# PSORIASIS

CHI Formulary Indication Review

مجلس الضمان الصحي
Council of Health Insurance

**INDICATION UPDATE**

**ADDENDUM- December 2023**

**To the CHI Original Clinical Guidance- Issued Psoriasis February 2020**

# Contents

## Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

## List of Tables



## List of Figures

# Abbreviations

| | |
|---|---|
| AAD | American Academy of Dermatology |
| bDMARD | Biological DMARD |
| BSA | Body Surface Area |
| CADTH | Canadian Agency for Drugs and Technologies in Health |
| CHF | Congestive Heart Failure |
| CHI | Council of Health Insurance |
| csDMARD | Conventional Synthetic DMARD |
| DLQI | Dermatology Life Quality Index |
| DMARD | Disease-Modifying Antirheumatic Drug |
| FAE | Fumaric Acid Esters |
| GPP | Good Practice Point |
| HAS | Haute Autorite de Sante |
| HTA | Health Technology Assessment |
| IBD | Inflammatory Bowel Disease |
| IDF | Insurance Drug Formulary |
| JAK | Janus Kinase |
| JAKi | JAK Inhibitor |
| LTBI | Latent Tuberculosis Infection |
| MS | Multiple Sclerosis |
| MTX | Methotrexate |
| NB-UVB | Narrow-band ultraviolet B |
| NPF | National Psoriasis Foundation |
| PASI | Psoriasis Area and Severity Index |

| | |
|---|---|
| PDE4 | Phosphodiesterase-4 |
| PGA | Physician Global Assessment |
| PMDA | Pharmaceuticals and Medical Devices Agency |
| PsA | Psoriatic Arthritis |
| PSI | Psoriasis Symptom Inventory |
| SFDA | Saudi Food and Drug Authority |
| SPC | Summary of Product Characteristics |
| TNF | Tumor Necrosis Factor |
| TNFi | TNF inhibitors |
| tsDMARD | Targeted Synthetic DMARD |

# Executive Summary

Psoriasis is a chronic proliferative and inflammatory condition of the skin. It is characterized by erythematous plaques covered with silvery scales, particularly over the extensor surfaces, scalp, and lumbosacral region.

The disorder can also affect the joints and eyes. Psoriasis has no cure and the disease waxes and wanes with flareups. Many patients with psoriasis develop depression as the quality of life is poor. There are several subtypes of psoriasis, but the plaque type is the most common and presents on the trunk, extremities, and scalp. Close examination of the plaques usually reveals white silvery scales. The eye is involved in about 10% of patients, mostly women. In general, the eye is rarely involved alone; it is almost always associated with skin features[1].

Signs and symptoms of psoriasis include worsening of a long-term erythematous scaly area, sudden onset of many small areas of scaly redness, pain (especially in erythrodermic psoriasis and in some cases of traumatized plaques or in the joints affected by psoriatic arthritis), pruritus (especially in eruptive, guttate psoriasis), afebrile (except in pustular or erythrodermic psoriasis, in which the patient may have high fever), dystrophic nails, which may resemble onychomycosis, long-term, steroid-responsive rash with recent presentation of joint pain, joint pain (psoriatic arthritis) without any visible skin findings, conjunctivitis or blepharitis[2].

The exact etiology is unknown, but it is thought to be an autoimmune disease mediated by T lymphocytes. There is an association of HLA antigens seen in many psoriatic patients, particularly in various racial and ethnic groups. Familial occurrence suggests its genetic predisposition. Injury in the form of mechanical, chemical, and radiational trauma induces lesions of psoriasis. Certain drugs like chloroquine, lithium, beta-blockers, steroids, and non-steroidal anti-inflammatory drugs (NSAIDs) can worsen psoriasis. Generally, summer improves psoriasis while winter aggravates it. Apart from the above factors' infections, psychological stress, alcohol, smoking, obesity, and hypocalcemia are other triggering factors for psoriasis[1].

Usually, diagnosis is made by clinical morphology and site of lesions. Histopathology is rarely necessary but may help to differentiate psoriasis from another dermatosis if the diagnosis is not easy. Characteristic changes in biopsy show parakeratosis, micro-abscess, the absence of granular lesions, regular elongation of ridges in the form of camel foot appearance, and spongiform pustules of Kogoj with dilated and tortuous capillaries in the dermal papilla[1].

Laboratory studies[1]

- CBC, renal, and liver function tests.
- Rheumatoid factor
- ESR may be elevated in erythrodermic and pustular psoriasis.
- Uric acid levels are high in psoriasis.
- If only hand and feet are involved, obtain scrappings for fungal studies
- Pregnancy test
- Hepatitis serology
- PPD (Purified Protein Derivative)

Complications of psoriasis include secondary infections, poor cosmesis, psoriatic arthritis, risk of lymphoma, increased risk of adverse cardiac events[1].

The global psoriasis prevalence rate is around 2–3% of the world population, reaching 8–11% in some Northern European countries[3]. In general, psoriasis burden is greatest in the age group of 60–69 years, with a relatively similar burden among men and women. The burden is disproportionately greater in high-income and high SDI index countries of North America and Europe. With advances in psoriasis therapeutics, objective evaluation of psoriasis disease burden is critical to track the progress at the population level[3].

The prevalence of psoriasis in the Kingdom of Saudi Arabia (KSA) varies from province to province with time, and there has been a continuous increasing trend in recent years. The highest reported to be 5.33% in Al-jouf (northern region). In the last decade, various studies have demonstrated the pattern of skin-related conditions in several parts of Saudi Arabia, including Asir, Riyadh, Madinah, Jeddah, Al-Khobar, Al-Baha, Qassim, Hail, Abha, Najran and Qunfudah, spanning the eastern and western province and southwestern Saudi Arabia. However, large-scale epidemiological studies on cutaneous manifestations of psoriasis in Saudi Arabia remain rare. In eastern and southwestern Saudi Arabia, psoriasis prevalence is estimated to be 1.5% and 3.4%. However, a study by Al-Saeed et al demonstrated a much lower prevalence of psoriasis (0.3%) in women. Later, Al-Hoqail et al reported a higher prevalence of psoriasis among women (3.2%) and men (5.5%). Following this, Alshamrani et al reported a total of 5.1% prevalence of psoriasis among Saudis[4].

Psoriasis Area Severity Index (PASI) is the most widely used measurement tool which assesses the severity of the condition and allows for the evaluation of treatment efficiency. Topical therapy is used in mild to moderate psoriasis. Emollients and moisturizers may help in improving barrier function and retain the hydration of the stratum corneum. Topical agents used are coal tar, dithranol, corticosteroids, vitamin D analog, and retinoids are used initially[1].

- In patients who do not respond to the above treatments, methotrexate can be effective[1].
- Cyclosporine can be used to induce a clinical response, but its use should be intermittent[1].
- When patients fail to respond to methotrexate, switch to biological agents; in some cases, combine with methotrexate[1].

Phototherapy includes PUVA therapy which combines psoralen (P) with exposure to ultraviolet A (UVA) light, as well as NBUVB (narrowband UVB light) with a range of 311 nanometers to 313 nanometers. NBUVB is equally effective without the side effects of psoralen like gastrointestinal upset, cataract formation, and carcinogenic effects. It can safely be given to children, pregnant and lactating females, and even older patients. Guttate psoriasis has been known to respond best to phototherapy[1].

Systemic drugs are used in extensive cases, the involvement of nails and psoriatic arthritis. Methotrexate, retinoids, cyclosporine, and fumarates are possible options. Routine blood, liver functions, and renal functions should be monitored in patients on systemic therapy[1].

Biologicals are manufactured proteins that interrupt the immune process in psoriasis which are infliximab, adalimumab, etanercept, and interleukin antagonists. Before starting any biological agent, the patient should be worked up for tuberculosis and hepatitis. There is a serious risk of infections in these patients and all precautions should be taken that the patient is not severely immunocompromised[1].

Prolonged use of steroids and other immunosuppressives may delay wound healing[1].

Ocular psoriasis requires aggressive treatment with topical corticosteroids[1].

Patients with psoriasis should avoid all skin trauma for fear of inducing the Kobner reaction. In addition, psoriatic patients should avoid the use of beta-blockers, chloroquine, or NSAIDs. They should also avoid alcohol because of the risk of developing fatty liver[1].

**CHI issued Psoriasis guidelines in Feb 2020 updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations. Below is a description of sections that need updates.**

**This report functions as an addendum to the prior CHI Psoriasis clinical guidance** and seeks to offer guidance for the effective management of **Psoriasis**. It provides an **update on the Psoriasis 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 **new guidelines** added to the report such as the Joint American Academy of Dermatology National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies (2020), the Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures (2021), the EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies (2019), the Saudi consensus statement on biologic treatment of chronic plaque psoriasis (2020), the EuroGuiDerm – Part 1: Treatment goals and treatment recommendations (2021), and the Japanese guidance for use of biologics for psoriasis (2019), British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update.

**After carefully examining clinical guidelines and reviewing the SFDA drug list, there are new SFDA registered drugs to include in the CHI formulary**; ***Bimekizumab***, ***Tildrakizumab*** **while removing** Alclometasone Ointment as it is no longer registered on the SFDA Drug List of December 2023. There have been new drugs that received FDA approval; ***Roflumilast, Deucravacitinib.***

There have been no changes and updates made to the previously listed drugs in terms of drug information and prescribing edits since February 2020.

**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 Psoriasis therapeutic management**.

Below is a table summarizing the major changes based on the different Psoriasis guidelines used to issue this report:

**Table 1.** General Recommendations for the Management of Psoriasis

| Management of Psoriasis | | |
|---|---|---|
| **General Recommendations** | **Level of Evidence/Grade of Recommendation** | **Reference** |
| *Topical corticosteroids*<br>• The use of class 1, class 2, and class 3-5 topical corticosteroids for up to 4 weeks is recommended for the treatment of plaque psoriasis not involving intertriginous areas.<br>• The use of class 1-7 topical corticosteroids for a minimum of 4 | A | Joint AAD-NPF Guidelines (2020) |

| | | |
|---|---|---|
| weeks is recommended as initial and maintenance treatment of scalp psoriasis. | | |
| The use of topical corticosteroids for > 12 weeks can be considered if done under the careful supervision of a physician. | C | Joint AAD-NPF Guidelines (2020) |
| *Topical pimecrolimus and tacrolimus*<br>The off-label use of 0.1% tacrolimus for psoriasis involving the face as well as inverse psoriasis for up to 8 weeks can be considered.<br>The off-label use of pimecrolimus for inverse psoriasis for 4-8 weeks is recommended. | B | Joint AAD-NPF Guidelines (2020) |
| The long-term use of topical vitamin D analogues (up to 52 weeks), including calcipotriene/ calcipotriene, calcitriol, tacalcitol, and maxacalcitol, is recommended for the treatment of mild to moderate psoriasis.<br>Use of calcipotriene foam and calcipotriene plus betamethasone dipropionate gel is recommended for 4-12 weeks for the treatment of mild to moderate scalp psoriasis.<br>Use of combination treatments with vitamin D analogues and potent class II and class III topical corticosteroids up to 52 weeks is recommended for the treatment of psoriasis.<br>Use of combination products with calcipotriol and corticosteroids is recommended for the treatment of psoriasis. | A | Joint AAD-NPF Guidelines (2020) |
| *Topical tazarotene*<br>The use of mid- or high-potency topical corticosteroid in combination with tazarotene for 8- 16 weeks is more effective than monotherapy | A | Joint AAD-NPF Guidelines (2020) |

| | | |
|---|---|---|
| with tazarotene and is recommended for the treatment of mild to moderate psoriasis.<br>The use of topical corticosteroids along with tazarotene is recommended to decrease the duration of treatment as well as increase the length of remission | | |
| Topical **salicylic acid** can be used for 8-16 weeks for the treatment of mild to moderate psoriasis | B | Joint AAD-NPF Guidelines (2020) |
| Topical **anthralin** for 8- 12 weeks can be used for the treatment of mild to moderate psoriasis. Short contact (up to 2 hours per day) anthralin is recommended to limit adverse side effects | B | Joint AAD-NPF Guidelines (2020) |
| Coal tar preparations are recommended for the treatment of mild to moderate psoriasis. | A | Joint AAD-NPF Guidelines (2020) |
| The addition of an ultrahigh potency (class 1) topical corticosteroid to standard dose etanercept for 12 weeks is recommended for the treatment of moderate to severe psoriasis. | A | Joint AAD-NPF Guidelines (2020) |
| We suggest using apremilast if an oral treatment is desired and “conventional” systemic agents led to an inadequate response or are contraindicated or not tolerated. | (↑), Strong consensus, consensus based. | EuroGuiDerm guidelines on the treatment of Psoriasis vulgaris (2021) |

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

# Section 1.0 Summary of Reviewed Clinical Guidelines & Evidence

This section is divided into two parts: the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Psoriasis report, and the second includes **newly added guidelines** that have helped generate this report.

## 1.1 Revised Guidelines

This section contains the **updated versions** of the guidelines mentioned in the February 2020 CHI Psoriasis Report and the corresponding recommendations:

**Table 2.** Guidelines Requiring Revision

| **Guidelines Requiring Revision** | |
|---|---|
| **Old Versions** | **Updated versions** |
| **Section 1.1** Clinical NICE Psoriasis: assessment and management Clinical guideline [CG153] (published 2012 last update **2017**) | N/A* |
| **Section 1.2** Joint American Academy of Dermatology-National Psoriasis Foundation (AAD-NPF) guidelines of care for the management and treatment of psoriasis with biologics **(2019)** | N/A* |
| **Section 1.3** Saudi practical guidelines on biologic treatment of psoriasis **(2014)** | N/A* |
| **Section 1.4** Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients **(2020)** | N/A* |

*: *No updated versions available*

## 1.2 Additional Guidelines

This part includes the added guidelines to the previous CHI Psoriasis report, along with their recommendations.

**Table 3.** List of Additional Guidelines

| Additional Guidelines |
|---|
| Joint **AAD-NPF** Guidelines of Care for the Management and Treatment of Psoriasis with **Topical Therapy and Alternative Medicine Modalities** for Psoriasis Severity Measures (**2020**) |
| Joint **AAD-NPF** Guidelines of Care for the Management of Psoriasis with **Systemic Nonbiologic Therapies** (**2020**) |
| **EuroGuiDerm** Guideline on the Systemic Treatment of Psoriasis Vulgaris – Part 1: **Treatment and Monitoring** Recommendations (**2020**) |
| **EuroGuiDerm** Guideline on the Systemic Treatment of Psoriasis Vulgaris – Part 2: **Specific Clinical and Comorbid Situations** (**2020**) |
| **Saudi Consensus Statement** on Biologic Treatment of Chronic Plaque Psoriasis (**2020**) |
| **British Association of Dermatologists** (BAD) Guidelines for Biologic Therapy for Psoriasis (**2020**): A Rapid Update |

### 1.2.1 American Academy of Dermatology (AAD)-National Psoriasis Foundation (NPF)

The American Academy of Dermatology (AAD) and the National Psoriasis Foundation (NPF) jointly published a series of clinical guidelines for the management of psoriasis. These include guidelines of care for the management and treatment of psoriasis with biologics (detailed in section 1.2 of the previous CHI report) and the management and treatment of psoriasis in pediatric patients (section 1.4 of the previous CHI report), the use of topical therapy and alternative medicine modalities (section 1.2.1.1 below), treatment with biologic agents (section 1.2.1.2 below).

Grading of recommendations issued by the AAD-NPF guidelines is done as in table 4:

**Table 4.** AAD-NPF Levels of Evidence and Grade of Recommendations

| Evidence and Grading of recommendations | |
|---|---|
| **Evidence was graded using a 3-point scale based on the quality of methodology (e.g., randomized control trial, case-control, prospective/retrospective cohort, case series, etc.) and the overall focus of the study (i.e., diagnosis, treatment/prevention/screening, or prognosis) as follows:** | |
| **I** | Good-quality patient-oriented evidence (i.e., evidence measuring outcomes that matter to patients: morbidity, mortality, symptom improvement, cost reduction, and quality of life) |
| **II** | Limited-quality patient-oriented evidence |
| **III** | Other evidence, including consensus guidelines, opinion, case studies, or disease-oriented evidence (i.e., evidence measuring intermediate, physiologic, or surrogate end points that may or may not reflect improvements in patient outcomes) |
| **Clinical recommendations were developed on the best available evidence tabled in the guideline. These are ranked as follows:** | |
| **A** | Recommendation based on consistent and good quality patient-oriented evidence |
| **B** | Recommendation based on inconsistent or limited quality patient-oriented evidence |
| **C** | Recommendation based on consensus, opinion, case studies, or disease-oriented evidence |

#### 1.2.1.1 Joint AAD-NPF Guidelines of Care for the Management and Treatment of Psoriasis with Topical Therapy and Alternative Medicine Modalities for Psoriasis Severity Measures (2020)

The Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities recommendations are outlined below[5]:

**I. TOPICAL AGENTS**

***Topical corticosteroids***

- The use of class 1, class 2, and class 3-5 topical corticosteroids for up to 4 weeks is recommended for the treatment of plaque psoriasis not involving intertriginous areas (A).
- The use of class 1-7 topical corticosteroids for a minimum of up to 4 weeks is recommended as initial and maintenance treatment of scalp psoriasis (A).

