma genitalium (only in symptomatic patients and always including macrolide resistance testing), syphilis, HBV, HCV, and HIV [1C]. **Recommended treatment for uncomplicated N. gonorrhoeae infections of the urethra, cervix and rectum in adults and adolescents when the antimicrobial susceptibility of the infection is unknown** • Ceftriaxone 1 g intramuscularly (IM) as a single dose together with azithromycin 2 g as a single oral dose [1C] • If gastrointestinal side effects are anticipated: ceftriaxone 1 g IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6–12h later may be used to limit gastrointestinal side effects OR • Ceftriaxone 1 g IM as a single dose [2C] NOTE: Only recommended in settings where: (i) comprehensive, recent and quality-assured local in vitro ceftriaxone susceptibility testing has shown lack of ceftriaxone resistance; (ii) TOC is mandatory; (iii) the patient is considered very likely to return for TOC; (iv) doxycycline 100 mg oral dose twice daily for 7 days is administered at the same time to cover any concomitant C. trachomatis infection, if C. trachomatis infection has not been excluded by NAAT. In other settings, ceftriaxone 1 g IM monotherapy is only an alternative option if azithromycin is not available or patient is unable to take oral medication. **Treatment when patient has history of severe hypersensitivity (e.g. anaphylaxis) to any b-lactam antimicrobial (penicillins,** **cephalosporins, monobactams or carbapenems** **Recommended treatment:** • Spectinomycin 2 g IM as a single dose [1B] together with azithromycin 2 g as a single oral dose [1C]

	• If gastrointestinal side effects are anticipated: spectinomycin 2 g IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6-12 h later may be used **Alternative treatment:** • Ciprofloxacin 500 mg as a single oral dose [1B] • Gentamicin 240 mg IMas a single dose together with azithromycin 2 g as a single oral dose [1B] • If gastrointestinal side effects are anticipated: gentamicin 240 mg IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6– 12 h later may be used **Treatment when administration of an intramuscular injection is contraindicated or refused** **Recommended treatment:** • Cefixime 400 mg as a single oral dose together with azithromycin 2 g as a single oral dose [1B] • If gastrointestinal side effects are anticipated: cefixime 400 mg single oral dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6-12 h later may be used **Alternative treatment:** • Ciprofloxacin 500 mg as a single oral dose [1B]. **Sexual contact notification and management of sex contact(s)** • Sexual contact notification should be performed and documented by appropriately trained professionals at the time of diagnosis to prevent reinfection and reduce onwards transmission [1B] • Sexual contacts should be contacted and offered (and encouraged to have) testing for gonorrhea (and other STIs) together with antimicrobial treatment if appropriate (i.e. if positive N. gonorrhoeae test or clinician considers contacts will not return for treatment after testing results are available) and receive counseling for gonorrhea and other STIs [1D] • All sexual contact(s) within the preceding 3 months of onset of symptoms or diagnosis should be tested and treated if positive [2D].
Addition of a new section:	**BV** Recommend 5–7 days of topical or oral metronidazole or seven days of intravaginal clindamycin

European (IUSTI/WHO) International Union against sexually transmitted infections (IUSTI) World Health Organisation (WHO) guideline on the management of vaginal discharge **(2018)**[16]	as first line for uncomplicated BV in women depending on personal choice and circumstances (Grade 1, quality of evidence: Grade A). **Recommended regimens for BV:** • Metronidazole 400–500 mg orally twice daily for 5–7 days Or • Intravaginal metronidazole gel (0.75%) once daily for five days Or • Intravaginal clindamycin cream (2%) once daily for seven days **Alternative regimens for BV**: • Metronidazole 2 g orally in a single dose or • Tinidazole 2 g orally in a single dose or • Tinidazole 1 g orally for five days or • Clindamycin 300 mg orally twice daily for seven days or • Dequalinium chloride 10 mg vaginal tablet one daily for six days **Recurrent BV** • Recommends current best treatment for persistent and recurrent BV in women is intravaginal metronidazole (Grade 2, quality of evidence: Grade B). • Recommends that the current best treatment for BV in pregnant women is clindamycin (Grade 2, quality of evidence: Grade C). **Management of sexual partners** Recommends that the current advice for women diagnosed with BV is that male sexual partners do not require treatment. Female partners may be treated if they have BV (Grade 2, quality of evidence: Grade B).
Addition of a	The antibiotics treatment should be based on local epidemiology and antibiotic susceptibility

new section: European guideline for the management of chancroid **(2017)**[22]	patterns. **Several antibiotic regimens have been recommended for confirmed cases of chancroid:** First line: • Ceftriaxone as a single intramuscular injection of 250 mg (Ib, A) or • Azithromycin, as a single 1 g oral dose, (Ib, A) Second line: • Ciprofloxacin 500 mg orally twice a day for three days (Ib, B), or • Erythromycin orally 500 mg four times a day for seven days (Ib, B) **Adjunctive therapy** • Patients with fluctuant buboes will experience symptomatic relief if these are emptied. Needle aspiration is effective but may need to be repeated. Incision and drainage is an alternative but some authorities believe that it may lead to sinus formation. Antibiotic cover is recommended if this is done (IV, C). • Sexual partners of patients who have chancroid should be examined and treated, regardless of whether symptoms of the disease are present, if they had sexual contact with the patient in the 10 days preceding the patient's onset of symptoms (IV, C).
Addition of a new guidelines: European guideline for the management of pelvic inflammatory disease **(2017)**[23]	**Information, explanation and advice for the patient** • Patients should be advised to avoid unprotected intercourse until they, and their partner(s), have completed treatment and symptoms have resolved (Evidence level IV, C). • A detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partner(s) should be provided, reinforced with clear and accurate written information. Appropriate information should include: fertility is usually well preserved in women with first-episode PID who receive prompt appropriate antimicrobial therapy the risk of impaired fertility increases significantly with each subsequent episode of PID (approximately) doubling with each new presentation

	the risk of impaired fertility is increased in clinically more severe PID chronic pelvic pain of varying severity affects around 30% of women following PID PID increases the relative risk of a subsequent pregnancy being an ectopic, but the absolute risk of ectopic pregnancy remains low at around 1% • Although laparoscopic division of hepatic adhesions has been performed in women with perihepatitis, there is insufficient clinical trial evidence to make specific recommendations for treatment beyond antibiotic therapy. Broad spectrum antibiotic therapy is required to cover N. gonorrhoeae, C. trachomatis and anaerobic infection. It is also desirable to include microbiological cover for other possible pathogens (e.g. M. genitalium, streptococci, staphylococci, E. coli, H. influenzae). The choice of an appropriate treatment regimen may be influenced by: · local antimicrobial sensitivity patterns · local epidemiology of specific infections in this setting · cost · patient preference and compliance · severity of disease **General measures include**: • rest is advised for those with severe disease (Evidence level IV, C) • if there is a possibility that the patient could be pregnant, a pregnancy test should be performed (Evidence level IV, C) • appropriate analgesia should be provided (Evidence level IV, C) • Admission for parenteral therapy, observation, further investigation and/or possible surgical intervention should be considered in the following situations (Evidence level IV, C): diagnostic uncertainty · clinical failure with oral therapy · severe symptoms or signs · presence of a tuboovarian abscess

	• inability to tolerate an oral regimen • pregnancy • In inpatients the treatment response can be monitored • by changes in C-reactive protein and white cell • count. In severe cases and cases with failure of the initial treatment, tuboovarian abscess should be excluded by vaginal ultrasonography, CT or MRI. • All patients should be offered testing for Chlamydia, gonorrhea, M. genitalium, syphilis and HIV (Evidence level IV, C). • It is likely that delaying treatment increases the risk • of long-term sequelae such as ectopic pregnancy, infertility and pelvic pain. Because of this, and the lack of definitive diagnostic criteria, a low threshold for empiric treatment of PID is recommended (Evidence level IV, C). **Recommended regimens** • Choice of treatment regimen should be influenced by the following: • Mild and moderate cases should be treated as outpatients with oral therapy (Evidence level Ib, A). • Intravenous therapy, when given, should be continued until 24 h after clinical improvement and then switched to oral (Evidence level IV, C). • Dosage recommendations may need to be adjusted depending on local licensing regulations and the availability of drug formulations, e.g. metronidazole may be dosed at 400 or 500 mg. • The optimal duration of treatment is not known but most clinical trials report a response to 10–14 days of therapy. • No difference in efficacy has been demonstrated between the recommended regimens. **Outpatient regimens** • i.m. ceftriaxone 500 mg single dose followed by oral doxycycline 100 mg twice daily plus metronidazole 500 mg twice daily for 14 days (Evidence level Ia, A)

	• oral ofloxacin 400 mg twice daily plus oral metronidazole 500 mg twice daily for 14 days (ofloxacin may be replaced by levofloxacina 500 mg once daily) (Evidence level Ib, A) • oral moxifloxacina 400 mg once daily for 14 days (Evidence level Ia, A) **Inpatient regimens** • i.v./i.m. ceftriaxone 1 g once daily plus i.v. doxycycline 100 mg twice daily (oral doxycycline may be used if tolerated) followed by • oral doxycycline 100 mg twice daily plus oral metronidazole 500 mg twice daily to complete 14 days (Evidence level Ia, A) • i.v. clindamycin 900 mg three times daily plus i.m./i.v. gentamicin (3–6 mg/kg as a single daily dose with renal monitoring) followed by either • (oral clindamycin 450 mg four times daily to complete 14 days) or (oral doxycycline 100mg twice daily plus oral metronidazole 500 mg twice daily to complete 14 days) (Evidence level Ia, A) **Alternative regimens** The evidence for alternative regimens is less robust than the regimens above. • i.v. ofloxacina 400 mg twice daily plus i.v. metronidazole 500 mg three times daily for 14 days (Evidence level Ib, A) • i.m. ceftriaxone 500 mg single dose plus oral azithromycin 1 g single dose followed by a second dose of oral azithromycin 1 g after one week (Evidence level Ib, A) **Partner notification** • Current partners of women with PID should be contacted and offered health advice and screening for gonorrhea and Chlamydia (and M. genitalium if the index patient is infected). Other recent sexual partners may also be offered screening – tracing of contacts within a six-month period of onset of symptoms is recommended but this time period is not evidence based and may be influenced by the sexual history, available resources or local practice

<table>
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Because many cases of PID are not associated with gonorrhea, Chlamydia or M. genitalium, broad spectrum empirical therapy should also be offered to male partners, e.g. doxycycline 100 mg twice daily for one week.
Partners should be advised to avoid unprotected intercourse until they and their partner have completed the treatment course.

</td></tr>
<tr><td>Addition of a new section:
Brazilian Protocol for Sexually Transmitted Infections, 2020: infections that cause cervicitis[8]</td><td>
<table>
<tr><td>chlamydia</td><td>Treatment</td></tr>
<tr><td>NON-complicated gonococcal infection (urethra, cervix, rectum, and pharynx)</td><td>Ceftriaxone 500mg, intramuscular (IM), a single dose plus Azithromycin 500mg, two pills, per os (PO), a single dose</td></tr>
<tr><td>Disseminated gonococcal infection</td><td>Ceftriaxone 1g, IM or intravenous (IV), per day, completing at least seven days of treatment plus Azithromycin 500mg, two pills, PO, a single dose</td></tr>
<tr><td>Chlamydia or mycoplasma infection</td><td>Azithromycin 500mg, two tablets, PO, a single dose or Doxycycline 100mg, PO, twice a day, for seven days (except pregnant women)a</td></tr>
</table>
</td></tr>
<tr><td>Addition of a new section:
Brazilian Protocol for Sexually Transmitted infections,</td><td>
<table>
<tr><td>Treatment</td><td>First option</td><td>Second option</td><td>Third option</td></tr>
<tr><td>Outpatient</td><td>Ceftriaxone 500mg, intramuscular (IM), single dose plus Doxycyclinea 100mg, 1 pill, per os</td><td>Cefotaxime 500mg, IM, single dose plus Doxycyclinea 100mg, 1 pill, PO, twice/day, for 14</td><td>-</td></tr>
</table>
</td></tr>
</table>

2020: pelvic inflammatory disease[18]		(PO), twice/day, for 14 days plus Metronidazoleb 250mg, 2 pills, PO, twice/day, for 14 days	days plus Metronidazoleb 250mg, two pills, PO, twice/day, for 14 days	
	Hospitalc	Ceftriaxone 1g, intravenous (IV), once/day, for 14 days plus Doxycyclinea 100mg, 1 pill, PO, twice/day, for 14 days plus Metronidazoleb 400mg, IV, each 12 hours	Clindamycin 900mg, IV, three times/day, for 14 days plus Gentamicind (IV or IM): 3-5mg/kg, once/day for 14 days	Ampicillin/sulbactam 3g, IV, each 6 hours, for 14 days plus Doxycyclinea 100mg, one pill, PO, twice/day, for 14 days
	• Treatment must start immediately, aiming at avoiding late complications, such as infertility, ectopic pregnancy, and chronic pelvic pain • Treatment of other common pelvic pain causes (ectopic pregnancy, acute appendicitis, ovarian cyst, and functional pain) is unlikely to be harmed by antimicrobial therapy for pelvic inflammatory disease. In addition to antibiotics, analgesic and anti-inflammatory drugs can be used for decreasing symptomatology. • Outpatient treatment applies to women that present light clinical pictures without signs of pelvic peritonitis • Pregnant women with pelvic inflammatory disease have a high risk of miscarriage, chorioamnionitis, and premature delivery, and they must be hospitalized and undergo intravenous broad-spectrum antibiotic treatment immediately. Doxycycline and			