- The use of topical corticosteroids for > 12 weeks can be considered if done under the careful supervision of a physician (C).

**Table 5.** Classification of Topical Corticosteroid

| WHO potency group | Classification | Topical corticosteroid |
|---|---|---|
| **Super-potent Ultrahigh** | Class 1 | 1. Augmented betamethasone dipropionate 0.05%[a,b]<br>2. Clobetasol propionate 0.05%[a,b,c,d,e,f,g,h,i]<br>3. Desoximetasone 0.25%[h]<br>4. Augmented diflorasone diacetate 0.05%[a]<br>5. Fluocinonide 0.1%[c]<br>6. Flurandrenolide 4 µg/cm2[j]<br>7. Halobetasol propionate 0.05%[a,c] |
| **High** | Class 2 | 1. Amcinonide 0.1%[a]<br>2. Betamethasone dipropionate 0.05%[a]<br>3. Augmented betamethasone dipropionate 0.05%[c,d]<br>4. Desoximetasone 0.25%[a,c]<br>5. Desoximetasone 0.05%[b]<br>6. Augmented diflorasone diacetate 0.05%[c]<br>7. Diflorasone diacetate 0.05%[a]<br>8. Fluocinonide 0.05%[a,b,c,f]<br>9. Halcinonide 0.1%[a,c]<br>10. Mometasone furoate 0.1%[a]<br>11. Triamcinolone acetonide 0.5%[a] |
| | Class 3 | 1. Amcinonide 0.1%[c,d]<br>2. Betamethasone dipropionate 0.05%[c,k]<br>3. Betamethasone valerate 0.1%[a]<br>4. Betamethasone valerate 0.12%[l]<br>5. Diflorasone diacetate 0.05%[c]<br>6. Fluticasone propionate 0.005%[a]<br>7. Triamcinolone acetonide 0.1%[a]<br>8. Triamcinolone acetonide 0.5%[c] |
| **Moderate (medium)** | Class 4 | 1. Betamethasone valerate 0.12%[l]<br>2. Desoximetasone 0.05%[c] |

| | | |
|---|---|---|
| | | 3. Fluocinolone acetonide 0.025%[a]<br>4. Flurandrenolide 0.05%[a]<br>5. Hydrocortisone valerate 0.2%[a]<br>6. Mometasone furoate 0.1%[c,d]<br>7. Triamcinolone acetonide 0.1%[c,m]<br>8. Triamcinolone acetonide 0.2%[h] |
| | Class 5 | 1. Betamethasone dipropionate 0.05%[k]<br>2. Betamethasone valerate 0.1%[c,d]<br>3. Clocortolone pivalate 0.1%[c]<br>4. Fluocinolone acetonide 0.025%[c]<br>5. Fluocinolone acetonide 0.01%[n,o]<br>6. Fluticasone propionate 0.05%[c,d]<br>7. Flurandrenolide 0.05%[c,d]<br>8. Hydrocortisone butyrate 0.1%[a,c,d,f]<br>9. Hydrocortisone probutate 0.1%[c]<br>10. Hydrocortisone valerate 0.2%[c]<br>11. Prednicarbate 0.1%[a,c]<br>12. Triamcinolone acetonide 0.025%[a]<br>13. Triamcinolone acetonide 0.01%[d] |
| **Low** | Class 6 | 1. Alclometasone dipropionate 0.05%[a,c]<br>2. Betamethasone valerate 0.05%[d]<br>3. Desonide 0.05%[a,b,c,d,e]<br>4. Fluocinolone acetonide 0.01%[c,f]<br>5. Triamcinolone acetonide 0.025%[c,d] |
| | Class 7 | 1. Dexamethasone sodium phosphate 0.1%[c]<br>2. Hydrocortisone 0.5%-2.5%[a,b,c,d,f]<br>3. Methylprednisolone acetate 0.25%[c] |

WHO, World Health Organization.
a Ointment.
b Gel.
c Cream.
d Lotion.
e Foam.
f Solution.
g Scalp solution application, in some classifications class 2.
h Spray.

i Shampoo 0.05%.

j Tape.

k Lotion, depending upon classification, class 3 or 5.

l Foam, depending upon classification, class 3 or 4.

m Kenalog ointment (manufactured by APOTHECON, a Bristol-Myers Squibb Company; Princeton, NJ).

n Oil.

o Shampoo

**Topical pimecrolimus and tacrolimus**

- The off-label use of 0.1% tacrolimus for psoriasis involving the face as well as inverse psoriasis for up to 8 weeks can be considered (B)
- The off-label use of pimecrolimus for inverse psoriasis for 4-8 weeks is recommended (B)
- Long-term use of tacrolimus or pimecrolimus can be considered for inverse psoriasis treatment as off-label use (C)
- The off-label combination of tacrolimus and 6% salicylic acid for 12 weeks may be used for the treatment of plaque psoriasis (B)

**Vitamin D analogues**

- The long-term use of topical vitamin D analogues (up to 52 weeks), including calcipotriene/ calcipotriene, calcitriol, tacalcitol, and maxacalcitol, is recommended for the treatment of mild to moderate psoriasis (A)
- Use of calcipotriene foam and calcipotriene plus betamethasone dipropionate gel is recommended for 4-12 weeks for the treatment of mild to moderate scalp psoriasis (A)
- Topical tacalcitol ointment or calcipotriene combined with hydrocortisone for 8 weeks can be used for the treatment of facial psoriasis.
- Use of combination treatments with vitamin D analogues and potent class II and class III topical corticosteroids up to 52 weeks is recommended for the treatment of psoriasis (A)
- Use of combination products with calcipotriol and corticosteroids is recommended for the treatment of psoriasis (A)
- The application of vitamin D analogues twice daily on weekdays in conjunction with high potency topical corticosteroids twice daily on weekends can be considered for maintenance treatment for psoriasis (B)

- The application of morning high-potency topical corticosteroids and evening topical vitamin D analogues is an effective treatment regimen that can be considered for the treatment of psoriasis (B)

**Topical tazarotene**

- Topical tazarotene can be used for the treatment of mild to moderate psoriasis (B)
- Topical tazarotene can be used for the treatment of nail psoriasis (B)
- The combination of topical tazarotene and NB-UVB has been shown to be effective and allow a reduction in total use of NB-UVB (B)
- The use of mid- or high-potency topical corticosteroid in combination with tazarotene for 8- 16 weeks is more effective than monotherapy with tazarotene and is recommended for the treatment of mild to moderate psoriasis (A)
- The use of topical corticosteroids along with tazarotene is recommended to decrease the duration of treatment as well as increase the length of remission (A)

**Emollient**

- The use of an emollient in conjunction with topical corticosteroids for 4 to 8 weeks can be used to help reduce itching, desquamation, and total body surface area and prevent quick relapse of psoriasis when topical corticosteroids are discontinued (B)

**Salicylic acid**

- Topical salicylic acid can be used for 8-16 weeks for the treatment of mild to moderate psoriasis (B)
- The combination of salicylic acid with topical corticosteroids can be used for the treatment of moderate to severe psoriasis (body surface area ≤20%) (B)

**Topical anthralin**

- Topical anthralin for 8- 12 weeks can be used for the treatment of mild to moderate psoriasis. Short contact (up to 2 hours per day) anthralin is recommended to limit adverse side effects (B)

**Coal tar**

- Coal tar preparations are recommended for the treatment of mild to moderate psoriasis (A)
- According to the joint AAD-NPF phototherapy guideline, there is sufficient evidence to recommend the use of Goeckerman therapy for the treatment of psoriasis (B)

**Combination of topical agents with biologics**

- The addition of an ultrahigh potency (class 1) topical corticosteroid to standard dose etanercept for 12 weeks is recommended for the treatment of moderate to severe psoriasis (A)
- The addition of calcipotriene/betamethasone to standard dose adalimumab for 16 weeks is recommended for the treatment of moderate to severe psoriasis to accelerate clearance of psoriatic plaques. (B)
- All topical corticosteroids can be used in combination with any biologics for the treatment of moderate to severe psoriasis (C)

**Combination of topical calcipotriene and methotrexate**

- The addition of topical calcipotriene to standard dose methotrexate therapy is recommended for the treatment of moderate to severe psoriasis. It may lead to lower cumulative doses of methotrexate and increased time to relapse after methotrexate discontinuation. (A)

**Combination of topical agents and cyclosporine**

- The addition of calcipotriene/ betamethasone dipropionate ointment to low dose (2 mg/kg/d) cyclosporine can be used for the treatment of moderate to severe psoriasis. (B)

**Combination of calcipotriene and acitretin**

- The addition of calcipotriene to standard dose acitretin is recommended for the treatment of moderate to severe psoriasis. (A)

**Body surface area (BSA) severity measure**

- BSA measurement of involved skin is recommended as an important measure of psoriasis severity to risk stratify patient for future comorbidities and to assess response to treatment. (B)

**Psoriasis Area and Severity Index (PASI) severity measure**

- PASI is a commonly used outcome measure in clinical trials. However, it is seldom used in clinical practice to assess psoriasis severity. (B)

**Physician Global Assessment (PGA) severity measure**

- PGA measurement of psoriasis is recommended as an important measure to assess psoriasis severity. (B)

**Physician Global Assessment (PGA) 3 body surface area (BSA) severity measure**

- PGA 3 BSA is recommended as an important measure of psoriasis severity. (B)

**Psoriasis Symptom Inventory (PSI) severity measure**

- PSI is recommended as an important patient-reported measure of psoriasis severity with utility in clinical trials. PSI is a new quality of life instrument and has potential to be used in clinical practice and clinical trials. (C)

**Dermatology Life Quality Index (DLQI) severity measure**

- DLQI measurement of psoriasis is recommended as an important measure of psoriasis severity with utility in clinical trials and is seldom used in clinical practice. (B)

**Pruritus assessment severity measure**

- Pruritus is a significant symptom of psoriasis. An itch severity assessment is recommended to appropriately assess the degree of pruritus when present. (B)

#### 1.2.1.2 Joint AAD-NPF Guidelines of Care for the Management and Treatment of Psoriasis with Systemic Nonbiologic Therapies (2020)

The main recommendations on the use of systemic nonbiologic therapies are outlined below[6]:

**Strength of recommendation for methotrexate in psoriasis therapy**

- Methotrexate is recommended for the treatment of moderate to severe psoriasis in adults. A
- Methotrexate is less effective than adalimumab and infliximab for cutaneous psoriasis. A
- Methotrexate is efficacious for treatment of psoriatic arthritis (peripheral arthritis, but not for axial involvement); in psoriatic arthritis, the efficacy of methotrexate is lower than TNF-inhibitors. B
- Recommended methotrexate dosage typically ranges from 7.5 to 25 mg weekly. The dose can be given as a single dose or in 3 doses over 24 hours. B
- Methotrexate can be administered orally or subcutaneously. A

- A test dose should be considered, especially in patients with impaired kidney function. B
- Administration of folic acid or folinic acid is recommended to reduce the incidence of GI and hepatic adverse effects. Large folic acid and folinic acid doses may reduce the efficacy of methotrexate. A
- Combination therapy with methotrexate and NB-UVB phototherapy can be considered for adult patients with generalized plaque psoriasis to enhance efficacy and lower cumulative doses of both treatments. B

**Strength of recommendation for the apremilast in psoriasis therapy**

- Apremilast is recommended for the treatment of moderate to severe psoriasis in adults. A

**Strength of recommendation for cyclosporine therapy in psoriasis**

- Cyclosporine is recommended for patients with severe, recalcitrant psoriasis. A
- Cyclosporine can be recommended for the treatment of erythrodermic, generalized pustular, and/or palmoplantar psoriasis. B
- Cyclosporine can be recommended as short-term interventional therapy in patients who flare up while on a pre-existing systemic therapy. C

**Strength of recommendations for acitretin in psoriasis therapy**

- Acitretin can be recommended as monotherapy for plaque psoriasis. B
- Acitretin can be recommended for treatment of erythrodermic, pustular, and palmar-plantar psoriasis. B
- Acitretin can be recommended as combination therapy with PUVA for psoriasis. B
- Acitretin can be combined with BB-UVB for plaque psoriasis. B

### 1.2.2 EuroGuiDerm Guidelines

These evidence- and consensus-based guidelines on the treatment of psoriasis vulgaris was developed following the EuroGuiDerm Guideline and Consensus Statement Development Manual. The first part of the guideline includes general information on the scope and purpose, health questions covered, target users and strength/limitations of the guideline. Suggestions for disease severity grading and treatment goals are provided. It presents the general treatment recommendations as well as detailed management and monitoring recommendations for the individual drugs. The treatment options discussed in this guideline are as follows:

acitretin, ciclosporin, fumarates, methotrexate, adalimumab, apremilast, brodalumab, certolizumab pegol, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab and ustekinumab. The second part of the guideline provides guidance for specific clinical and comorbid situations such as treating psoriasis vulgaris patient with concomitant psoriatic arthritis, concomitant inflammatory bowel disease, a history of malignancies or a history of depression or suicidal ideation. It further holds recommendations for concomitant diabetes, viral hepatitis, disease affecting the heart or the kidneys as well as concomitant neurological disease.

**Table 6.** EuroGuiDerm Strength of Recommendations

| Strength of Recommendation | Wording | Symbols | Definition |
|---|---|---|---|
| **Strong recommendation for the use of an intervention** | "We recommend …" | ↑↑ | We believe that all or almost all informed people would make a choice in favour of using this intervention. Clinicians will not have to spend as much time on the process of decision-making with the patient and may devote that time instead to overcoming barriers to implementation and adherence. In most clinical situations, the recommendation can be adopted as a policy |
| **Weak recommendation for the use of an intervention** | "We suggest …" | ↑ | We believe that most informed people would make a choice in favour of using this intervention, but a substantial number would not. Clinicians and other health care providers will need to devote more time to the process of shared decision-making. Policy makers will have to involve |

| | | | |
|---|---|---|---|
| | | | many stakeholders and policy making will require substantial debate. |
| **Open recommendation/no recommendation** | "We cannot make a recommendation for or against …" | 0 | Currently, a recommendation in favour of or against using this intervention cannot be made due to certain circumstances (for example, unclear or balanced benefit-risk ratio, no data available) |
| **Weak recommendation against the use of an intervention** | "We suggest against …" | ↓ | We believe that most informed people would make a choice against using this intervention, but a substantial number would not. |
| **Strong recommendation against the use of an intervention** | "We recommend against …" | ↓↓ | We believe that all or almost all informed people would make a choice against using this intervention. This recommendation can be adopted as a policy in most clinical situations. |

#### 1.2.2.1 EuroGuiDerm Guideline on the Systemic Treatment of Psoriasis Vulgaris – Part 1: Treatment and Monitoring Recommendations (2020)

The EuroGuiDerm Guideline on the systemic treatment of psoriasis vulgaris–Part 1: treatment and monitoring recommendations are outlined below[7].

**General recommendations**

- ↑↑ We recommend taking account of efficacy and safety, time until onset of treatment response, comorbidities and individual patient factors when choosing a systemic treatment for moderate to severe psoriasis. Consensus, evidence- and consensus-based
- ↑↑ We recommend initiating a systemic treatment in patients with moderate to severe. Strong consensus, consensus-based

- ↑↑ For patients who require systemic treatment, we generally recommend initiating a “conventional” systemic agent. Strong consensus, evidence- and consensus-based
- ↑↑ We recommend initiating a biologic if conventional systemic agents were inadequate in response or if they are contraindicated or not tolerated. Strong consensus, evidence- and consensus-based
- ↑ In cases of psoriasis where conventional treatments are not expected to lead to a sufficient response*, we suggest initiating a biologic agent that has a “first-line label”.** *e.g., particularly severe disease (e.g., PASI ≥ 20) or rapid worsening of disease; severe involvement of the nails, the genital area or the scalp; or a particularly strong impact on quality of life (e.g., DLQI ≥ 15) **“First line label” refers to the therapeutic indication as approved by the EMA (European Medicines Agency). Strong consensus, consensus-based
- ↑ We suggest using apremilast if an oral treatment is desired and “conventional” systemic agents led to an inadequate response or are contraindicated or not tolerated. Strong consensus, consensus based.

**Conventional systemic therapy**

➔ **Acitretin**

*Pre-treatment*

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History and clinical examination should focus on musculoskeletal problems. If a patient reports complaints, further imaging investigations may be performed.
- Exclude pregnancy/breastfeeding: patient must be informed explicitly and extensively about the teratogenic risk of the medication, the necessity of effective long-term contraception (for three years after cessation of treatment), and the possible consequences of becoming pregnant while taking retinoids; written documentation of this informational interview should be obtained.
- Inform patient that during treatment and for three years after cessation of treatment, blood donation is not permitted.
- Laboratory parameters including pregnancy test.
- Check need for vaccinations.

*During treatment*

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- The capsules should be taken with a meal containing some fat or with whole milk to improve absorption }
- To prevent elevation of serum lipids and liver enzymes, alcohol abstinence and a low-fat and low carbohydrate diet are advised.
- Preventing pregnancy is mandatory. After satisfactory contraception for at least one month prior to treatment, start treatment on second or third day of the menstrual cycle. Double contraception is recommended (e.g., condom + pill; IUD/Nuva Ring + pill; Cave: no low-dosed progesterone preparations/mini-pills) during and up to three years after end of therapy; effectiveness of oral contraceptives is reduced by acitretin.
- Ask patients about spine and joint complaints at follow-up visits. If a patient reports complaints, further imaging investigation may be performed. }
- Laboratory parameters including monthly pregnancy test.