<table>
<tr><td></td><td>quinolones are a contraindication during pregnancy</td></tr>
<tr><td>Addition of a new section: European guideline on the management of Mycoplasma genitalium infections (2021)[13]</td><td>
<table>
<tr><th>RECOMMENDATIONS</th><th>GRADE</th></tr>
<tr><td colspan="2">MANAGEMENT OF PATIENTS</td></tr>
<tr><td>Patients with M. genitalium infection should abstain from unprotected sexual contact until they and their partners have completed treatment, their symptoms have resolved and their test of cure (TOC) is negative</td><td>1D</td></tr>
<tr><td>Patients with M. genitalium infection (and their sexual contacts) should be given verbal and written information about the infection, including details about transmission, prevention and complications.</td><td>1D</td></tr>
<tr><td>Patients with M. genitalium infection should be screened for other STIs, including C. trachomatis, N. gonorrhoeae, syphilis and HIV, plus T. vaginalis where appropriate</td><td>1D</td></tr>
<tr><td>M. genitalium infections during pregnancy may be treated with azithromycin or pristinamycin. Treatment may be postponed until after delivery, but the neonate should be observed for signs of infection, primarily conjunctivitis and respiratory tract infection</td><td>1D</td></tr>
<tr><td colspan="2">INDICATIONS FOR THERAPY</td></tr>
<tr><td>Detection of M. genitalium-specific nucleic acid in a clinical specimen</td><td>1B</td></tr>
<tr><td>Current partners of M. genitalium-positive patients should be treated with the same antimicrobial as the index patient</td><td>1B</td></tr>
<tr><td colspan="2">THERAPY</td></tr>
<tr><td>Uncomplicated M. genitalium infection in the absence of macrolide resistance mutations or resistance testing</td><td></td></tr>
<tr><td>Azithromycin 500 mg on day one, then 250 mg od days 2-5 (oral)</td><td>1B</td></tr>
<tr><td>Josamycin 500 mg 3 times daily for 10 days (oral)</td><td>2C</td></tr>
</table>
</td></tr>
</table>

	Uncomplicated M. genitalium infection in the presence of macrolide resistance mutations	
	Moxifloxacin 400 mg od for 7 days (oral)	1B
	Second-line treatment for uncomplicated persistent M. genitalium infection after azithromycin treatment	
	Moxifloxacin 400 mg od for 7 days (oral)	1B
	Third-line treatment for persistent M. genitalium infection after azithromycin and moxifloxacin treatment	
	Pristinamycin 1 g four times daily for 10 days (oral), 75% cure	1B
	Minocycline 100 mg two times daily for 14 days (oral), 70% cure	2B
	Doxycycline 100 mg two times daily for 14 days (oral), 40% cure	2B
	Complicated M. genitalium infection (PID, epididymitis)	
	Moxifloxacin 400 mg od for 14 days (oral)	1C
	Partner notification	
	Current partner(s) should always be tested and treated with the same antimicrobial as the index patient	2B
	FOLLOW-UP AND TEST OF CURE	
	A TOC should be considered in all patients	2C
	TOC samples should be collected no earlier than three weeks after completion of treatment	1B
Addition of a new section: Australian STI Management Guidelines for use in Primary Care; Pelvic	Primary treatment choices: in the case of an infection, the recommended treatments differ depending on the severity. **For Mild to Moderate Cases (Outpatient Treatment):** - Ceftriaxone: 500 mg administered intramuscularly with 2 mL of 1% lignocaine, or 500 mg given intravenously as a single dose. - In addition to Ceftriaxone: - Metronidazole: Take 400 mg orally twice daily for 14 days.	

Inflammatory Disease (2021) [20]	- Doxycycline: Take 100 mg orally twice daily for 14 days. **For Severe Cases (Inpatient Treatment):** - Inpatient treatment is necessary for severe cases, and the options are as follows: - Ceftriaxone: Administer 2 g intravenously daily. - Alternatively, Cefotaxime: Administer 2 g intravenously three times daily. - Along with Ceftriaxone or Cefotaxime: - Azithromycin: Administer 500 mg intravenously daily. - Metronidazole: Administer 500 mg intravenously twice daily. **Treatment Recommendations:** • Commence treatment promptly based on a provisional diagnosis, without waiting for test results. • For patients who are breastfeeding or may not comply with a doxycycline regimen, consider substituting with Azithromycin 1g as a single oral dose, followed by another dose one week later. • Contemplate the removal of an intrauterine device (IUD) if there is no response to treatment within 48-72 hours. Weigh the decision in consideration of the risk of pregnancy and consider oral emergency contraception. • Think about admitting the patient if: - The diagnosis is uncertain. - A surgical emergency cannot be ruled out. - There is suspicion or a confirmed diagnosis of a pelvic abscess. - The patient is severely ill or does not respond to outpatient management. - There is intolerance to oral therapy. - The patient is pregnant or lacks stable housing. Other Immediate Measures: • Advise the patient to abstain from sexual intercourse for one week following treatment or until symptoms improve. • Provide rest and simple pain relief as needed, such as non-steroidal anti-inflammatory

	drugs or paracetamol. • Implement contact tracing.