*Post-treatment*

- Reliable contraception and monthly pregnancy test in women of child-bearing age for three years after cessation of therapy. Double contraception, as described above, is recommended.
- Remind patients that blood donation is not permitted for three years after cessation of therapy.

➔ **Ciclosporin (CsA)**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis). } Measure HRQoL (e.g., using DLQI/ Skindex-29 or -17). }
- History and clinical examination should focus on previous and concomitant diseases (e.g., arterial hypertension; severe infections; malignancies, including cutaneous malignancies; renal and liver diseases) and concomitant medication (see drug interactions in long version of the guideline).
- Measure blood pressure on two separate occasions. } Laboratory parameters (see long version of the guideline).

- Reliable contraception (caution: reduced efficacy of progesterone-containing contraceptives).
- Regular gynaecologic screening according to current EuroGuiDerm guidelines.
- Consultation on vaccination; susceptibility to infections (take infections seriously, seek medical attention promptly if necessary); drug interactions (inform other treating physicians about therapy); avoidance of excessive sun exposure; use of sun protection measures.

*During treatment:*

- During therapy with low dose ciclosporin (CsA; 2.5 to 3 mg/kg body weight daily), follow-up intervals may be extended to two months or more. Shorter intervals may be needed in patients with risk factors, after dose increases, or those who must take concomitant medications that are likely to contribute to adverse drug reactions.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g. using DLQI/Skindex-29 or -17).
- Clinical examination should focus on status of skin and mucous membranes (hypertrichosis, gingival changes, malignancies), signs of infections, gastrointestinal or neurological symptoms (tremor, dysesthesia), musculoskeletal/joint pain.
- Repeat recommendation for need for sun avoidance and sun protection
- Repeat check of concomitant medication.
- Measure blood pressure.
- Laboratory parameters (see long version of guideline).
- Reliable contraception.
- Regular gynaecologic screening according to current EuroGuiDerm guidelines.
- If creatinine is significantly elevated or patient has been on therapy for more than one year, perform creatinine clearance (or creatinine-EDTA clearance where available).
- Determination of the CsA level is advisable in selected cases.

*Post-treatment:*

- After discontinuation of CsA, patients should be followed up for skin cancer, especially in case of high cumulative doses of prior UV therapy or natural UV exposure.

➔ **Dimethyl fumarate/fumaric acid esters**

Pre-treatment:

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History and clinical examination.
- Reliable contraception.
- Laboratory parameters (see long version of the guideline).
- Check need for vaccinations.

During treatment:

- Objective assessment of the severity of disease (such as PASI/BSA/PGA).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Clinical examination.
- Reliable contraception.
- Laboratory parameters

Post-treatment: None

➔ **Methotrexate (MTX)**

*Pre-treatment*

- Consider enrolling the patient in a psoriasis registry.
- History and clinical examination.
- Objective assessment of the severity of the disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Laboratory parameters (see long version of the guideline).
- Exclude tuberculosis
- Chest X-ray.

- Reliable contraception in women of child-bearing age (starting after menstruation).
- If abnormalities in liver screening are found, the patient should be referred to a specialist for further evaluation.
- Check need for vaccinations.

*During treatment:*

- Objective assessment of the severity of disease (such as
- PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Check concomitant medication.
- Clinical examination.
- Laboratory parameters (see long version of the guideline).
- Reliable contraception in women of child-bearing age.
- 5 mg folic acid once weekly 24 hours after MTX.
- Advise alcohol abstinence.

*Post-treatment:*

- Women should be advised not to become pregnant and men should be advised not to conceive for at least three months after cessation of therapy with MTX*

*EMA recommends six months as a means of precaution; the practice of the guideline group differs from this.

*Biological therapy and small molecules*

➔ **Adalimumab**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History and clinical examination should focus on prior exposure to other treatments, malignancies, infections, congestive heart failure (CHF) and neurological disease or symptoms. }

- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters (see long version of the guideline) – Exclude tuberculosis – Check for evidence of active infection – Check need for vaccinations.
- Reliable contraception

*During treatment:*

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis). }
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17)
- Clinical examination should focus on malignancies, risk factors for serious infections, congestive heart failure, and neurological symptoms.
- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters.
- Reliable contraception

*Post-treatment*:

- After cessation of adalimumab therapy, patients should be followed up with medical history and physical examination.

➔ **Apremilast**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Medical history and physical examination including: – Check for skin cancer – Check for evidence of active and chronic infection – Check for contraception and breastfeeding – Check for need for vaccinations – Check for hypersensitivity, metabolic, gastrointestinal and renal disorders/dysfunction and underweight – Check for depression, anxiety – Check for co-medication: CYP3A4 enzyme inducers – Laboratory parameters including pregnancy test

*During treatment:*

- Objective assessment of the severity of the disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/ Skindex-29 or -17).

- Medical history and physical examination focusing on malignancies, infections, contraception, depression, and anxiety.
- Laboratory parameters only when indicated on medical history or physical examination.
- Reliable Contraception

➔ **Brodalumab**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Medical history and clinical examination including prior exposure to treatments, malignancies, infections (e.g. candidiasis), inflammatory bowel disease, depression and/or suicidal ideation or behaviour.
- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters – Exclusion of tuberculosis– Check for evidence of active infection – Check need for vaccinations.
- Reliable contraception.

*During treatment*:

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters (see long version of the guideline).
- Medical history and physical examination focusing on infections (in particular upper respiratory tract infections, candida, tuberculosis), contraception, symptoms of depression and/or suicidal behaviour and signs or symptoms of inflammatory bowel disease.

*Post-treatment*:

- After cessation of brodalumab therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation.

➔ **Certolizumab pegol**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History and clinical examination should focus on prior exposure to treatments, malignancies, infection, congestive heart failure, and neurological disease or symptoms.
- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters (see long version of the guideline) – Exclusion of tuberculosis– Check for evidence of active infections – Check need for vaccinations
- Discuss contraception

*During treatment:*

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Clinical examination should focus on lymphadenopathy, malignancies, especially skin cancer, premalignant lesions, risk factors for serious infections, congestive heart failure, and neurological symptoms.
- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters.
- Discuss contraception

*Post-treatment:*

- After cessation of certolizumab pegol therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation.

➔ **Etanercept**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17)
- History and clinical examination should focus on prior exposure to treatments, malignancies, infection, congestive heart failure, and neurological symptoms. }
- Other recommended measures include: – Check for malignancy, mainly skin cancer, and premalignant lesions – Check for lymphadenopathy – Laboratory parameters (see long version of the guideline) – Exclusion of tuberculosis – Check for evidence of active infection – Check need for vaccinations
- Reliable contraception

*During treatment:*

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Clinical examination should focus on lymphadenopathy, malignancies, especially skin cancer, premalignant lesions, risk factors for serious infections, congestive heart failure, and neurological symptoms.
- Other recommended measures include: – Laboratory parameters (see long version of the guideline)
- Reliable contraception.

Post-treatment:

- After cessation of etanercept therapy, patients should be followed up with medical history and physical examination.

➔ **Guselkumab**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Medical history and physical examination including prior exposure to treatments, malignancies, infections.
- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters (see long version of the guideline)

– Exclusion of tuberculosis– Check for evidence of active infection – Check need for vaccinations

- Reliable contraception.

*During treatment*:

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters
- Medical history and physical examination including infections, including monitoring signs and symptoms of tuberculosis.
- Reliable contraception.

*Post-treatmen*t:

- After cessation of guselkumab therapy, patients should be followed up with medical history and physical examination.

➔ **Infliximab**

*Pre-treatment*:

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History focuses on prior exposure to treatments.
- History and clinical examination should focus on malignancies, infection, congestive heart failure, and neurological symptoms.
- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters– Exclusion of tuberculosis– Check for evidence of active infection – Check need for vaccinations
- Reliable contraception.

*During treatment*:

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/ Skindex-29 or -17).
- Clinical examination should focus on malignancies, risk factors for serious infections, congestive heart failure, and neurological symptoms.

- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters.
- Reliable contraception.

*Post-treatment:*

- After cessation of infliximab therapy, patients should be followed up with medical history and physical examination.

➔ **Ixekizumab**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Medical history and physical examination including prior exposure to treatments, malignancies, infection (e.g. candidiasis), inflammatory bowel disease.
- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters (see long version of the guideline) – Exclusion of tuberculosis – Check for evidence of active infection – Check need for vaccinations
- Reliable contraception.

*During treatment:*

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters (see long version of the guideline).
- Medical history and physical examination focusing on infections (in particular upper respiratory tract infections, candida, tuberculosis), contraception, signs or symptoms of inflammatory bowel disease.

*Post-treatment*:

- After cessation of ixekizumab therapy, patients should be followed up with medical history and physical examination.

➔ **Risankizumab**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (such as DLQI, Skindex-29 or 17)
- Medical history and physical examination including prior exposure to treatments, malignancies, infections.
- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters (see long version of the guideline) – Exclusion of tuberculosis– Check for evidence of active infection – Check need for vaccinations.
- Reliable contraception.

*During treatment*:

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17)
- Laboratory parameters (see long version of the guideline)
- Medical history and physical examination including infections, including monitoring signs and symptoms of tuberculosis.
- Reliable contraception.

*Post-treatment:*

- After cessation of risankizumab therapy, patients should be followed up with medical history and physical examination.

➔ **Secukinumab**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Medical history and physical examination including prior exposure to treatments, malignancies, infections (e.g. candidiasis), inflammatory bowel disease. } Other recommended measures include: – Check for skin cancer –

Check for lymphadenopathy – Laboratory parameters– Exclusion of tuberculosis– Check for evidence of active infection – Check need for vaccinations

- Reliable contraception.

*During treatment:*

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters (see long version of the guideline).
- Medical history and physical examination focusing on infections (upper respiratory tract infections, candida, tuberculosis), contraception, signs or symptoms of inflammatory bowel disease. Post-treatment:
- After cessation of secukinumab therapy, patients should be followed up with medical history and physical examination.

➔ **Tildrakizumab**

*Pre-treatment:*

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Medical history and physical examination including prior exposure to treatments, malignancies, infections.
- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters– Exclusion of tuberculosis – Check for evidence of active infection – Check need for vaccinations.
- Reliable contraception.

*During treatment:*

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters (see long version of the guideline)
- Medical history and physical examination including infections, including monitoring signs and symptoms of tuberculosis.

- Reliable contraception.

*Post-treatment:*

- After cessation of tildrakizumab therapy, patients should be followed up with medical history and physical examination.

➔ **Ustekinumab**

*Pre-treatment*:

- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Medical history and physical examination including prior exposure to treatments, malignancies, infections.
- Other recommended measures include: – Check for skin cancer – Check for lymphadenopathy – Laboratory parameters (see long version of the guideline) – Exclusion of tuberculosis – Check for evidence of active infection – Check need for vaccinations.
- Reliable contraception.

*During treatment*:

- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17)
- Laboratory parameters (see long version of the guideline)
- Medical history and physical examination including infections, including monitoring signs and symptoms of tuberculosis. } Reliable contraception. Post-treatment
- After cessation of ustekinumab therapy, patients should be followed up with medical history and physical examination.

### 1.2.2.2 EuroGuiDerm Guideline on the Systemic Treatment of Psoriasis Vulgaris – Part 2: Specific Clinical and Comorbid Situations (2020)

Recommendations from part 2 of the EuroGuiDerm guidelines are outlined below[8]:

The EuroGuiDerm guideline development group considers the time a treatment has been available a relevant factor when considering different treatment options as shown in figures 1 and 2.

| Specific circumstances \ Therapy | Conventional systemic agents | | | |
|---|---|---|---|---|
| | Acitretin | Ciclosporin | Fumarates | Methotrexate |
| Concomitant psoriatic arthritis | | | | ↑↑ peripheral active joint involvement |
| Chronic inflammatory bowel disease: Crohn's Disease | ↑ especially cases with mild paradoxical psoriasis | | | ↑ 2nd choice oral treatment |
| Chronic inflammatory bowel disease: Ulcerative colitis | ↑ especially cases with mild paradoxical psoriasis | ↑ 2nd choice oral treatment | | |
| Diabetes mel./metabolic syndrome | | ↓ | | ↓ |
| Dyslipidaemia | ↓ | | | |
| Advanced heart failure | ↑ | ↓ | | ↑ |
| Heart Disease: Ischemic heart disease | | ↓ | | ↑ |
| Concomitant latent / treated TB | ↑ | | ↑ | |
| Pregnancy | ↓↓ | ↑ preferred conventional | ↓ | ↓↓ |

| Symbols | Implications[1] |
|---|---|
| ↑↑ | We believe that all or almost all informed people would make that choice. |
| ↑ | We believe that most informed people would make that choice, but a substantial number would not. |
| | See background text and specific recommendations |
| ↓ | We believe that most informed people would make a choice against that intervention, but a substantial number would not. |
| ↓↓ | We believe that all or almost all informed people would make a choice against that choice. |

[1]Adapted from GRADE

***Figure 1.*** *Overview of 'conventional' treatment options and the expert assessment of their suitability in specific treatment circumstances (retrieved from the EuroGuiDerm guidelines)*

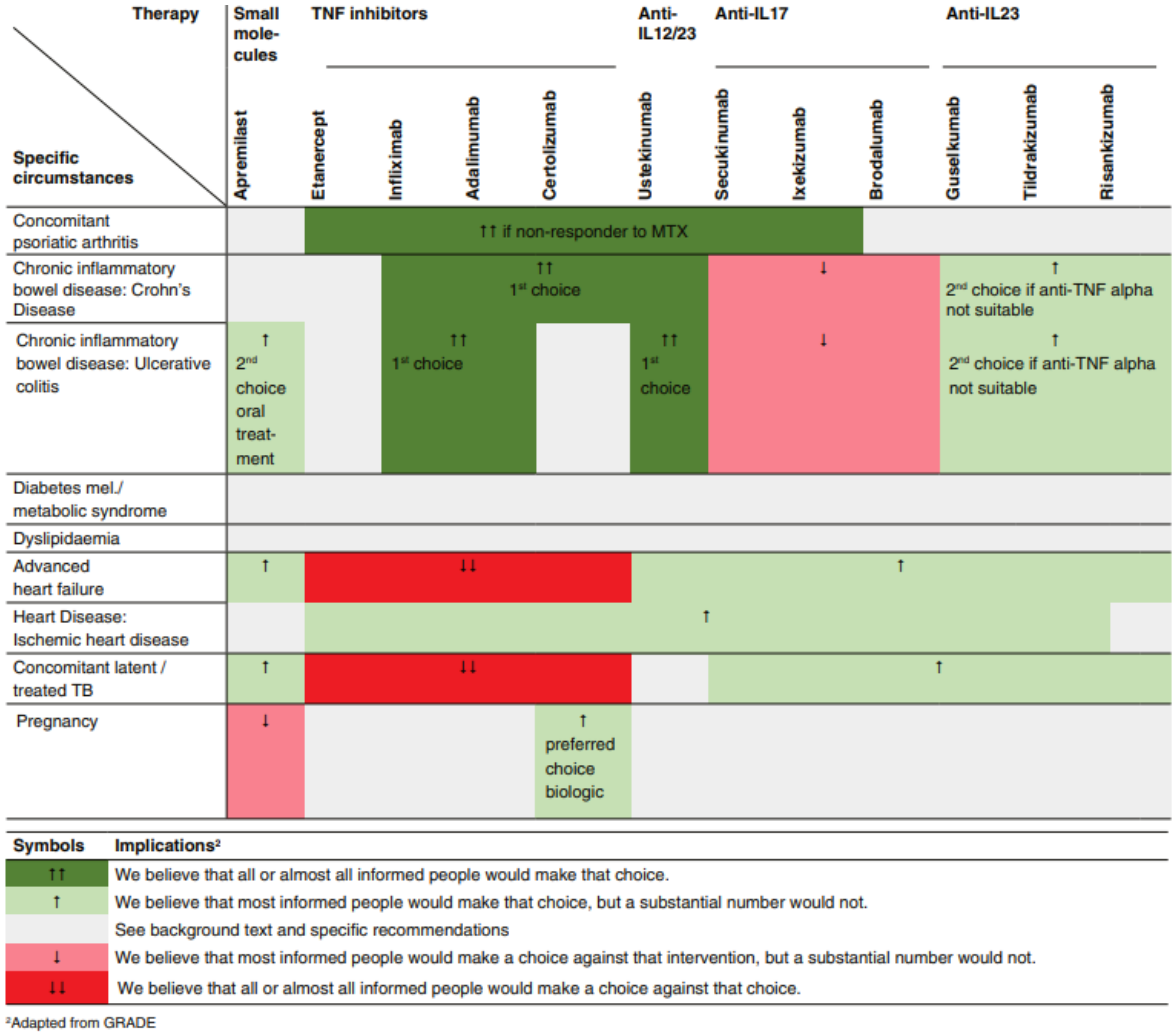


***Figure 2.*** *Overview of 'biologics' treatment options and the expert assessment of their suitability in specific treatment circumstances (decision grid II) (retrieved from the EuroGuiDerm guideline)*

- ↑↑ We recommend interdisciplinary cooperation with a rheumatologist for the confirmation of the diagnosis of psoriatic arthritis and the selection of a suitable treatment whenever needed. Strong consensus (Due to personal–financial conflict of interest 4 abstentions) EXPERT CONSENSUS 100% agreement.
- ↓↓ We recommend starting a conventional synthetic DMARD (MTX) early to prevent progression of disease and erosive destruction of joints for patients with moderate to severe psoriasis and peripheral active joint involvement (PsA) despite the usage of NSAIDs, or glucocorticoid site injections if applicable and/or potential poor prognosis due to polyarthritis, increased inflammatory markers and erosive changes, and extra-articular

musculoskeletal manifestations. Strong consensus EVIDENCE AND EXPERT CONSENSUS Table 3 100% agreement

- ↑↑ For inadequately responding patients after at least one synthetic DMARD, we recommend the use of biological DMARDs as monotherapy or in combination with synthetic DMARDs. Strong consensus 100% agreement EVIDENCE AND EXPERT CONSENSUS Table 3
- ↑↑ For the selection of a bDMARD for patients with moderate to severe psoriasis of the skin and active joint involvement (PsA), we recommend taking aspects of efficacy with regard to skin and the joints, comorbidity, practicability and safety into account. Strong consensus EXPERT CONSENSUS 100% agreement

*Inflammatory bowel disease: How should psoriasis patients be managed with concomitant inflammatory bowel disease?*

All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.

- ↑↑ We recommend working in collaboration with the treating gastroenterologist when prescribing a systemic therapy in psoriasis patients with concomitant chronic inflammatory bowel disease. Strong consensus1 EXPERT CONSENSUS
- ↑↑ In patients with psoriasis and active IBD or a history of IBD, we recommend to preferentially use approved targeted therapies with a documented efficacy in these conditions: Crohn's disease: anti-TNF (infliximab, adalimumab, certolizumab) and anti-IL-12/23p40 (ustekinumab). Ulcerative colitis: anti-TNF (infliximab, adalimumab) and anti-IL-12/23p40 (ustekinumab).
- ↑ If these first-choice treatments cannot be used, we suggest the following treatments to be considered as second choice targeted treatment options in patients with psoriasis and IBD: Crohn's disease: Anti-IL-23p19 (preferred risankizumab, guselkumab; also possible: tildrakizumab) Ulcerative colitis: Anti-IL-23p19 (preferred risankizumab, guselkumab; also possible: tildrakizumab)
- ↑ If these first-choice treatments cannot be used, we suggest the following treatments to be considered as second choice oral treatment options in patients with psoriasis and IBD Crohn's disease: Methotrexate Active ulcerative colitis: Ciclosporine (preferred), apremilast (also possible)
- ↑ In combination with other treatments, we suggest acitretin as an adjunct therapy for patients with IBD and psoriasis, especially in cases with mild paradoxical psoriasis.

- ↓ We suggest against the use of anti-IL 17 antibodies in patients with inflammatory bowel disease.

*Cancer: How should psoriasis patients with a history of malignancies be managed?*

All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.

- ↑↑ We recommend taking the burden of psoriasis, and the risk of cancer worsening or recurrence (pre-cancer vs low risk vs high risk) into account for shared therapeutic decision making.
- ↑↑ For patients with recent malignancy we recommend topical therapies, phototherapy (narrow band UVB) * and/ or acitretin. *except patients with a recent, and/or high risk of cutaneous malignancy
- ↑↑ We recommend discussing the decision to initiate immunosuppressive therapies, in psoriasis patients with a current or recent diagnosis of cancer in the previous five years case-by-case with cancer specialists and to reach an informed decision, respecting the patient's preference.
- ↑ In case of inadequate response to topical therapies, phototherapy, (narrow band UVB) and/or acitretin we suggest using MTX in psoriasis patients with a previous history of cancer. * (*for patients with history of non-melanoma skin cancer, see background text)
- ↓ We suggest apremilast can be used in psoriasis patients with a previous history of cancer despite the lack of long-term experience based on pathophysiological considerations on a case-by-case basis including discussion with cancer specialist.
- ↓ We suggested against using ciclosporin in psoriasis patients with a previous history of cancer.
- ↑ We suggest anti-TNF, Ustekinumab can be used based on existing safety data on a case-by-case basis including discussion with cancer specialist. We suggest anti-IL17, anti IL23, can be used in psoriasis patients with a previous history of cancer despite the lack of long-term experience based on pathophysiological considerations on a case-by-case basis including discussion with a cancer specialist.

*Depression: How should psoriasis patients with a history of depression and/or suicidal ideation be managed?*

All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.

- ↑↑ We recommend being aware of signs and symptoms of anxiety and depression in patients with psoriasis and monitor for symptoms of depression

and/or suicidal ideation or anxiety during systemic treatments for psoriasis especially in those with a history of any of the above.

- ↑ We suggest using alternatives to brodalumab and apremilast in patients with a history of depression and/or suicidal ideation.

*Diabetes: How should psoriasis patients with diabetes mellitus be managed?*

- ↓ We suggest against using ciclosporin or MTX as a first line treatment in patients with diabetes and/or features of the metabolic syndrome. Consensus 89% agreement EXPERT CONSENSUS
- ↓ We suggest against using acitretin as a first line treatment in patients with dyslipidemia. Strong Consensus 100% agreement EXPERT CONSENSUS

*Heart disease: How should psoriasis patients with ischemic heart disease and/or congestive heart failure be managed?*

All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.

- ↓ We suggest cyclosporine or acitretin as preferred treatments in patients with psoriasis and ischemic heart disease.
- ↑ We suggest methotrexate as preferred first-line therapy in patients with psoriasis and ischemic heart disease* if other patient characteristics do not preclude its use.
- ↑ We suggest anti-TNFs, Ustekinumab, and IL-17 inhibitors as preferred targeted therapies in patients with psoriasis and ischemic heart disease* (*In case of concomitant congestive heart failure, also note the recommendations from the respective section)

➔ ***Heart failure***

All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.

- ↓ We suggest against using cyclosporine in patients with psoriasis and advanced congestive heart failure.
- ↑ We suggest that methotrexate, acitretin and apremilast are considered as treatment in patients with psoriasis and advanced congestive heart failure.
- ↑ We suggest that ustekinumab, inhibitors of IL-17 and of IL-23 are considered as treatment in patients with psoriasis and advanced congestive heart failure.
- ↓↓ We recommend against using anti-TNFs in patients with psoriasis and advanced congestive heart failure.

- ↑↑ We recommend discussing the choice of a systemic therapy in psoriasis patients with advanced congestive heart failure with a cardiologist.

*Kidney disease: How should psoriasis patients with kidney failure/ renal impairment be managed?*

All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.

- ↑↑ We recommend ensuring an accurate assessment of renal function in any psoriasis patient with known or suspected chronic kidney disease prior to therapy.
- ↑↑ We recommend working in collaboration with the nephrologist when prescribing systemic therapy in any psoriasis patient with chronic kidney disease of stage 3 (Egfr (eGFR <60 mL/min/1.73 $m^2$) or more.
- ↑ We suggest acitretin*, apremilast, fumarates*, methotrexate* may be used in psoriasis patients with mild to moderate renal impairment (eGFR ≥30 mL/min/1.73$m^2$). *(careful dosing/dose adjustment may be needed)
- ↑ We suggest using biologics in psoriasis patients with chronic kidney disease and all stages of renal impairment.
- ↓ ↓ We recommend against using ciclosporin, fumarates, or methotrexate in psoriasis patients with chronic kidney disease and severe renal impairment (eGFR <30 mL/min/1.73$m^2$).

*Neurological diseases: Which treatments are appropriate for psoriasis patients with neurological diseases?*

All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement

- ↑ We suggest using fumarates in psoriasis patients with multiple sclerosis.
- ↓ ↓ We recommend against using TNF antagonist therapy in psoriasis patients with a diagnosis of multiple sclerosis or other demyelinating disease.
- ↓ In psoriasis patients with a first degree relative with multiple sclerosis or other demyelinating disease, we suggest against the use of TNF antagonist therapy if other suitable treatment options are available.

*Viral hepatitis: How should patients who test positive be managed?*

All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.

- ↑↑ We recommend that treatment decision for patients with positive test result for HBsAg or positive HBV DNA should always be taken together with a hepatologist.

- ↑ Depending on the individual health care setting and personal experience and training, we suggest consulting with a hepatologist to choose a systemic treatment for patients that have a positive anti-HBc with a neg. HBsAG/HBV-DNA test. We suggest, based on the common practice within the guideline group, acitretin, apremilast, fumarates, MTX, ustekinumab and the anti-IL 17 and anti-IL 23 antibodies as preferred systemic treatment options for this patient group. Strong consensus EVIDENCE AND CONSENSUS BASED, see METHODS & EVIDENCE REPORT
- ↑↑ We recommend regular testing for HBsAG/HBV-DNA (e.g. every three months) during systemic treatment.
- ↑↑ We recommend recording all treatment initiations and follow up visits of psoriasis patients with concomitant hepatitis B or C cases in drug registries.

Tuberculosis: How to manage psoriasis in patients with positive tuberculosis test results?

All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.

- ↓ ↓ We recommend against TNF alpha antagonists as a treatment for patients with latent TB unless there are no other suitable treatment options.
- ↑↑ We recommend remaining alert to signs and symptoms of tuberculosis activation or re-infection during therapy.
- ↑ We suggest acitretin, apremilast or fumarates or a treatment from the anti-IL 17 and anti-IL 23 group for patients with latent TB that require a systemic antisporiatic treatment.

Wish for child/pregnancy: How should psoriasis patients with a wish for pregnancy in the near future or who are pregnant be managed?

All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.

- ↑ We suggest ciclosporin as a first line convention agent in women planning conception and when it is necessary to start systemic therapy during the 2nd and 3rd trimester of pregnancy.
- ↓ ↓ Methotrexate and acitretin are contra-indicated in women planning conception. We recommend using these.
- ↓ Fumarates and apremilast are contra-indicated in women planning conception. We suggest against using these.

- ↑↑ We recommend consultation and information sharing across specialties, including with an obstetrician with expertise in caring for pregnant women with medical problems.
- ↑↑ We recommend the collection of maternal exposure to medications and pregnancy outcome data in national safety registries where available.
- ↑ We suggest certolizumab pegol as a first line choice when starting biologic therapy in women planning conception (when a biologic is considered essential to use in pregnancy) and when it is necessary to start a systemic therapy during the second or third trimester.
- ↑ We suggest stopping biologic therapy in the second and third trimester (except certolizumab pegol) to minimise fetal exposure and limit potential infection risk to the neonate.
- ↓ We suggest against using live or live attenuated vaccines in infants (up to 6 months of age) whose mothers received biologic therapy beyond 16 weeks gestation, unless the benefit of the vaccination clearly outweighs the theoretical risk of administration.
- ↑↑ We recommend consultation and information sharing across specialties, including with an obstetrician with expertise in caring for pregnant women with medical problems.
- ↑↑ We recommend the collection of maternal exposure to medications and pregnancy outcome data in national safety registries where available.
- ↑↑ It is recommended that men discontinue methotrexate 3 months before attempting conception. * *EMA recommends 6 months as a means of precaution; the practice of the guideline group differs from this.
- ↑ As a precaution, it is suggested that men receiving acitretin use barrier forms of contraception post-conception to limit exposure via direct contact with semen during pregnancy.
- ↑↑ We recommend the collection of paternal exposure to medications during conception and pregnancy outcome data in national safety registries where available.

### 1.2.3 Saudi Consensus Statement on Biologic Treatment of Chronic Plaque Psoriasis (2020)

The overall aim of this consensus document is to deliver evidence-based recommendations on the use, screening, and monitoring of biologic therapy in patients with moderate-to-severe plaque psoriasis. These recommendations also address the use of biologic therapy in special patient populations[9]. During

workshops, the formal consensus methodology of the nominal group technique was used to agree upon the recommendations. All work group members were entitled to vote on the recommendations. A statement was regarded as consented when the agreement was achieved by at least 75% of the voting experts. The strength of recommendation was not expressed.

Therapeutic use of biologics for the management of psoriasis Overview of biologic agents available for psoriasis in Saudi Arabia:

***Treatment algorithm:***

- In current routine clinical practice, near-complete skin clearance with the least side effects should be the treatment goal for patients with moderate-to-severe psoriasis. In addition to defining treatment goals, and to improve psoriasis outcomes, it is important to implement strategies to promptly alter treatment regimens if goals are not met within about 12–16 weeks. When the clinical response of treatment with the chosen biologic therapy is unsatisfactory (suboptimal outcomes, primary or secondary treatment failure, or drug-related side effects), the possible courses of action that may be followed to improve the results are: (a) dose optimization, (b) combination strategies with non-biologic treatment, (c) switching to another biologic therapy.
- *Apremilast* may be considered for a select group of patients. Apremilast is an oral phosphodiesterase inhibitor approved for Pso & PsA and has a PASI 75 response of 33.1% at 16 weeks. Subgroup analysis of pivotal studies data showed some response in palmoplantar, scalp, and nail psoriasis. There is no restriction to using it in patients with malignancies. Additionally, institution formulary restrictions may need to be considered when selecting apremilast (i.e. in MOH, apremilast is non-formulary).

**Transitioning**

*Benefits of transitioning*

Switching psoriasis treatment is a common, accepted practice for improving patient outcomes (e.g. when patients are experiencing suboptimal efficacy and/or intolerability with a given therapy). There are no evidence-based studies on the duration of the interval between discontinuation of the previous medication and initiation of biologic therapy. This may depend on the treatment that is being discontinued, disease severity, and response to prior treatment, as well as on expert opinion, and it should be assessed on a case-by-case basis. Therefore, whereas some experts will start administration of a new biologic as soon as it is available for the patient, others may wait for a period of 3 or 4 half-lives of the previous therapy before the transition.

*Transitioning from conventional systemic therapy to biologic therapy*

General considerations: Recommendations for transitioning from conventional systemic therapy to biologic therapy will differ depending on the reason for transition. For example:

- When transitioning due to safety reasons (development of medication-related side effects), a treatment-free interval may be necessary until the safety parameter has normalized or stabilized.
- When transitioning due to lack of efficacy, which could be primary or secondary inefficacy, or due to suboptimal response; transitioning directly or with an overlap period can be considered.
- Additionally, if a patient develops psoriatic arthritis, transitioning to a therapy that is efficacious in both psoriasis and psoriatic arthritis is required.
- Irrespective of the reason for transitioning, approved induction dosages should be used for the new drug.

***Transitioning from cyclosporine to biologic therapy:*** Transitioning from cyclosporine to TNF antagonists and ustekinumab can be performed without a washout period. A short overlap period (e.g. 2–8 weeks) of cyclosporine with TNF antagonists or ustekinumab can be considered to reduce the risk of the rebound in partial responders but the overlap period should be minimized, and the dose of cyclosporine tapered down as soon as possible. Transitioning from MTX to biologic therapy: Transitioning from MTX to TNF antagonists and ustekinumab can be performed without a washout period. MTX can be overlapped or used concurrently with TNF antagonists or ustekinumab.

***Transitioning from one biologic therapy to another:***

General considerations before transitioning: In the case of suboptimal response to a biologic therapy (etanercept, infliximab, adalimumab, and ustekinumab), dose optimization or combination strategies with non-biologic treatment is preferred before transitioning to another biologic therapy. This decision should be made with consideration to patient situation/ preference and the cost inflation by dose optimization. Recommendations for dose optimization include:

- For adalimumab, an increase of dosage from 40 mg every other week to 40 mg/week
- For etanercept, an increase of dosage from 50 mg/week to 50 mg twice weekly

- For ustekinumab, with partial responders, an increase of dosage from 45 to 90 mg with 12-week dosing intervals. If this is unsuccessful, the interval can be shortened to 8 weeks.
- For infliximab, a reduction of the dosing intervals from every 8 weeks to every 6 weeks with 5 mg/kg can be considered in secondary non-responders, defined as the loss of at least 50% of the initial improvement. In special cases, an increase of the dosage >5 mg/kg can be considered (64). The dose can be increased in some circumstances up to 10 mg/kg/dose and the interval can be shortened to 4 weeks
- For secukinumab, dose optimization includes shortening the interval to every 2 weeks
- For ixekizumab, a single report of administrating it every 2 weeks instead of 4 weeks
- For IL-23 inhibitors, no data yet
- *General considerations after the decision to transition have been made*
  Recommendations for transitioning from one biologic therapy to another will differ depending on the reason for transition. For example:
    - When transitioning due to lack of efficacy, no washout period is necessary; transition to the new biologic therapy at the time of the next scheduled dose of the original therapy, using the standard induction dose, followed by the maintenance dose.
    - When transitioning due to safety reasons (development of medication-related side effects), a treatment-free interval may be necessary until the safety issue has been resolved.