Appendix C. PubMed Search Methodology Terms

Query	Filters	Search Details	Results
(Gonorrhea[MeSH Terms]) OR (Neisseria gonorrhoeae Infection[Title/Abstract])	Guideline, in the last 5 years	("gonorrhea"[MeSH Terms] OR "neisseria gonorrhoeae infection"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	2
(((Chlamydia Infections[MeSH Terms]) OR (Infections, Chlamydia[Title/Abstract])) OR (Chlamydia Infection[Title/Abstract])) OR (Infection, Chlamydia[Title/Abstract])	Guideline, in the last 5 years	("chlamydia infections"[MeSH Terms] OR "infections chlamydia"[Title/Abstract] OR "chlamydia infection"[Title/Abstract] OR "infection chlamydia"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	4
(((((((((Vaginosis, Bacterial[MeSH Terms]) OR (Bacterial Vaginitides[Title/Abstract])) OR (Vaginitides, Bacterial[Title/Abstract])) OR (Bacterial Vaginosis[Title/Abstract])) OR (Vaginitis, Nonspecific[Title/Abstract])) OR (Nonspecific Vaginitis[Title/Abstract])) OR (Bacterial Vaginoses[Title/Abstract])) OR (Vaginoses, Bacterial[Title/Abstract])) OR (Bacterial Vaginitis[Title/Abstract])) OR (Vaginitis, Bacterial[Title/Abstract])	Guideline, in the last 5 years	("vaginosis, bacterial"[MeSH Terms] OR (("Bacterial"[All Fields] OR "bacterially"[All Fields] OR "bacterials"[All Fields]) AND "Vaginitides"[Title/Abstract]) OR (("vagina"[MeSH Terms] OR "vagina"[All Fields] OR "vaginal"[All Fields] OR "vaginally"[All Fields] OR "vaginals"[All Fields] OR "Vaginitis"[MeSH Terms] OR "Vaginitis"[All Fields] OR "Vaginitides"[All Fields]) AND "Bacterial"[Title/Abstract]) OR "bacterial vaginosis"[Title/Abstract] OR "vaginitis nonspecific"[Title/Abstract] OR "nonspecific vaginitis"[Title/Abstract] OR "bacterial vaginoses"[Title/Abstract] OR ("Vaginoses"[All Fields] AND "Bacterial"[Title/Abstract]) OR "bacterial vaginitis"[Title/Abstract] OR "vaginitis bacterial"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	5
(Syphilis[MeSH Terms]) OR (Great Pox[Title/Abstract])	Guideline, in the last 5 years	("syphilis"[MeSH Terms] OR "great pox"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	1
Chancroid[MeSH Terms]	Guideline, in the last 5 years	("chancroid"[MeSH Terms]) AND ((y_5[Filter]) AND (guideline[Filter]))	0
((((((((((Pelvic Inflammatory Disease[MeSH Terms]) OR (Disease, Pelvic Inflammatory[Title/Abstract])) OR (Diseases, Pelvic	Guideline, in the last 5 years	("pelvic inflammatory disease"[MeSH Terms] OR "disease pelvic inflammatory"[Title/Abstract] OR "diseases pelvic inflammatory"[Title/Abstract] OR	10

Inflammatory[Title/Abstract])) OR (Inflammatory Diseases, Pelvic[Title/Abstract])) OR (Pelvic Inflammatory Diseases[Title/Abstract])) OR (Inflammatory Pelvic Disease[Title/Abstract])) OR (Disease, Inflammatory Pelvic[Title/Abstract])) OR (Diseases, Inflammatory Pelvic[Title/Abstract])) OR (Inflammatory Pelvic Diseases[Title/Abstract])) OR (Pelvic Diseases, Inflammatory[Title/Abstract])) OR (Pelvic Disease, Inflammatory[Title/Abstract])) OR (Inflammatory Disease, Pelvic[Title/Abstract])) OR (Adnexitis[Title/Abstract])		"inflammatory diseases pelvic"[Title/Abstract] OR "pelvic inflammatory diseases"[Title/Abstract] OR "inflammatory pelvic disease"[Title/Abstract] OR (("Disease"[MeSH Terms] OR "Disease"[All Fields] OR "Diseases"[All Fields] OR "disease s"[All Fields] OR "diseased"[All Fields]) AND "inflammatory pelvic"[Title/Abstract]) OR "diseases inflammatory pelvic"[Title/Abstract] OR "inflammatory pelvic diseases"[Title/Abstract] OR (("pelvics"[All Fields] OR "pelvis"[MeSH Terms] OR "pelvis"[All Fields] OR "Pelvic"[All Fields]) AND "diseases inflammatory"[Title/Abstract]) OR (("pelvics"[All Fields] OR "pelvis"[MeSH Terms] OR "pelvis"[All Fields] OR "Pelvic"[All Fields]) AND "disease inflammatory"[Title/Abstract]) OR "inflammatory disease pelvic"[Title/Abstract] OR "Adnexitis"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	
Mycoplasma genitalium[MeSH Terms]	Guideline, in the last 5 years	("mycoplasma genitalium"[MeSH Terms]) AND ((y_5[Filter]) AND (guideline[Filter]))	3
((Granuloma Inguinale[MeSH Terms]) OR (Granuloma Venereum[Title/Abstract])) OR (Donovanosis[Title/Abstract])	Guideline, in the last 5 years	("granuloma inguinale"[MeSH Terms] OR "granuloma venereum"[Title/Abstract] OR "Donovanosis"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	0
(Urethritis[MeSH Terms]) OR (Urethritides[Title/Abstract])	Guideline, in the last 5 years	("urethritis"[MeSH Terms] OR "Urethritides"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	0
Uterine Cervicitis[MeSH Terms]	Guideline, in the last 5 years	("uterine cervicitis"[MeSH Terms]) AND ((y_5[Filter]) AND (guideline[Filter]))	0
(Epididymitis[MeSH Terms]) OR (Epididymitides[Title/Abstract])	Guideline, in the last 5 years	("epididymitis"[MeSH Terms] OR "Epididymitides"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	0