**Adjusting biologic therapy**

*Dose reduction*

- During successful maintenance with biologics as monotherapy, a dose reduction can be considered to limit drug exposure. However, long-term efficacy and safety data have only been generated for the approved doses. Moreover, there is a risk of decreasing efficacy. In addition, there is some evidence to support that a longer interval might increase the risk of anti-drug antibody formation. Decreasing the dose may be considered in patients on combination therapy.
- In clinical practice, dosing intervals have been increased with adalimumab and etanercept while maintaining clinical response. With infliximab monotherapy, intervals should not be increased over the recommended intervals. The dose of infliximab may be reduced from 5 mg/kg body weight to

a minimum of 3 mg/kg bodyweight particularly if combined with methotrexate. With ustekinumab, the dose for a responding patient may be reduced from 90 to 45 mg. Moreover, few reports exist for the prolongation of intervals between injections.

Dose discontinuation/interruption

In cases of sustained response/clearance:

- Discontinuation of biologic therapy is not generally recommended due to the risk of recurrence or failure to recapture the initial response.
- However, if agreed with the patient, and after achieving a clinical response of clear or almost clear with good QoL for a prolonged period (i.e. a minimum of 1 year), discontinuing biologic therapy can be considered with careful follow-up.
- There is little evidence to suggest which subgroups of patients can discontinue the biologic medication. These subgroups include:
- Patient preference , Patients with a history of disease-free intervals or previously stable plaque-type psoriasis, Absence of PsA , Low impact of disease on QoL, No worsening of the disease after previous dose reductions and treatment withdrawals, However, because biologic therapies are typically considered for patients with more severe disease, and as a second line after failing conventional systemic therapy; patients on biologics are less likely to fulfill these criteria. Furthermore, fewer treatment options are available in case of relapse after discontinuation. Another consideration is that the risk of antibody formation increases with intermittent therapy. This is particularly important for the use of infliximab monotherapy where a higher risk of infusion reactions has been observed with intermittent therapy.

Efficacy with biologic therapy following treatment discontinuation/interruption:

- In patients receiving biologic therapy, there is a high likelihood of disease recurrence within several months of discontinuation of treatment, although some patients may maintain disease control for a prolonged period. Generally, maintaining PASI-90 response for a longer duration is documented with IL-17 as compared to anti-TNF inhibitors, as well as a higher percentage of patients will recapture PASI-90 after restarting IL-17 in comparison to anti-TNF
- Continuous biologic therapy generally results in greater improvements in efficacy over time compared with intermittent therapy.
- In clinical trials with primary responder patients, up to 20% fail, to regain a PASI 75 response after the re-initiation of the same biologic monotherapy. This decrease in efficacy may be greater with intermittent use of the drug

- Where therapy has been withdrawn and restarted, an induction dosing schedule should be used for re-introduction of the biologic therapy, except for infliximab (because of the increased risk of infusion reactions.

**Use of biologics in special patient populations**

This section of the guidelines covers the choice of biologic therapy in pregnancy and lactation, as well as in pediatrics and adolescents. In addition, recommendations of the choice of treatment are presented for patients with the following comorbidities: metabolic syndrome (including obesity), malignancy, demyelinating disease (multiple sclerosis), cardiovascular disease, congestive heart failure, inflammatory bowel disease, and lupus erythematosus. This section also provides insights for choosing appropriate biologic therapy for the treatment of moderate-to-severe psoriasis in the setting of chronic infections, such as hepatitis and tuberculosis.

**Pregnancy and lactation**

- TNF- α inhibitors can be used during lactation. They are safe in men attempting conception with their partners. There is a greater theoretical risk with use during the third trimester of pregnancy owing to transplacental transfer of TNF-a inhibitors. Certolizumab pegol has shown minimal to no placental transfer, so it is labeled as the best choice for pregnant psoriatic patients. Etanercept is considered an alternative to certolizumab if certolizumab is not available.
- IL-12/IL-23 inhibitors: The safety of IL-12/IL-23 inhibitors during pregnancy and lactation is uncertain. They are acceptable for men attempting conception with their partners.
- IL-17 inhibitors: There are no studies with these agents in human pregnancy. All IL-17 inhibitors are likely acceptable for men attempting conception with their partners. The presence of IL-17 inhibitors in excreted human milk has not been studied.
- IL-23 inhibitors: Safety during pregnancy for IL-23 inhibitors is unknown. The presence of IL-23 inhibitors in secreted human milk has not been studied (13). However, antibodies are effectively secreted during lactation, but generally have no significant impact.

**Pediatric and adolescent patients**

Recommendations on the choice of biologic therapy for pediatrics and adolescents are summarized in the table below:

**Table 7.** Summary of Recommendations for Choice of Biologic Therapy in Pediatrics and Adolescents

| FDA approved for moderate-to-severe pediatric plaque psoriasis | | Doses in children (subcutaneous) |
|---|---|---|
| **Adalimumab** | ≥ 4 years | 10–<15 kg<br>10 mg every other week<br>15–<30 kg<br>20 mg every other week<br>30 kg<br>40 mg every other week |
| **Etanercept** | ≥ 4 years | 0.8 mg/kg weekly, with a maximum of 50 mg per week |
| **Ustekinumab** | ≥ 6 years | <60 kg<br>0.75 mg/kg<br>60 kg<br>as adult<br>The dosing frequency is the same as in adults at weeks 0 and 4, then every<br>12 weeks thereafter |
| **Ixekizumab** | ≥ 6 years | <25 kg<br>40 mg at day 0 then 20 mg every 4 weeks<br>25–50 kg<br>80 mg at day 0 then 40 mg every 4 weeks<br>>50 kg<br>160 mg (two 80 mg syringes) at day 0 then 80 mg every 4 weeks |
| **Secukinumab** | ≥ 6 years | <50 kg<br>75 mg at weeks 0,1,2,3,4 followed by monthly maintenance doses.<br>50 kg<br>150 mg (can be increased to 300 mg) at weeks 0, 1, 2, 3, 4 followed by<br>monthly maintenance doses |

**Malignancy**: It is best to avoid all biologic therapy in patients with concurrent malignancy. In cases with a recent history of malignancy, it is recommended to

discuss the decision to initiate immunosuppressive therapies with the treating oncologist.

**Patients undergoing surgery:** For elective high-risk surgery, it is better to discontinue biologic therapy for about 4–5 half-lives before surgeries. This is despite the use of biologic therapy does not appear to affect the rates of surgical complications, like infections. For non-high-risk surgeries, biologics can be continued.

**Patients with hepatitis**: It is generally accepted that biologics should not be initiated in patients with active hepatitis B infection. The risk of developing severe hepatitis due to reactivation of HBV infection with biologic agents cannot be excluded, therefore management of psoriatic patients with a hepatologist should be considered in the cases of chronic carriers of HBV or those with positive serology and positive symptoms, such as nausea, appetite loss, and pruritus. The infliximab insert warns about HBV reactivation and recommends monitoring of HBV carriers during and several months after therapy. There is no clear consensus regarding the management of patients with HCV. However, the risk of developing severe hepatitis is not as critical for patients with HCV as for those with HBV. If the HCV-infected patient has already been successfully treated with antiviral therapy, the risk seems to be even lower. There are several published reports of successful treatment of HCV-infected psoriatic patients with adalimumab and etanercept. The safety profile of ustekinumab in patients with hepatitis is controversial. IL-17 inhibitors appear to have a favorable safety profile, but the available data is limited. Data are also limited on IL-23 inhibitor use in patients with hepatitis.

**Tuberculosis** Patients who receive anti -TNF biologic therapy is at increased risk of LTBI reactivation; the risk may be greater with the monoclonal antibodies (infliximab and adalimumab) than etanercept. Also, ustekinumab may facilitate the reactivation of tuberculosis. The atypical clinical presentation of infection with extrapulmonary and disseminated disease in patients treated with TNF antagonist's incidence is higher. There are no reported LTBI cases with IL-17 and IL-23 so far. If patients with LTBI have normal chest radiographs and no symptoms or signs of active TB, treatment of LTBI is indicated. Treatment with isoniazid (INH) for 9 months or rifampin for 4 months (only when INH regimen is not feasible and after consulting with a TB specialist due to high risk of rifampicin-resistance), aim to complete one month of treatment before starting the biologic therapy. If active TB is suspected, treatment with biologics should be deferred, and chest x-ray, sputum AFB stain, and culture must be repeated to rule out any new infection or reactivation. Referral to a TB expert is indicated in the case of LTBI or active TB.

Patients with demyelinating diseases/multiple sclerosis (MS)

- Do not use TNF-a antagonists in patients with demyelinating diseases and review alternative interventions in patients who have an affected first-degree

relative with the demyelinating disease. Stop treatment and seek specialist advice if neurological symptoms suggestive of the demyelinating disease develop during TNF-a antagonist therapy.

- IL 12/23 inhibitors may be used in patients with MS as it does not improve or worsen MS. IL-17 inhibitors can be used with some benefit in MS symptoms. Data are limited for the IL-23 inhibitors, but there are no reports of MS worsening with these drugs.

Patients at elevated cardiovascular risk

- TNF-α inhibitors are preferred systemic agents for the treatment of psoriasis in patients with coexisting cardiovascular risk factors. IL-12/23 inhibitor has some potential cardioprotective benefit, but more long-term data are needed. More data is needed for the use of IL-17 and IL-23 inhibitors.

Congestive heart failure (CHF)

- Avoid TNF-a antagonist therapy in people with severe cardiac failure (New York Health Association [NYHA] class III and IV) and discontinue TNF-a antagonist therapy in the event of new or worsening preexisting heart failure and seek specialist advice. IL 12/23, IL-17, and IL-23 inhibitors appear to be safe to use in patients with CHF.

Inflammatory bowel disease (IBD)

- Patients with a history of concomitant IBD might benefit from TNF-a inhibitor therapy. In fact, adalimumab, infliximab, and certolizumab are approved by the US FDA for the treatment of IBD. Etanercept is not as effective as other TNF-a inhibitors for Crohn's Disease.
- IL 12/23 inhibitor is also approved for Crohn's disease but not ulcerative colitis. IL-23 inhibitor use in Crohn's disease has promising results in preliminary studies, but more data are needed to draw definite conclusions (104). Exercise caution and consult a gastroenterology specialist before using IL-17 inhibitors in patients with IBD, or those with first-degree relatives with IBD.

Lupus erythematosus

- There is a concern for the development of de novo lupus or flare-up of lupus during treatment with TNF- a blockers, also known as anti TNF- a induced lupus (ATIL). IL-12/23 inhibitor is the safest treatment option for concomitant lupus and psoriasis as it reportedly improves SLE symptoms, specifically oral ulcerations, anemia or thrombocytopenia, and lupus arthritis. There is not enough data regarding the use of IL-17 and IL-23 inhibitors in patients with SLE, but no new cases of lupus induction or flare have been reported yet.

### 1.2.4 British Association of Dermatologists Guidelines for Biologic Therapy for Psoriasis (2020)

The overall aim of the guideline is to provide up-to-date, evidence-based recommendations on the use of biologic therapies targeting tumour necrosis factor (TNF) (**adalimumab**, **etanercept**, **certolizumab** pegol, **infliximab**), interleukin (IL)-12/23p40 (**ustekinumab**), IL-17A (**ixekizumab**, **secukinumab**), IL-17RA (**brodalumab**) and IL-23p19 (**guselkumab, risankizumab, tildrakizumab**) in adults, children and young people for the treatment of psoriasis; consideration is given to the specific needs of people with psoriasis and psoriatic arthritis[10].

British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020's recommendations are outlined below:

**Table 8.** British Association of Dermatologists (BAD) guidelines strength of recommendation ratings

| Strength | Wording | Symbols | Definition |
|---|---|---|---|
| **Strong recommendation for the use of an intervention** | 'Offer' (or similar, e.g. 'use', 'provide', 'take', 'investigate', etc.) | ↑↑ | Benefits of the intervention outweigh the risks; most patients would choose the intervention, while only a small proportion would not; for clinicians, most of their patients would receive the intervention; for policy makers, it would be a useful performance indicator |
| **Weak recommendation for the use of an intervention** | 'Consider' | ↑ | Risks and benefits of the intervention are finely balanced; most patients would choose the intervention but many would not; clinicians would need to consider the pros and cons for the patient in the context of the evidence; for policy makers it would be a poor performance |

| | | | |
|---|---|---|---|
| | | | indicator where variability in practice is expected |
| **No recommendation Θ Insufficient evidence to support any recommendation Strong recommendation against the use of an intervention** | 'Do not offer' | Θ<br>↓↓ | Insufficient evidence to support any recommendation Strong recommendation against the use of an intervention 'Do not offer' ↓↓ Risks of the intervention outweigh the benefits; most patients would not choose the intervention, while only a small proportion would; for clinicians, most of their patients would not receive the intervention |

**Using biologic therapy**

- (↑↑) Initiation and supervision of biologic therapy for people with psoriasis should be undertaken by specialist physicians experienced in the diagnosis and treatment of psoriasis. Routine monitoring may be delegated to other healthcare professionals, for example clinical nurse specialists. Manage psoriatic arthritis and/or multimorbidity in consultation with the relevant healthcare professionals.
- (↑↑) Agree and formalize arrangements for drug administration, monitoring and follow-up between health carers and the person receiving treatment.

**Criteria for biologic therapy**

- (↑↑) Offer biologic therapy to people with psoriasis requiring systemic therapy if methotrexate and ciclosporin have failed, are not tolerated or are contraindicated and the psoriasis has a large impact on physical, psychological or social functioning [for example, Dermatology Life Quality Index (DLQI) or Children's DLQI > 10 or clinically relevant depressive or anxiety symptoms] and one or more of the following disease severity criteria apply: • the psoriasis is extensive [defined as body surface area (BSA) > 10% or Psoriasis Area and Severity Index (PASI) ≥ 10] • the psoriasis is severe at localized sites and associated with significant functional impairment and/or high levels of distress (for example nail disease or involvement of high impact and difficult-to-treat sites such as the face, scalp, palms, soles, flexures and genitals).

- (↑) Consider biologic therapy earlier in the treatment pathway (e.g. if methotrexate has failed, is not tolerated or is contraindicated) in people with psoriasis who fulfil the disease severity criteria and who also have active psoriatic arthritis (see the NICE musculoskeletal conditions overview)8 or who have psoriasis that is persistent, i.e. that relapses rapidly (defined as > 50% baseline disease severity within 3 months of completion of any treatment) off a therapy that cannot be continued in the long term *(e.g. narrowband ultraviolet B and ciclosporin*)

**Prescribing biologic therapy**

- (↑↑) Be aware of the benefits of, contraindications to and adverse effects associated with biologic therapies and reference the drug specific SPCs.
- (↑↑) Provide high-quality, evidence-based information to people being prescribed biologic therapies. Explain the risks and benefits to people undergoing this treatment (and their families or carers where appropriate), using absolute risks and natural frequencies when possible. Explain the treatment regimen and importance of treatment adherence. Allow them adequate time to consider the information.
- (↑↑) Support and advice should be offered to people with psoriasis (and their families or carers where appropriate) by healthcare professionals who are trained and competent in the use of biologic therapies.

**Reviewing biologic therapy**

- (↑↑) Assess initial response to biologic therapy in people with psoriasis at time points appropriate for the drug in question, and then on a regular basis during therapy (e.g. every 6 months)
- (↑↑) Review the response to biologic therapy by considering:
    - psoriasis disease severity compared with baseline (e.g. PASI baseline to endpoint score)
    - the agreed treatment goal
    - control of psoriatic arthritis disease activity and/or inflammatory bowel disease (in consultation with a rheumatologist and/or gastroenterologist)
    - the impact of psoriasis on the person's physical, psychological and social functioning
    - the benefits vs. the risks of continued treatment

    - the views of the person undergoing treatment (and their family or carers, where appropriate)
    - adherence to the treatment
- (↑↑) Assess whether the minimal response criteria have been met, as defined by:
    - a 50% or greater reduction in baseline disease severity (e.g. PASI 50 response, or percentage BSA where PASI is not applicable) and
    - clinically relevant improvement in physical, psychological, or social functioning (e.g. ≥ 4-point improvement in DLQI or resolution of low mood).
- (↑) Consider changing to an alternative therapy, including another biologic therapy, if any of the following applies:
    - The psoriasis does not achieve the minimum response criteria.
    - the psoriasis initially responds but subsequently loses this response (secondary failure)
    - The current biologic therapy cannot be tolerated or becomes contraindicated.

**Choice of biologic therapy: general considerations**

- (↑↑) Before initiating or making changes to biologic therapy, consider both psoriasis and psoriatic arthritis and manage treatment in consultation with a rheumatologist or pediatric rheumatologist. Be aware that the presence of and phenotype of psoriatic arthritis (e.g. peripheral vs. axial disease) may influence access to, choice of and dose of biologic therapy. Actively screen for psoriatic arthritis (in people without this diagnosis), using a validated tool, e.g. Psoriasis Epidemiology Screening Tool (PEST), and be aware that the PEST may not detect axial arthritis/inflammatory back pain.
- (↑↑) Tailor the choice of agent to the needs of the person.

  *Psoriasis factors:* • the goal of therapy [for example, Physician's Global Assessment of clear or nearly clear], disease phenotype and pattern of activity, disease severity and impact, the presence of psoriatic arthritis (in consultation with an adult or pediatric rheumatologist), the outcomes of previous treatments for psoriasis.