Appendix D. Bacterial Genital Tract Infections Treatment Algorithm

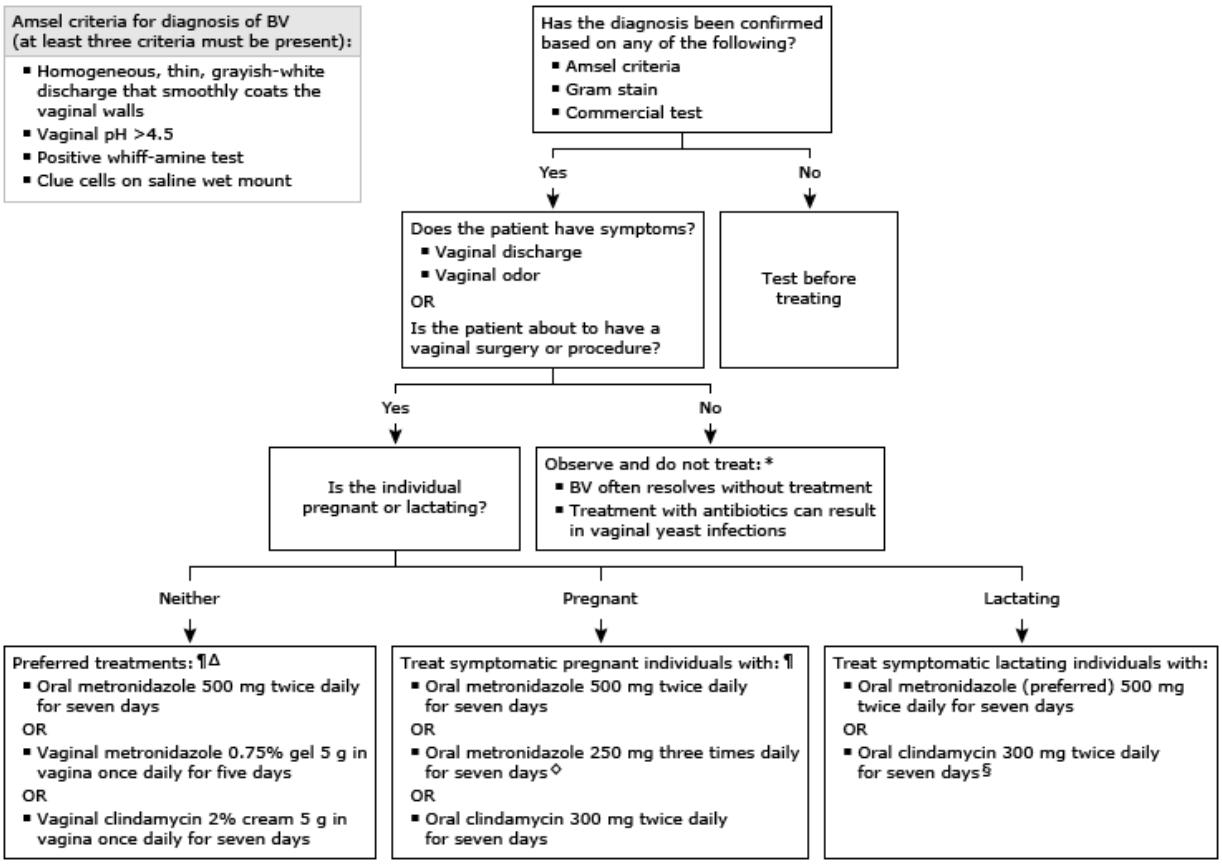


Figure 1. Treatment Algorithm for Bacterial Vaginosis

* We do not routinely treat asymptomatic individuals, including pregnant and lactating persons. However, others may reasonably elect to treat asymptomatic pregnant individuals as the supporting data conflict, particularly for those with a history of preterm birth.

¶ As treatment efficacy is similar between metronidazole and clindamycin, the choice of medication is based on availability, patient preference, side effects, cost, and history of response or adverse reactions.

Δ For additional treatment options, please refer to related UpToDate content on treatment of bacterial vaginosis.

◊ Pregnant individuals who are unable to tolerate metronidazole 500 mg twice daily because of gastrointestinal symptoms may be able to tolerate metronidazole 250 mg three times daily.

§ Breastfeeding infants may develop side effects from maternal clindamycin treatment and should be monitored for possible symptoms, including diarrhea, candidiasis (thrush, diaper rash), or rarely, colitis.

¥ Until definitive data are available, we treat patients who have undergone gender-affirming surgery based on their revised anatomy. As example, patients with neo-vaginas are treated as female and those with neophalluses are treated as male.

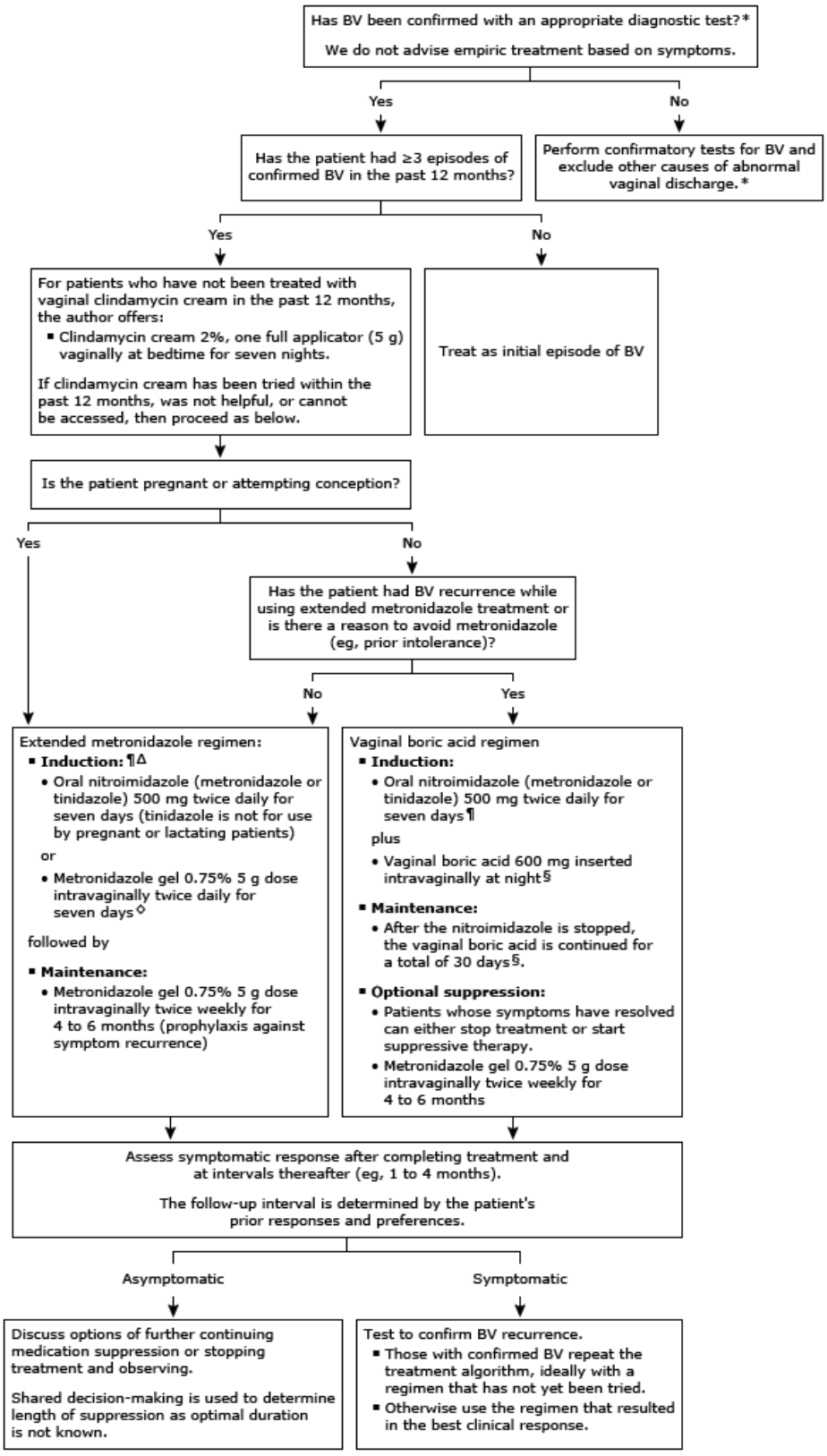
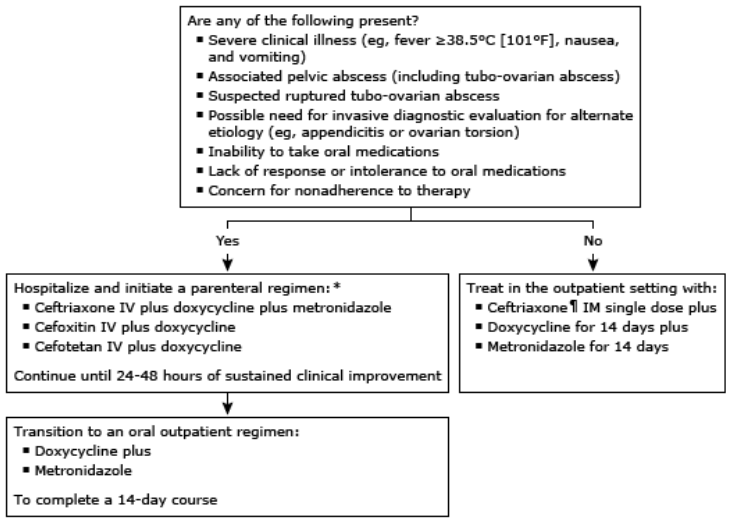


Figure 2. Treatment Algorithm for Recurrent Bacterial Vaginosis

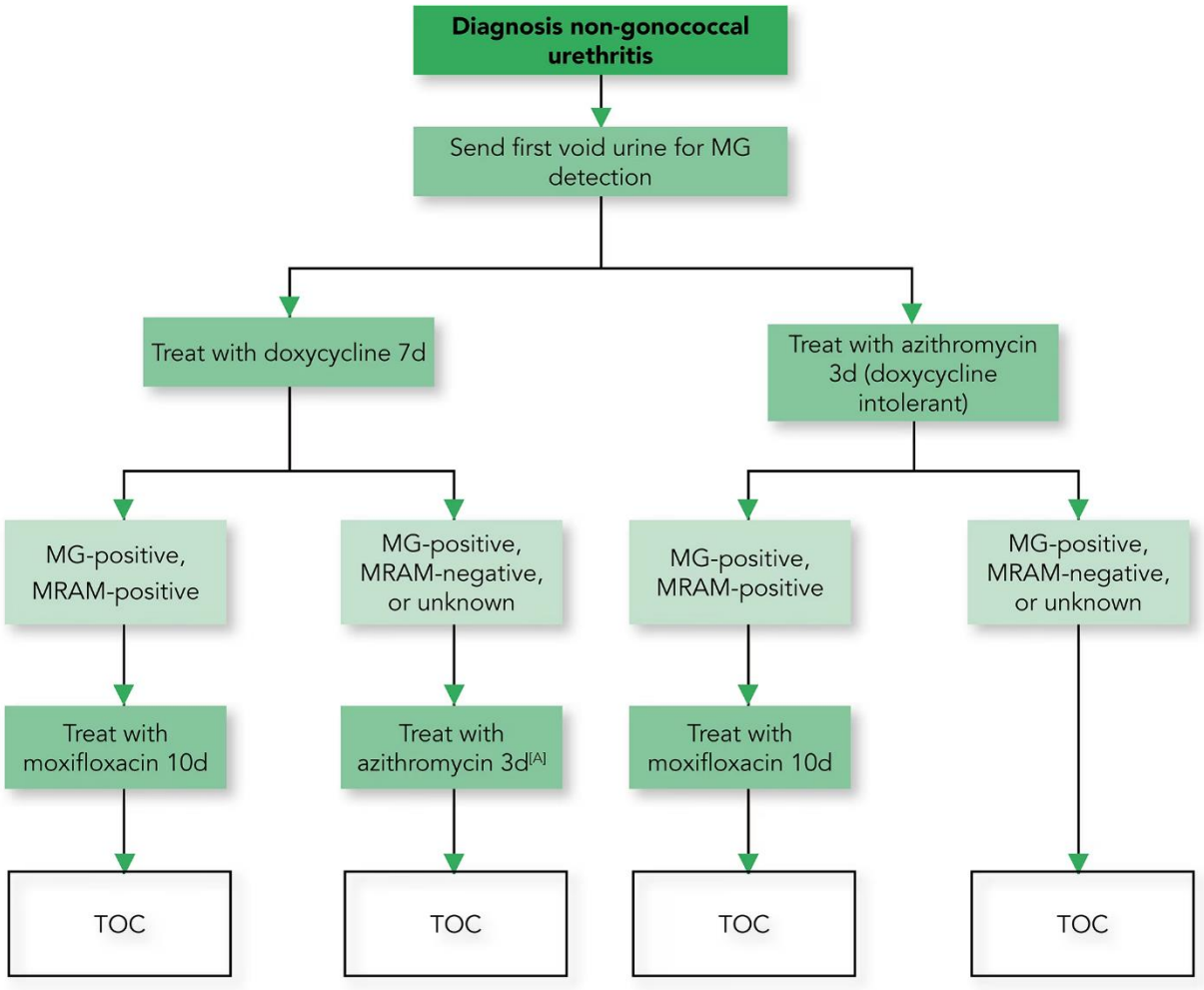
* Discussion of testing options to confirm bacterial vaginosis and/or other causes of abnormal vaginal discharge are presented in related UpToDate content on abnormal vaginal discharge.
¶ Choice of metronidazole or tinidazole is based on prior patient response (if any), availability, and cost.
Δ If response to a drug was inadequate in the past, then we select a different drug if available.
◊ Patients often prefer oral rather than vaginal treatment but both are effective.
§ **Critical warning:** Boric acid is for **vaginal** use only. Boric acid can cause death if taken orally. Commercially available vaginal suppository preparation is preferred but compounded products are an acceptable alternative. Vaginal boric acid should not be used by people who are pregnant or attempting conception. Boric acid should be stored safely away from children. Optimal treatment duration is not known.