  *Other individual factors:* person's age, past or current comorbid conditions (e.g. inflammatory bowel disease, heart failure), conception plans, body weight, the person's views and any stated preference on administration route or frequency, likelihood of adherence to treatment.

*Drug costs:* including administration costs, dosage, price per dose and commercial arrangements.

**Choice of biologic therapy in adults**

- (↑↑) Offer any of the currently licensed biologic therapies as first-line therapy) to adults with psoriasis who fulfil the criteria for biologic therapy, using the Decision Aid shown in the figure 3 below to inform treatment choice.

This is a decision aid to help clinicians and patients decide their treatment choice and not a comprehensive data source or replacement for the individual drug Summary of Product Characteristics. Please use in conjunction with the published guidelines, pathway algorithm and discussions in the online supporting information document (see File S2, Appendix D).

| | How do I take it? | | How effective is it? | | How common are the side effects? | | Is there anything else to consider? | |
|---|---|---|---|---|---|---|---|---|
| Questions you might want to ask | How often do I need to inject the treatment?[a] | For how long has this treatment been around?[b] | Roughly what proportion of people becomes clear or nearly clear (PASI90) after 3-4 months?[c] | What is the likelihood of staying on this treatment past 1 year?[d] | Roughly what proportion of people stops their treatment in the first 3-4 months due to unwanted effects?[c] | Roughly what proportion of people gets a serious infection in the first 3-4 months?[e] | What are *some* of the conditions that would make your doctor hesitant about giving you the treatment?[f] | What if I have psoriatic arthritis? |
| **TNF** | | | | | | | | |
| **Adalimumab** | 1 injection under the skin, every other week | Since 2008 | 41% | 77-81% chance[1] | 2% | < 1% | Moderate or severe heart failure, multiple sclerosis (or other conditions affecting the nerves) | Recommended treatment for psoriatic arthritis |
| **Certolizumab pegol** | 1 or 2 injections under the skin, every 2 weeks | Since 2019 | 41-48% | Not known at present | 2% | < 1% | Moderate or severe heart failure, multiple sclerosis (or other conditions affecting the nerves) | Recommended treatment for psoriatic arthritis |
| **Etanercept** | 1 injection under the skin, once or twice a week | Since 2004 | 23% | 67-73% chance[1] | 2% | < 1% | Moderate or severe heart failure, multiple sclerosis (or other conditions affecting the nerves) | Recommended treatment for psoriatic arthritis |
| **Infliximab** | 1 injection in the vein,[g] every 8 weeks | Since 2006 | 53% | 54-74% chance[1] | 5% | Not known at present | Moderate or severe heart failure, multiple sclerosis (or other conditions affecting the nerves) | Recommended treatment for psoriatic arthritis |
| **IL12/23** | | | | | | | | |
| **Ustekinumab** | 1 injection under the skin, every 12 weeks | Since 2009 | 46% | 86-92% chance[1] | 1% | < 1% | No particular condition | Recommended treatment for psoriatic arthritis only when TNF inhibitors have failed |
| **IL17** | | | | | | | | |
| **Brodalumab** | 1 injection under the skin, every 2 weeks | Since 2018 | 73% | Not known at present | 2% | < 1% | Inflammatory bowel disease (e.g. Crohn's disease or ulcerative colitis), recurrent candida infection (i.e. thrush) | This treatment is not licensed[h] for psoriatic arthritis |
| **Ixekizumab** | 1 injection under the skin, every 4 weeks | Since 2016 | 72% | Not known at present | 3% | < 1% | Inflammatory bowel disease (e.g. Crohn's disease or ulcerative colitis), recurrent candida infection (i.e. thrush) | Recommended treatment for psoriatic arthritis |
| **Secukinumab** | 2 injections under the skin, every month | Since 2015 | 60% | Not known at present | 2% | < 1% | Inflammatory bowel disease (e.g. Crohn's disease or ulcerative colitis), recurrent candida infection (i.e. thrush) | Recommended treatment for psoriatic arthritis |
| **IL23** | | | | | | | | |
| **Guselkumab** | 1 injection under the skin, every 8 weeks | Since 2018 | 68% | Not known at present | 2% | < 1% | No particular condition | This treatment is not licensed[h] for psoriatic arthritis |
| **Risankizumab** | 2 injections under the skin, every 12 weeks | Since 2019 | 74% | Not known at present | 1% | < 1% | No particular condition | This treatment is not licensed[h] for psoriatic arthritis |
| **Tildrakizumab** | 1 or 2 injections under the skin, every 12 weeks | Since 2019 | 39% | Not known at present | 2% | < 1% | No particular condition | This treatment is not licensed[h] for psoriatic arthritis |
| **Placebo** | | | | | | | | |
| **No active treatment** | Does not apply | Does not apply | 2% | Does not apply | 2% | < 1% | Does not apply | Does not apply |

NICE eligibility criteria, infliximab: PASI ≥20, DLQI >18; other biologic therapies: PASI ≥10, DLQI >10
[a]Only licensed maintenance doses are featured; see File S1: Table S1 for information on initiation dosing schedules.
[b]First approval of the drug for moderate to severe plaque psoriasis.
[c]The evidence is drawn from clinical trials including a mixed biologic-naïve and experienced population; figures quoted are based on anticipated absolute effects derived from network meta-analyses of licensed biologic doses.
[d]The evidence is drawn from a real-world UK biologic-naïve population; it may not apply to biologic choice for subsequent lines of treatment.
[e]The evidence is drawn from clinical trials including a mixed biologic-naïve and experienced population; figures quoted are based on Peto odds ratio analyses of all biologic doses.
[f]Please refer to individual drugs' summary of product characteristics for a more comprehensive list (www.medicines.org.uk).
[g]Requires attendance to hospital.
[h]A treatment that is not licensed for a particular condition means it has not been awarded a Market Authorisation from the U.K. Medicines Healthcare Products Regulatory Agency (MHRA) for that condition. Once awarded, the licensed treatment can be marketed and sold in the U.K.

***Figure 3.*** *Decision aid – biological therapy for psoriasis (retrieved from the BAD 2020 guideline)*

- (↑↑) Offer any of the currently licensed biologic therapies when psoriasis has not responded to a first biologic therapy. Use the Decision Aid shown in figure 2 and consider all factors detailed in R14 to select the most appropriate agent.
- (↑↑) Offer a TNF antagonist or an IL-17 antagonist* as a first-line therapy to adults with psoriasis and who also have psoriatic arthritis, using the Decision Aid shown the figure 2 below to inform treatment choice.10–13 *Please note that brodalumab is not licensed for psoriatic arthritis.

- (↑) Consider etanercept for use in people where a TNF antagonist is indicated and other available biological agents have failed or cannot be used, or where a short half-life is important.
- (↑↑) Reserve infliximab for use in people with very severe disease, or where other available biological agents have failed or cannot be used, or where weight-based dosing is a priority.

**When to consider dose escalation/interval reduction**

- (↑) Consider escalating the dose of or reducing the interval for biologic therapy in adults and when an inadequate primary response might be due to insufficient drug exposure (e.g. in people who are obese and/or whose psoriasis relapses during the treatment cycle and/or if the drug level is known to be subtherapeutic). Consider that this may be associated with an increased risk of infection/adverse events and, depending on the drug, off-licence and may not be approved by NICE and therefore not funded.

**Table 9.** Dose-Escalation/Interval-Reduction Strategy (Adapted from the BAD 2020 Guideline)

| Biological agent | Suggested dose-escalation/interval-reduction strategy |
|---|---|
| Adalimumab 40 mg every other week | Adalimumab 40 mg weekly |
| Certolizumab pegol 200 mg every 2 weeks | Certolizumab pegol 400 mg every 2 weeks |
| Etanercept 50 mg once weekly | Etanercept 50 mg twice weekly |
| Infliximab 5 mg $kg^{-1}$ every 8 weeks | [a] Infliximab 5 mg $kg^{-1}$ every 6 weeks |
| Ixekizumab 80 mg every 4 weeks | [a] Ixekizumab 80 mg every 2 weeks |
| Tildrakizumab 100 mg every 12 weeks | Tildrakizumab 200 mg every 12 weeks (high disease burden or ≥ 90 kg) |
| Ustekinumab 45 mg every 12 weeks (≤ 100 kg) | [a] Ustekinumab 90 mg every 8 or 12 weeks (≤ 100 kg) |
| Ustekinumab 90 mg every 12 weeks (> 100 kg) | [a] Ustekinumab 90 mg every 8 weeks (> 100 kg) |
| [a] Off-license use. | |

**What to do when a second or subsequent biologic therapy fails in adults**

- (↑↑) When a person's psoriasis responds inadequately to a second or subsequent biological agent, review treatment goals, seek advice from a

dermatologist with expertise in biologic therapy and consider any of the following strategies: reiterate advice about modifiable factors contributing to poor response such as obesity and poor adherence (intentional or nonintentional), consider whether drug exposure is adequate, optimize adjunctive therapy (e.g. switch from oral to subcutaneous methotrexate), switch to an alternative biological agent, alternative or supplementary nonbiologic therapy approaches (e.g. inpatient topical therapy, phototherapy or systemic therapies).

**Choice of biologic therapy in children and young people**

- (↑↑) Offer adalimumab (age ≥ 4 years), etanercept (≥ 6 years) or Ustekinumab (≥ 12 years) to children and young people who fulfil the criteria for biologic therapy.
- (↑↑) When a child's or young person's psoriasis responds inadequately to a first or subsequent biological agent seek advice from a dermatologist with expertise in biologic therapy in this age group and consider any of the following strategies: reiterate advice about modifiable factors contributing to poor response (e.g. obesity and poor adherence), optimize adjunctive therapy (e.g. switch from oral to subcutaneous methotrexate), switch to an alternative biological agent, alternative or supplementary nonbiologic therapy approaches (e.g. inpatient topical therapy or systemic therapies).

**Transitioning to or between biologic therapies**

- (↑↑) When choosing the transitioning strategy from one drug therapy to another and whether a therapy washout (or no washout) should be used, take into consideration: the pharmacology of the drugs that are being stopped and started, the person's clinical circumstances, the person's views on the risks and benefits of transitioning option(s)
- (↑) When transitioning from standard systemic therapy to biologic therapy consider these:
    - In stable disease, aim to allow 1 month to elapse between the last dose of any current standard systemic immunosuppressant psoriasis therapy (except methotrexate) and the planned date of biologic initiation.
    - Start a biologic therapy with no drug washout period in people taking methotrexate, or in people on other therapies where this would lead to unstable disease.
    - When standard, systemic immunosuppressant therapy cannot be stopped (e.g. in people for whom a disease flare would be severe or

hazardous), rationalize use of therapy and stop as soon as possible (e.g. when a minimum response has been achieved).

- (↑) When transitioning to a new biologic therapy (from a previous biologic therapy) consider using a 1-month washout period, or the length of the treatment cycle (whichever is longer), between the last dose of the current biologic therapy and the planned date of biologic initiation.

**Conception and pregnancy**

- (↑↑) Advise women of childbearing potential, who are starting biologic therapy for psoriasis, to use effective contraception and to discuss conception plans with the consultant supervising their care. There are no known interactions between biologic therapies and contraceptive methods.
- (↑↑) For women planning conception or who are pregnant, provide information about what is known about the effects of biologic therapy, including these:
    - the importance of controlling severe or unstable psoriasis to maintain maternal health.
    - most of the available evidence relates to TNF antagonists in women with rheumatological or inflammatory bowel disease.
    - most pregnancies reported in women exposed to TNF antagonists at conception and/or during pregnancy have successful outcomes, with no increase in stillbirths, congenital malformations, preterm births or neonatal infections.
    - exposure to TNF antagonists during pregnancy may increase the risk of maternal infection.
    - maternal IgG, and therefore biological drugs currently licensed for psoriasis (with the exception of certolizumab pegol), is actively transferred to the developing fetus during the second and third trimesters and the impact of this on neonatal development and risk of infection has not been adequately studied.
    - certolizumab pegol transfer across the placenta is low or negligible.
    - in general, live vaccines must be avoided for the first 6 months of life in infants born to mothers taking biologic therapy beyond 16 weeks' gestation.
- (↑↑) Discuss the risks and benefits of using biologic therapy in women who are planning conception or who are pregnant. Offer advice on a case-by-case basis by taking into account the woman's views and: the available evidence,

her current disease status, the course of psoriasis disease and the fetal outcome during any prior pregnancies, the risk of severe or unstable psoriasis without biologic therapy, her physical, psychological and social functioning without biologic therapy, the options for alternative treatment strategies in the event of disease flare.

- (↑) If the decision to use biologic therapy when planning conception or during pregnancy has been made: consider using certolizumab pegol as a first-line choice when starting biologic therapy in women planning conception, consider stopping biologic therapy in the second/third trimester to minimize fetal exposure and limit the potential risk to the neonate, taking into account individual biologics' pharmacokinetics and transfer across the placenta, consider using ciclosporin or certolizumab pegol as firstline options when it is necessary to start a systemic therapy during the second or third trimester.
- (GPP) Consider continuing or restarting biologic therapy in women wishing to breastfeed. Explain the benefits of breastfeeding and that the small amounts of biologic therapy present in breast milk are unlikely to be absorbed systemically by the infant.
- (↑↑) Ensure consultation and information sharing across specialties, including with an obstetrician who has expertise in caring for pregnant women with medical problems. Collect pregnancy outcome data for safety registries.
- (↑↑) Be aware that limited evidence reports that use of TNF antagonist therapy by men around the time of conception resulted in successful outcomes in most pregnancies, with no increased risk of congenital malformations, preterm births or small for gestational age infants.

**Biologic therapy and cancer risk**

- (↑↑) Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to:
    - their past or current history of cancer and/or
    - any future risk of cancer
- (↑↑) Provide information to people with psoriasis about the importance of participating in national cancer screening programs.
- (↑↑) Exercise caution and discuss with the relevant cancer specialist when prescribing biologics in people with psoriasis and:
    - a history of cancer, particularly if this has been diagnosed and treated less than 5 years previously and/or
    - where the baseline risk of skin cancer is increased

- (↑↑) Discuss the risks and benefits of continuing vs. stopping biologic therapy in patients who develop or have completed recent treatment for cancer. Offer advice on a case-by-case basis by considering the advice from the treating oncologist, multidisciplinary team discussion and patient choice considering: the risk of severe or unstable psoriasis if the biologic therapy were stopped, the physical, psychological, and social functioning if the biologic therapy were stopped, the options for alternative treatment strategies, the impact of cancer progression/recurrence.

**Biologic therapy and infections**

- (↑↑) Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to risk factors for infection (e.g. comorbidities, cotherapy, lifestyle and travel), known infections (past or current), signs or symptoms suggestive of infection.

**Biologic therapy and chronic viral infections – hepatitis B, hepatitis C and HIV**

- (↑↑) Test for hepatitis B (surface antigen and core antibody), hepatitis C (IgG) and HIV (HIV-1 and HIV-2 antibodies and HIV-1 antigen) infection in people starting biologic therapy.
- (↑) Consider ongoing screening (e.g. annually) for hepatitis B, hepatitis C and HIV, particularly in people who are at increased risk of infection.
- (↑↑) Retest for viral hepatitis in any person who develops unexplained transaminitis (raised alanine aminotransferase and/or aspartate aminotransferase); retest for HIV infection in any person who has symptoms or other conditions that might represent HIV seroconversion/infection.
- (↑↑) Consult a hepatitis specialist when treating all people with biologic therapy who have hepatitis B or C infection, whether newly diagnosed or previously known.
- (↑↑) Provide treatment options to people with psoriasis who are HIV seropositive on a case-by-case basis; be aware that severe psoriasis can occur in people with uncontrolled HIV infection. Involve relevant specialists and ensure HIV viral load is suppressed on antiretroviral therapy before considering biologic therapy.
- (GPP) Test for varicella zoster (VZ) virus antibody in people with a negative or uncertain history for chickenpox before starting biologic therapy. Consider varicella vaccination before initiating biologic therapy in those who are not varicella immune and seek expert advice. Be aware of the indications for postexposure prophylaxis in VZ-susceptible individuals taking biologics, with VZ immunoglobulin or oral aciclovir/valaciclovir.

**Use of biologic therapy and tuberculosis**

- (↑) Consider screening for latent tuberculosis (TB) with an interferon-gamma release assay (IGRA) alone, or with an IGRA and concurrent Mantoux test; be aware of the individual's risk factors for TB when interpreting results.
- (↑↑) Apply local policy on the use of a plain chest radiograph for screening for TB to rule out abnormalities at baseline including granulomas indicative of prior infection and other confounding lung diseases. If positive, assess for active TB and/or management of latent TB in consultation with a TB specialist (see NICE tuberculosis guideline).
- (GPP) In people who require treatment for latent TB [3 months of isoniazid (with pyridoxine) and rifampicin, or 6 months of isoniazid (with pyridoxine)], aim to complete 2 months of treatment before commencing biologic therapy.
- (GPP) Any symptoms or signs suggestive of TB, new exposure to TB or prolonged residence in a high-incidence setting should prompt further clinical assessment and investigation, including a repeat IGRA. Be aware that active TB on TNF antagonist therapy is often disseminated and extrapulmonary; symptoms may include unexplained weight loss, night sweats, nonrevolving cough, haemoptysis and lymphadenopathy.
- (GPP) Inform people that they should seek medical advice if symptoms of TB develop during or after treatment with a biologic therapy and issue a patient alert card in line with Medicines and Healthcare products Regulatory Agency guidance.