Dosing of antimicrobials	
Ceftriaxone IV	1 g intravenously every 24 hours
Cefoxitin IV	2 g intravenously every 6 hours
Cefotetan IV	2 g intravenously every 12 hours
Ceftriaxone IM	500 mg intramuscularly once (if <150 kg)
	1 g intramuscularly once (if ≥150 kg)
Doxycycline$^{\Delta}$	100 mg orally twice daily
Metronidazole$^{\Delta}$	500 mg orally twice daily

Figure 3. Antimicrobial therapy for pelvic inflammatory disease in adults and adolescents

This algorithm represents our approach to antimicrobial selection for nonpregnant patients with PID. Treatment should be tailored to the individual. Refer to other UpToDate content on PID therapy for details on and doses for alternative regimens, including management of PID in pregnant individuals (which is uncommon).
PID: pelvic inflammatory disease; IM: intramuscular; IV: intravenous.
* Alternative regimens include clindamycin plus gentamicin, ampicillin-sulbactam plus doxycycline, and if *Neisseria gonorrhoeae* has been ruled out, azithromycin plus metronidazole. Because of various drawbacks, we reserve these for patients who cannot take preferred regimens.
¶ We prefer ceftriaxone because it has the best and most established activity against *N. gonorrhoeae*. Other appropriate long-acting intramuscular cephalosporins include cefoxitin (with probenecid), cefotaxime, and ceftizoxime.
Δ Doxycycline and metronidazole can also be given intravenously at the same doses for those who cannot take oral medications.



Abbreviations: azithromycin 3d=azithromycin 1 g, then 500 mg once daily for 2 days; doxycycline 7d=doxycycline 100 mg twice daily for 7 days; MG=*Mycoplasma genitalium*; moxifloxacin 10d=moxifloxacin 400 mg once daily for 10 days; MRAM=macrolide resistance-associated mutation; TOC=test of cure

[A] Azithromycin 3d should be started within 2 weeks of finishing doxycycline

Figure 4. Treatment Pathway for Men Presenting with Non-gonococcal Urethritis Who Subsequently Test Positive for M. Genitalium

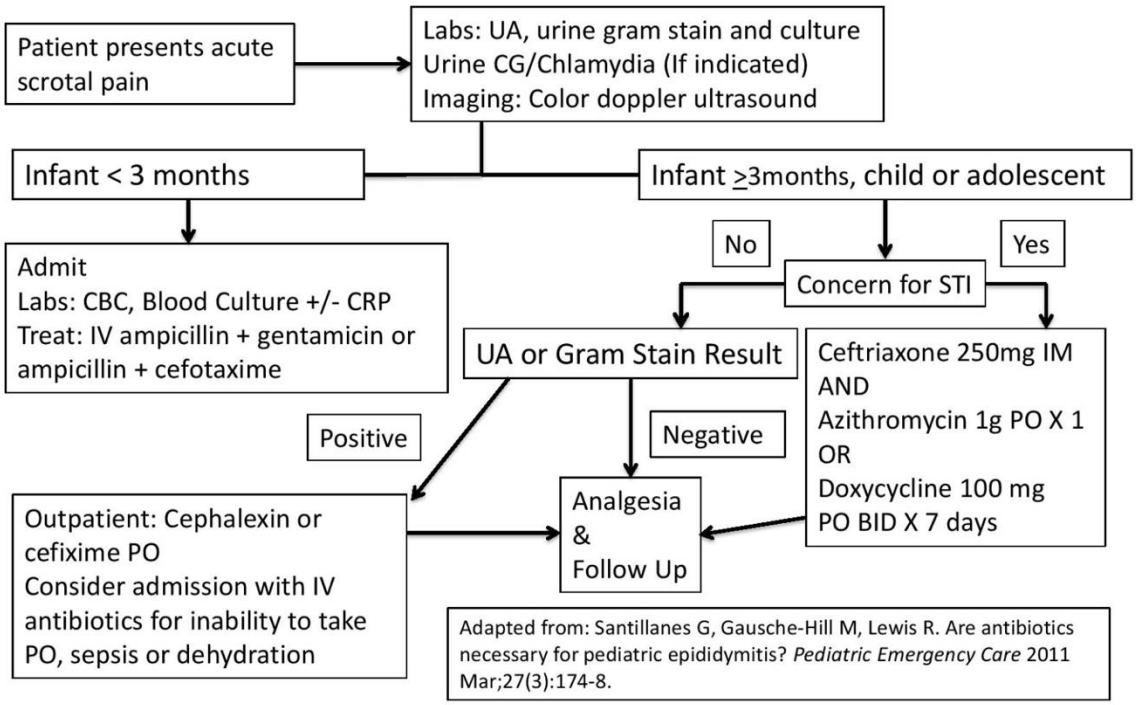


Figure 5. Epididymitis treatment algorithm for infants, children and adolescents

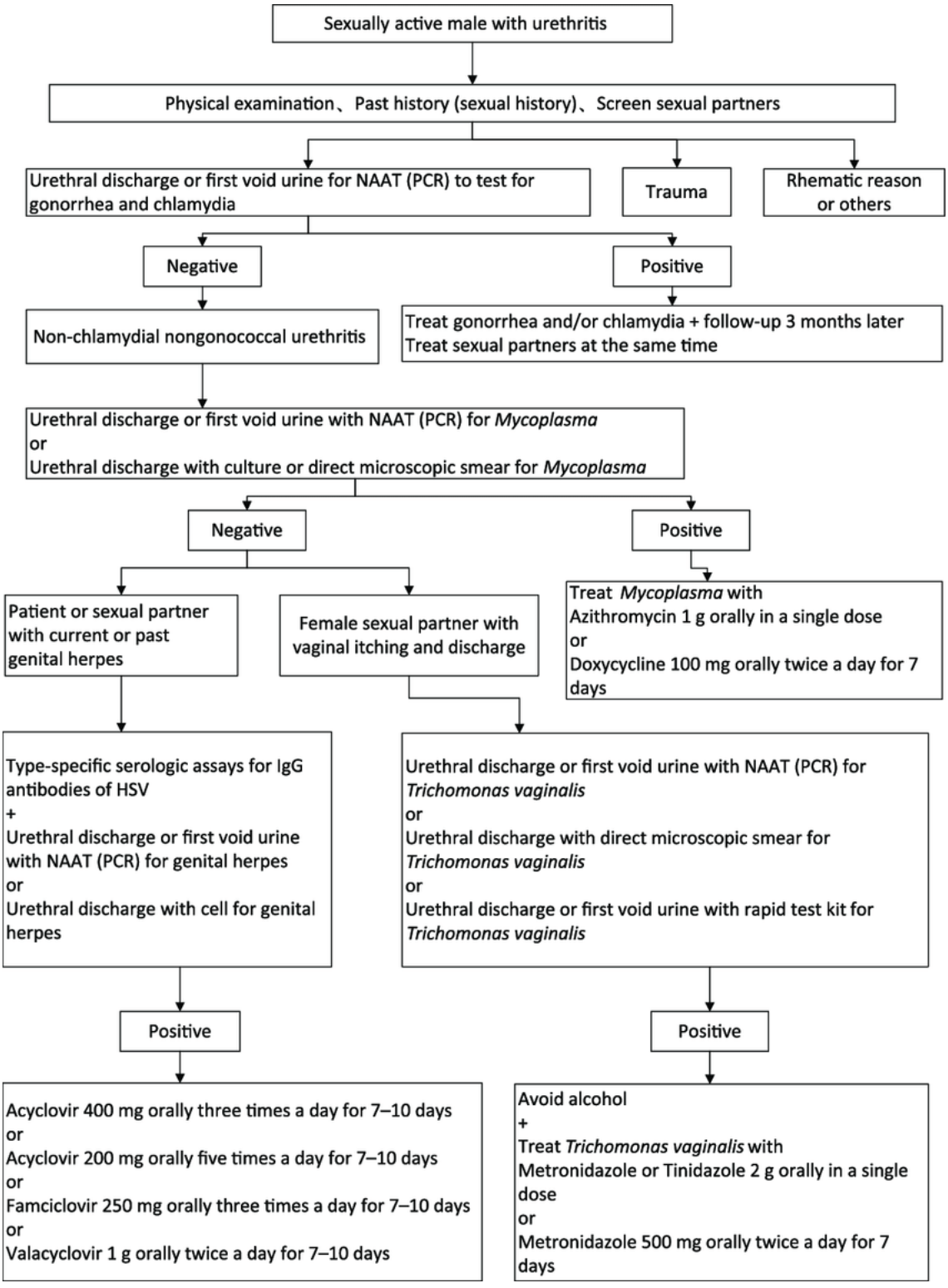
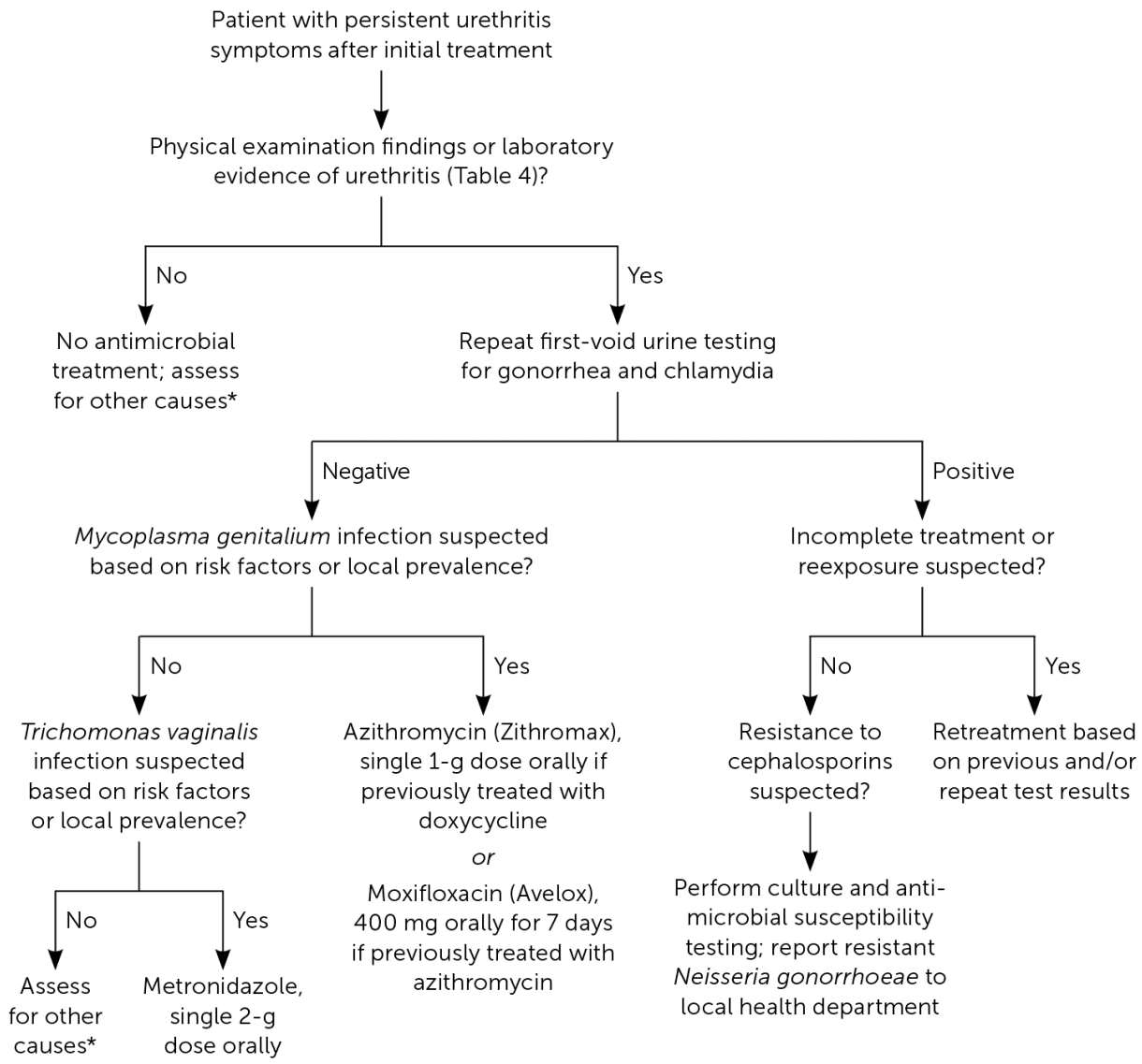


Figure 6. Treatment algorithm for Non-chlamydial nongonococcal urethritis in men



*—For all patients with persistent urethritis symptoms, consider:

- Workup for chronic prostatitis/chronic pelvic pain syndrome
- Obtaining a urethral specimen for herpes simplex virus culture
- Consulting a urologist, an infectious disease specialist, or an experienced colleague

Figure 7. Evaluation and treatment of patients with persistent urethritis symptoms after initial treatment

Figure 8. Management of syphilis

*--Alternative treatments for nonpregnant penicillin-allergic patients: doxycycline (Vibramycin), 100 mg taken orally twice daily for 2 weeks, or tetracycline, 500 mg taken orally four times daily for 2 weeks; limited data support efficacy for ceftriaxone (Rocephin), 1 g once daily IM or IV for 8 to 10 days, or azithromycin (Zithromax), 2 g orally (single dose).

†--Alternative treatments for nonpregnant penicillin-allergic patients: doxycycline, 100 mg taken orally twice daily for 4 weeks, or tetracycline, 500 mg taken orally four times daily for 4 weeks.