**Biologics and vaccination**

- (↓↓) Do not give live vaccines to people on biologic therapy or to infants (up to 6 months of age) whose mothers have received biologic therapy beyond 16 weeks' gestation. Please check individual drug SPC.
- (↑↑) Stop biologic therapy for 6–12 months before giving live vaccines, e.g. the varicella and shingles (herpes zoster) vaccine. Be aware that the UK Green Book (Immunization Against Infectious Disease) has recently advised increasing the interval from 6 to 12 months; expert opinion suggests the interval required will vary depending on the pharmacokinetic/pharmacodynamic profile of each drug and should be determined on a case-by-case basis, taking into account the SPC drug specifications and expert advice. Biologic therapy can be started 4 weeks after administration of a live vaccine.
- (↑↑) Provide people on biologic therapy with information on safe use of vaccinations including which vaccination should be used and which to avoid.

- (↑↑) Where possible, complete all required vaccinations prior to initiation of biologic therapy and review vaccination requirements during therapy with reference to the Green Book19 and the clinical risk category 'immunosuppression'.

**Important contraindications to biologic therapies**

- (GPP) Do not use TNF antagonists in people with demyelinating diseases and consider alternative interventions in people who have a first-degree relative with demyelinating disease.
- (GPP) Stop treatment and seek specialist advice if neurological symptoms suggestive of demyelinating disease develop during TNF antagonist therapy. Symptoms include loss or reduction of vision in one eye with painful eye movements; double vision; ascending sensory disturbance and/or weakness; problems with balance, unsteadiness, or clumsiness; altered sensation travelling down the back and sometimes into the limbs when bending the neck forwards.
- (GPP) Avoid TNF antagonist therapy in people with severe cardiac failure [New York Heart Association (NYHA) class III and IV].
- (GPP) Assess people with well-compensated (NYHA class I and II) cardiac failure and consult with a cardiology specialist before using TNF antagonist therapy.
- (GPP) Stop TNF antagonist therapy in the event of new or worsening pre-existing heart failure and seek specialist advice.
- (GPP) Exercise caution and consult a gastroenterology specialist before using brodalumab, ixekizumab or secukinumab in people with inflammatory bowel disease.
- (GPP) In people undergoing elective surgery, balance the risk of postoperative infection against the risk of developing severe or unstable disease by stopping biologic therapy. Advise stopping biologic therapy 3–5 times the half-life of the drug in question or the length of the treatment cycle (whichever is longer) between the last dose of therapy and the planned surgery. Inform the surgical team that the patient may be at a higher risk of infection postoperatively. Restart biologic therapy postoperatively if there is no evidence of infection and wound healing is satisfactory.

# Section 2.0 Drug Therapy in Psoriasis

This section comprises three subsections: the first one contains the newly recommended drugs, the second one covers drug modifications, and the third one outlines the drugs that have been withdrawn from the market.

## 2.1 Additions

Since February 2020, there have been new drugs for the management of psoriasis have received FDA approval. These include a phosphodiesterase-4 (PDE4) inhibitor, **roflumilast**, where the **topical formulation** has received FDA approval in 2022 for plaque psoriasis and in 2023 for plaque psoriasis in children. A tyrosine kinase 2 (TYK2) inhibitor, **deucravacitinib**, was approved in September 2022 for the treatment of adults with moderate-to-severe plaque psoriasis. These two agents have not yet been registered by the SFDA and are discussed in section 2.4 below.

In addition, an interleukin-23 antagonist, **tildrakizumab**, approved in March 2018 for the treatment of adults with moderate to severe plaque psoriasis, and an interleukin-17A and interleukin-17F antagonist, **bimekizumab**, approved for the same indication in October 2023, were **registered by the SFDA**. Hence, relevant information pertaining to this drug can be found below.

### 2.1.1 Bimekizumab

This section includes pertinent information regarding the use of ***Bimekizumab in*** Psoriasis[11].

**Table 10**. Bimekizumab Drug Information

| SCIENTIFIC NAME<br>Bimekizumab | |
|---|---|
| **SFDA Classification** | Prescription |
| **SFDA Approval** | Yes |
| **US FDA** | Yes |
| **EMA** | Yes |
| **MHRA** | Yes |
| **PMDA** | No |
| **Indication (ICD-10)** | L40 |
| **Drug Class** | Monoclonal Antibody |
| **Drug Sub-class** | - |
| **ATC Code** | L04AC |

| | |
|---|---|
| **Pharmacological Class (ASHP)** | Humanized Monoclonal Antibody |
| **DRUG INFORMATION** | |
| **Dosage Form** | Solution for injection in pre-filled pen |
| **Route of Administration** | Subcutaneous use |
| **Dose (Adult) [DDD]*** | 320 mg (given as two 160 mg injections) once every 4 weeks for the first 16 weeks, and then every 8 weeks thereafter. |
| **Maximum Daily Dose Adults*** | 320 mg |
| **Dose (pediatrics)** | N/A |
| **Maximum Daily Dose Pediatrics*** | N/A |
| **Adjustment** | There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).<br>**Obesity:** Plaque psoriasis, moderate to severe: ≥120 kg: SUBQ: 320 mg (given as two 160 mg injections) once every 4 weeks**.** |
| **Prescribing edits*** | **AGE, MD, PA, ST, QL** |
| **AGE (Age Edit):** The safety and efficacy of bimekizumab in children and adolescents below the age of 18 years have not been established. No data are available. | |
| **CU (Concurrent Use Edit):** N/A | |
| **G (Gender Edit):** N/A | |
| **MD (Physician Specialty Edit**): Biological agents for psoriasis should be initiated and supervised only by dermatologists experienced in the diagnosis and treatment of psoriasis. | |
| **PA (Prior Authorization):** Bimekizumab should be given for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy when the disease has not responded to other systemic treatments, not tolerated or are contraindicated at a dose of 320 mg (given as two 160 mg injections) once every 4 weeks for the first 16 weeks, and then every 8 weeks thereafter. Bimekizumab should be prescribed by dermatologists experienced in the diagnosis and treatment of psoriasis. | |
| **QL (Quantity Limit:** 320 mg (given as two 160 mg injections) once every 4 weeks for the first 16 weeks, and then every 8 weeks thereafter. | |
| **ST (Step Therapy):** Treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy when the | |

| | |
|---|---|
| disease has not responded to other systemic treatments, were not tolerated, or are contraindicated. | |
| **EU (Emergency Use Only):** N/A | |
| **PE (Protocol Edit):** N/A | |
| **SAFETY** | |
| **Main Adverse Drug Reactions (Most common and most serious)** | **Most common:**<br>• Immunologic: Antibody development (45%; neutralizing: 16%)<br>• Infection: Infection (36%; including herpes simplex infection [1%], oral candidiasis [9%], serious infection [<1%], and upper respiratory tract infection [15%])<br>**Most serious:**<br>• **Infections**<br>• **Liver biochemical abnormalities**<br>• **Suicidal ideation**<br>• **Tuberculosis** |
| **Drug Interactions** | **Category X**<br>XAbrocitinib<br>XAdenovirus (Types 4, 7) Vaccine<br>XAnifrolumab<br>XBaricitinib<br>XBCG (Intravesical)<br>XBCG Vaccine (Immunization)<br>XBrivudine<br>XChikungunya Vaccine (Live)<br>XCholera Vaccine<br>XCladribine<br>XDengue Tetravalent Vaccine (Live)<br>XDeucravacitinib<br>XEbola Zaire Vaccine (Live)<br>XEtrasimod<br>XFilgotinib<br>XInFLIXimab<br>XInfluenza Virus Vaccine (Live/Attenuated)<br>XJapanese Encephalitis Virus Vaccine (Live/Attenuated) |

| | |
|---|---|
| | **X** Measles, Mumps, and Rubella Virus Vaccine<br>**X** Measles, Mumps, Rubella, and Varicella Virus Vaccine<br>**X** Mumps Virus Vaccine<br>**X** Nadofaragene Firadenovec<br>**X** Natalizumab<br>**X** Pimecrolimus<br>**X** Poliovirus Vaccine (Live/Bivalent/Oral)<br>**X** Poliovirus Vaccine (Live/Trivalent/Oral)<br>**X** Ritlecitinib<br>**X** Rotavirus Vaccine<br>**X** Ruxolitinib (Topical)<br>**X** Smallpox Vaccine Live<br>**X** Tacrolimus (Topical)<br>**X** Talimogene Laherparepvec<br>**X** Tertomotide<br>**X** Tofacitinib<br>**X** Typhoid Vaccine<br>**X** Upadacitinib<br>**X** Varicella Virus Vaccine<br>**X** Yellow Fever Vaccine<br>**X** Zoster Vaccine (Live/Attenuated)<br>**Category D**<br>**D** Anthrax Vaccine Adsorbed<br>**D** Anthrax Vaccine Adsorbed (Adjuvanted)<br>**D** Belimumab<br>**D** Coccidioides immitis Skin Test<br>**D** COVID-19 Vaccine (Adenovirus Vector)<br>**D** COVID-19 Vaccine (mRNA)<br>**D** Denosumab<br>**D** Diphtheria and Tetanus Toxoids<br>**D** Diphtheria and Tetanus Toxoids, Acellular Pertussis, and Poliovirus Vaccine<br>**D** Diphtheria and Tetanus Toxoids, Acellular Pertussis, Hepatitis B (Recombinant), Poliovirus (Inactivated), |

| | |
|---|---|
| | and Haemophilus influenzae B Conjugate (Adsorbed) Vaccine<br>**D**Diphtheria and Tetanus Toxoids, Acellular Pertussis, Poliovirus and Haemophilus b Conjugate Vaccine<br>**D**Diphtheria and Tetanus Toxoids, and Acellular Pertussis Vaccine<br>**D**Diphtheria and Tetanus Toxoids, Whole-Cell Pertussis, Hepatitis B (Recombinant), and Haemophilus influenzae b Conjugate Vaccine<br>**D**Diphtheria, Tetanus Toxoids, Acellular Pertussis, Hepatitis B (Recombinant), and Poliovirus (Inactivated) Vaccine<br>**D**Haemophilus b Conjugate Vaccine<br>**D**Hepatitis A and Hepatitis B Recombinant Vaccine<br>**D**Hepatitis A Vaccine<br>**D**Hepatitis B Vaccine (Recombinant [Adjuvanted])<br>**D**Hepatitis B Vaccine (Recombinant)<br>**D**Hepatitis B Vaccine (Trivalent [Recombinant])<br>**D**Human Papillomavirus Vaccine (9-Valent)<br>**D**Human Papillomavirus Vaccine (Bivalent)<br>**D**Human Papillomavirus Vaccine (Quadrivalent)<br>**D**Influenza A Virus Vaccine (H5N1)<br>**D**Influenza Virus Vaccine (Inactivated)<br>**D**Influenza Virus Vaccine (Recombinant)<br>**D**Japanese Encephalitis Virus Vaccine (Inactivated)<br>**D**Leflunomide<br>**D**Meningococcal (Groups A / B / C / W / Y) Vaccine<br>**D**Meningococcal (Groups A / C / Y and W-135) Conjugate Vaccine<br>**D**Meningococcal Group B Vaccine |

| | |
|---|---|
| | **D**Meningococcal Group C Conjugate Vaccine<br>**D**Poliovirus Vaccine (Inactivated)<br>**D**Polymethylmethacrylate<br>**D**Q Fever Vaccine<br>**D**Rabies Vaccine<br>**D**Respiratory Syncytial Virus Vaccine (Recombinant [Adjuvanted])<br>**D**Respiratory Syncytial Virus Vaccine (Recombinant)<br>**D**Sipuleucel-T<br>**D**Smallpox and Monkeypox Vaccine (Live)<br>**D**Tetanus Toxoid (Adsorbed)<br>**D**Tick-Borne Encephalitis Vaccine<br>**D**Travelers' Diarrhea and Cholera Vaccine<br>**D**Typhoid and Hepatitis A Vaccine<br>**D**Zoster Vaccine (Recombinant) |
| **Special Population** | Older adults were more likely to experience the following adverse effects compared to younger adults: Oral candidiasis, dermatitis, and eczema. Age did not affect efficacy or clearance of the drug. |
| **Pregnancy** | Bimekizumab is a humanized monoclonal antibody ($IgG_1$). Human IgG crosses the placenta. Fetal exposure is dependent upon the IgG subclass, maternal serum concentrations, placental integrity, newborn birth weight, and GA, generally increasing as pregnancy progresses. The lowest exposure would be expected during the period of organogenesis and the highest during the third trimester.<br>Data collection to monitor pregnancy and infant outcomes following exposure to bimekizumab is ongoing. Health care providers are encouraged to enroll |

| | |
|---|---|
| | patients exposed to bimekizumab during pregnancy in the Organization of Teratology. |
| **Lactation** | It is not known if bimekizumab is present in breast milk.<br>Bimekizumab is a humanized monoclonal antibody ($IgG_1$). Human IgG is present in breast milk; concentrations are dependent upon IgG subclass and postpartum age. According to the manufacturer, the decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of treatment to the mother. |
| **Contraindications** | There are no contraindications listed in the manufacturer's labeling.<br>*Canadian labeling:* Additional contraindications (not in US labeling): Hypersensitivity to bimekizumab or any component of the formulation. |
| **Monitoring Requirements** | Prior to initiating therapy: Tuberculosis (TB) screening (chest X-ray if TB positive); evaluate for depression and suicidal ideation, obtain baseline liver transaminases; ensure age-appropriate vaccinations are up to date (live vaccines should not be administered during therapy).<br>During therapy: Periodic liver transaminases if clinically indicated; signs and symptoms of active TB or other active infections, or inflammatory bowel disease. Monitor for emergence or worsening of depression, suicidal ideation, or behavior; if symptoms occur patient should be referred to an appropriate mental health care provider. |
| **Precautions** | ***Concerns related to adverse effects:*** |

| | |
|---|---|
| | • Infections: May increase the risk of infections. A higher rate of infections was observed with bimekizumab treatment in clinical trials, including upper respiratory tract, oral candidiasis, tinea, gastroenteritis, and herpes simplex infections. Bimekizumab should not be initiated in patients with untreated, active infections.<br>• Liver biochemical abnormalities: Use of bimekizumab is associated with an increase in liver serum transaminases >3 × ULN, which occurred between 28 and 198 days after initiating therapy and resolved with discontinuation.<br>• Suicidal ideation: Patients without a prior history of suicidal ideation or behavior experienced a higher rate of suicidal ideation during therapy.<br>• Tuberculosis: Patients should be evaluated for tuberculosis (TB) infection (latent TB) prior to initiating therapy; do not initiate therapy in patients with TB disease (active TB). Consider antituberculosis therapy if an adequate course of treatment cannot be confirmed in patients with a history of TB infection or disease.<br>***Other warnings/precautions:***<br>Immunizations: Patients should be brought up to date with all immunizations before initiating therapy. Live vaccines should not be given concurrently. |
| **Black Box Warning** | **N/A** |
| **REMS** | **N/A** |

## HEALTH TECHNOLOGY ASSESSMENT (HTA)

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

**Table 11.** Bimekizumab HTA Analysis

| MEDICATION | AGENCY | DATE – HTA RECOMMENDATION |
|---|---|---|
| **Bimekizumab** | NICE[12] | **01 September 2021 -** Bimekizumab is **recommended** as an option for treating plaque psoriasis in adults, only if:<br>• the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and<br>• the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated and<br>• the company provides the drug according to the commercial arrangement.<br>Stop bimekizumab treatment at 16 weeks if the psoriasis has not responded adequately. An adequate response is defined as:<br>• a 75% reduction in the PASI score (PASI 75) from when treatment started or<br>• a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started.<br>Choose the least expensive treatment if patients and their clinicians consider bimekizumab to be one of a range of suitable treatments (considering availability of biosimilar products, administration costs, dosage, price per dose and commercial arrangements).<br>Consider how skin color could affect the PASI score and make any appropriate clinical adjustments. |

| | | |
|---|---|---|
| | | Consider any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DLQI and make any appropriate adjustments.<br>These recommendations are not intended to affect treatment with bimekizumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop. |
| | CADTH[13] | **February 14, 2022 -** For the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.<br>**Conditions for reimbursement**<br>Initiation: Eligibility for reimbursement of bimekizumab should be based on the criteria used by each of the public drug plans for reimbursement of other IL-17 inhibitors for the treatment of adult patients with moderate to severe plaque psoriasis.<br>Renewal: Bimekizumab should be renewed in a similar manner to other IL-17 inhibitors currently reimbursed for the treatment of adult patients with moderate to severe plaque psoriasis.<br>Prescribing: Patients should be under the care of a dermatologist. Bimekizumab should not be used in combination with other biologic treatments for moderate to severe plaque psoriasis.<br>Pricing: Price reduction.<br>Feasibility of adoption: The feasibility of adoption of bimekizumab must be addressed. |
| | HAS[14] | **3/15/2023** - **Favorable opinion for reimbursement** in the "Treatment of moderate to severe plaque psoriasis in adults who require systemic treatment."<br>**2/09/2022** - Favorable opinion for reimbursement in the treatment of plaque psoriasis in adults, in severe chronic forms only, defined by: |

| | | |
|---|---|---|
| | | • Failure (insufficient response, contraindication or intolerance) to at least two treatments including non-biologic systemic therapies and phototherapy,<br>• and an extensive form and/or significant psychosocial impact.<br>Unfavorable opinion for reimbursement in other forms of plaque psoriasis in adults.<br>This opinion is issued pending re-evaluation by the Committee of the reimbursement scope and role in the strategy of all the biologics not included in the PSOBIOTEQ 1 observational study, including BIMZELX (bimekizumab). |
| | IQWIG[15] | **3/3/2022** - Adult patients with moderate to severe plaque psoriasis<br>Result of dossier assessment:<br>• Patients who are not candidates for conventional treatment in the framework of an initial systemic therapy: hint of minor added benefit.<br>• Patients who have had an inadequate response or who have been intolerant to systemic therapy: added benefit not proven. |
| | PBS[16] | N/A |

**Conclusion Statement – Bimekizumab**

NICE recommends the use of Bimekizumab as an option for treating plaque psoriasis in adults under certain conditions, only if: the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated and the company provides the drug according to the commercial arrangement. CADTH, HAS and IQWIG had favorable opinions about the use of Bimekizumab for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

### 2.1.2 Tildrakizumab

This section includes pertinent information regarding the use of ***Tildrakizumab*** *in* Psoriasis[11].

**Table 12.** Tildrakizumab Drug Information

| SCIENTIFIC NAME<br>Tildrakizumab | |
|---|---|
| **SFDA Classification** | Prescription |
| **SFDA Approval** | Yes |
| **US FDA** | Yes |
| **EMA** | Yes |
| **MHRA** | Yes |
| **PMDA** | No |
| **Indication (ICD-10)** | L40 |
| **Drug Class** | Antipsoriatic Agent |
| **Drug Sub-class** | Interleukin-23 Inhibitor; Monoclonal Antibody |
| **ATC Code** | L04AC17 |
| **Pharmacological Class (ASHP)** | Interleukin-23 Inhibitor; |
| **DRUG INFORMATION** | |
| **Dosage Form** | Solution for injection in pre-filled syringe |
| **Route of Administration** | Subcutaneous use |
| **Dose (Adult) [DDD]*** | 100 mg at weeks 0, 4, and then every 12 weeks thereafter. |
| **Maximum Daily Dose Adults*** | 100 mg (1 syringe at Weeks 0 & 4, every 12 weeks) |
| **Dose (pediatrics)** | N/A |
| **Maximum Daily Dose Pediatrics*** | N/A |
| **Adjustment** | **Dosing: Altered Kidney Function: Adult**<br>There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).<br>**Dosing: Hepatic Impairment: Adult** |

| | |
|---|---|
| | There are no dosage adjustments provided in the manufacturer's labeling (has not been studied). |
| **Prescribing edits*** | **AGE, MD, PA, ST, QL** |
| **AGE (Age Edit):** The safety and efficacy of tildrakizumab in children and adolescents below the age of 18 years have not yet been established. No data are available. | |
| **CU (Concurrent Use Edit):** N/A | |
| **G (Gender Edit):** N/A | |
| **MD (Physician Specialty Edit**): Biological agents for psoriasis should be initiated and supervised only by dermatologists experienced in the diagnosis and treatment of psoriasis. | |
| **PA (Prior Authorization):** Tildrakizumab should be given for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy when the disease has not responded to other systemic treatments, not tolerated**,** or are contraindicated 100 mg at weeks 0, 4, and then every 12 weeks thereafter. Tildrakizumab should be prescribed by dermatologists experienced in the diagnosis and treatment of psoriasis. | |
| **QL (Quantity Limit:** 100 mg at weeks 0, 4, and then every 12 weeks thereafter. | |
| **ST (Step Therapy):** Treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy when the disease has not responded to other systemic treatments, were not tolerated**,** or are contraindicated. | |
| **EU (Emergency Use Only):** N/A | |
| **PE (Protocol Edit):** N/A | |
| **SAFETY** | |
| **Main Adverse Drug Reactions (Most common and most serious)** | **Most common:**<br>• Infection: Infection (23%)<br>• Respiratory: Upper respiratory tract infection (14%)<br>**Most serious:**<br>• **Antibody formation**<br>• **Hypersensitivity**<br>• **Infections** |
| **Drug Interactions** | **Category X**<br>• XAdenovirus (Types 4, 7) Vaccine<br>• XAnifrolumab<br>• XBCG Vaccine (Immunization)<br>• XChikungunya Vaccine (Live) |

| | |
|---|---|
| | • XCholera Vaccine<br>• XDengue Tetravalent Vaccine (Live)<br>• XEbola Zaire Vaccine (Live)<br>• XInFLIXimab<br>• XInfluenza Virus Vaccine (Live/Attenuated)<br>• XJapanese Encephalitis Virus Vaccine (Live/Attenuated)<br>• XMeasles, Mumps, and Rubella Virus Vaccine<br>• XMeasles, Mumps, Rubella, and Varicella Virus Vaccine<br>• XMumps Virus Vaccine<br>• XPoliovirus Vaccine (Live/Bivalent/Oral)<br>• XPoliovirus Vaccine (Live/Trivalent/Oral)<br>• XRotavirus Vaccine<br>• XSmallpox Vaccine Live<br>• XTyphoid Vaccine<br>• XVaricella Virus Vaccine<br>• XYellow Fever Vaccine<br>• XZoster Vaccine (Live/Attenuated)<br>**Category D**<br>• DBelimumab |
| **Special Population** | Subjects ≥ 65 years of age made up ~10% (109 out of 1,083) of all subjects exposed to tildrakizumab in phase 2 and 3 clinical trials. This enrollment is insufficient to determine if differences in safety or efficacy exist between younger and older adults. |
| **Pregnancy** | Tildrakizumab is a humanized monoclonal antibody ($IgG_1$). Human IgG crosses the placenta. Fetal exposure is dependent upon the IgG subclass, maternal serum concentrations, placental integrity, newborn birth weight, and GA, generally increasing as pregnancy progresses. The lowest |

| | |
|---|---|
| | exposure would be expected during the period of organogenesis and the highest during the third trimester |
| **Lactation** | It is not known if tildrakizumab is present in breast milk.<br>Tildrakizumab is a humanized monoclonal antibody ($IgG_1$). Human IgG is present in breast milk; concentrations are dependent upon IgG subclass and postpartum age.<br>According to the manufacturer, the decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of treatment to the mother. |
| **Contraindications** | Serious hypersensitivity to tildrakizumab or any component of the formulation. |
| **Monitoring Requirements** | CBC with differential (baseline); complete metabolic panel (baseline); tuberculosis (TB) screening prior to initiating and during therapy (chest X-ray if TB positive); hepatitis B virus (HBV)/hepatitis C virus screening prior to initiating (all patients), HBV carriers (during and for several months following therapy); HIV screening in high-risk patients (baseline). |
| **Precautions** | ***Concerns related to adverse effects:***<br>• Antibody formation: Formation of neutralizing anti-drug antibodies may occur with tildrakizumab and may be associated with loss of efficacy.<br>• Hypersensitivity: Hypersensitivity, including anaphylaxis and angioedema, has been reported. Discontinue immediately with signs/symptoms of a serious |

| | |
|---|---|
| | hypersensitivity reaction and treat appropriately, as indicated.<br>• Infections: May increase the risk of infections; upper respiratory tract infections have occurred more frequently. Consider the risks versus benefits prior to treatment initiation in patients with a history of chronic or recurrent infection; treatment should not be initiated in patients with clinically important active infections until it is resolved or treated. Monitor for infections; patients should seek medical attention for signs/symptoms of a clinically important infection (acute or chronic). If a serious infection develops or is unresponsive to appropriate therapy for the infection, monitor closely and consider discontinuing use until the infection resolves.<br>***Disease-related concerns:***<br>Tuberculosis: Patients should be evaluated for tuberculosis (TB) infection (latent TB) prior to initiating therapy. Do not administer to patients with TB disease (active TB). Treatment for TB infection should be administered prior to administering tildrakizumab. Consider anti-TB therapy prior to treatment initiation in patients with a history of TB infection or disease in whom an adequate course of TB treatment cannot be confirmed. Monitor closely for signs/symptoms of TB disease during and after treatment.<br>***Concurrent drug therapy issues:***<br>Immunizations: Patients should be brought up to date with all immunizations before initiating therapy. |

| | |
|---|---|
| | Live vaccines should not be given concurrently; there are no data available concerning secondary transmission of infection by live vaccines in patients receiving therapy. |
| **Black Box Warning** | **N/A** |
| **REMS** | **N/A** |

## HEALTH TECHNOLOGY ASSESSMENT (HTA)

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

**Table 13.** Tildrakizumab HTA Analysis

| MEDICATION | AGENCY | DATE – HTA RECOMMENDATION |
|---|---|---|
| **Tildrakizumab** | NICE[12] | **17 April 2019 -** Tildrakizumab is recommended as an option for treating plaque psoriasis in adults, only if:<br>• the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and<br>• the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated and<br>• the company provides the drug according to the commercial arrangement.<br>Consider stopping tildrakizumab between 12 weeks and 28 weeks if there has not been at least a 50% reduction in the PASI score from when treatment started.<br>Stop tildrakizumab at 28 weeks if the psoriasis has not responded adequately. An adequate response is defined as: |

| | | |
|---|---|---|
| | | • a 75% reduction in the PASI score (PASI 75) from when treatment started or<br>• a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started.<br>If patients and their clinicians consider tildrakizumab to be one of a range of suitable treatments, the least expensive should be chosen (considering administration costs, dosage, price per dose and commercial arrangements).<br>When using the PASI, healthcare professionals should consider skin color and how this could affect the PASI score and make the clinical adjustments they consider appropriate.<br>When using the DLQI, healthcare professionals should consider any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DLQI and make any adjustments they consider appropriate.<br>These recommendations are not intended to affect treatment with tildrakizumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop |
| | CADTH[13] | **June 21, 2021 -** Tildrakizumab is expected to be indicated for the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. |
| | HAS[14] | **5/10/2023** - Favorable opinion for reimbursement in the treatment of moderate to severe plaque psoriasis in adults who require systemic treatment. |
| | IQWIG[15] | N/A |
| | PBS[16] | N/A |

**Conclusion Statement – Tildrakizumab**

NICE recommends the use of Tildrakizumab as an option for treating plaque psoriasis in adults, only if: the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated and the company provides the drug according to the commercial arrangement. CADTH and HAS also had favorable opinions about the use of Tildrakizumab for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

## 2.2 Modifications

Modifications made since the publication of the previous CHI report in February 2020 include the removal of "Prior Authorization (PA)" as a prescribing edit from acitretin, apremilast, ciclosporin, methotrexate, and keeping/replacing it with "MD" for the immunosuppressants.

## 2.3 Delisting

The medications below are no longer SFDA registered[17], therefore, it is advisable to delist the following drugs from CHI formulary. *Please refer to* ***Drugs in the disease - section 2*** *of CHI Psoriasis original clinical guidance*

Alclomethasone Ointment 0.05%

Dexamethasone, Salicylic Acid

## 2.4 Other Drugs

FDA approved drugs:

- *A phosphodiesterase-4 (PDE4) inhibitor****, Roflumilast*** **(Topical application)**
  - ***October 06, 2023*** WESTLAKE VILLAGE, Calif., Oct. 06, 2023 (GLOBE NEWSWIRE) — Arcutis Biotherapeutics, Inc. (NASDAQ: ARQT), an early commercial-stage biopharmaceutical company focused on developing meaningful innovations in immuno-dermatology, today announced the U.S. Food and Drug Administration (FDA) has approved the supplemental new drug application (sNDA) to expand the indication of ZORYVE (roflumilast) cream 0.3% for the topical treatment of plaque psoriasis, including intertriginous areas, to children ages 6 to 11 years. ZORYVE, a once-daily, steroid-free cream that is effective, safe, and well tolerated, is designed to simplify management of plaque psoriasis. The approval of the expanded

indication is based on data from a 4-week Maximal Usage Systemic Exposure (MUSE) study in children ages 6 to 11 years with plaque psoriasis. Pharmacokinetic, safety, tolerability, and efficacy data from this study were generally consistent with data from the DERMIS-1 and DERMIS-2 pivotal Phase 3 trials in adults. Results from a second MUSE study, in children ages 2 to 5 years, as well as data from an ongoing open label extension study to assess the long-term safety of roflumilast cream 0.3% in individuals with plaque psoriasis 2 years of age and older (ARQ-151-306), will be the subject of a future FDA review.[18]

- *Tyrosine kinase 2 (TYK2) inhibitor,* ***deucravacitinib***
  - Deucravacitinib (SOTYKTU™) is a first-in-class, highly selective, oral tyrosine kinase 2 (TYK2) inhibitor. It acts via an allosteric mechanism, binding to the catalytically inactive pseudokinase regulatory domain of TYK2 and stabilizing an inhibitory interaction between the regulatory and catalytic domains. Deucravacitinib is being developed by Bristol Myers Squibb for the treatment of multiple immune-mediated diseases, including psoriasis, psoriatic arthritis, lupus, and inflammatory bowel disease.

It received its first approval (in the USA on 9 September 2022) for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. On 26 September 2022, it was subsequently approved in Japan for the treatment of plaque psoriasis, generalized pustular psoriasis and erythrodermic psoriasis. The Marketing Authorization Application for deucravacitinib for the treatment of adults with moderate to severe plaque psoriasis has been validated in the EU, and clinical development of the drug for the treatment of multiple immune-mediated diseases is underway in numerous countries worldwide. This article summarizes the milestones in the development of deucravacitinib leading to this first approval for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.[19]

## Section 3.0 Key Recommendations Synthesis

***Topical corticosteroids***

- The use of class 1, class 2, and class 3-5 topical corticosteroids for up to 4 weeks is recommended for the treatment of plaque psoriasis not involving intertriginous areas A. [5]
- The use of class 1-7 topical corticosteroids for a minimum of up to 4 weeks is recommended as initial and maintenance treatment of scalp psoriasis A.[5]
- The use of topical corticosteroids for [12 weeks can be considered if done under the careful supervision of a physician C.[5]

***Topical pimecrolimusf and tacrolimus***

- The off-label use of 0.1% tacrolimus for psoriasis involving the face as well as inverse psoriasis for up to 8 weeks can be considered B.[5]
- The off-label use of pimecrolimus for inverse psoriasis for 4-8 weeks is recommended B.[5]
- Long-term use of tacrolimus or pimecrolimus can be considered for inverse psoriasis treatment as off-label use C.[5]
- The off-label combination of tacrolimus and 6% salicylic acid for 12 weeks may be used for the treatment of plaque psoriasis B.[5]

***Vitamin D analogues***

- The long-term use of topical vitamin D analogues (up to 52 weeks), including calcipotriene/ calcipotriene, calcitriol, tacalcitol, and maxacalcitol, is recommended for the treatment of mild to moderate psoriasis A[5]
- Topical tacalcitol ointment or calcipotriene combined with hydrocortisone for 8 weeks can be used for the treatment of facial psoriasis.
- Use of combination treatments with vitamin D analogues and potent class II and class III topical corticosteroids up to 52 weeks is recommended for the treatment of psoriasis A[5]
- Use of combination products with calcipotriol and corticosteroids is recommended for the treatment of psoriasis A[5]
- The application of vitamin D analogues twice daily on weekdays in conjunction with high potency topical corticosteroids twice daily on weekends can be considered for maintenance treatment for psoriasis B.[5]

- The application of morning high-potency topical corticosteroids and evening topical vitamin D analogues is an effective treatment regimen that can be considered for the treatment of psoriasis B.[5]

***Topical tazarotene***

- Topical tazarotene can be used for the treatment of mild to moderate psoriasis B.[5]
- The use of topical corticosteroids along with tazarotene is recommended to decrease the duration of treatment as well as increase the length of remission A[5]

***Emollient***

- The use of an emollient in conjunction with topical corticosteroids for 4 to 8 weeks can be used to help reduce itching, desquamation, and total body surface area and prevent quick relapse of psoriasis when topical corticosteroids are discontinued B.[5]

***Salicylic acid***

- Topical salicylic acid can be used for 8-16 weeks for the treatment of mild to moderate psoriasis B.[5]
- The combination of salicylic acid with topical corticosteroids can be used for the treatment of moderate to severe psoriasis (body surface area ≤20%) B.[5]

***Coal tar***

- Coal tar preparations are recommended for the treatment of mild to moderate psoriasis A.[5]

**Combinations**

- The addition of an ultrahigh potency (class 1) topical corticosteroid to standard dose etanercept for 12 weeks is recommended for the treatment of moderate to severe psoriasis. A.[5]
- All topical corticosteroids can be used in combination with any biologics for the treatment of moderate to severe psoriasis C.[5]
- The addition of topical calcipotriene to standard dose methotrexate therapy is recommended for the treatment of moderate to severe psoriasis. It may lead to lower cumulative doses of methotrexate and increased time to relapse after methotrexate discontinuation. A[5]
- *The addition of calcipotriene/ betamethasone dipropionate ointment to low dose (2 mg/kg/d) cyclosporine can be used for the treatment of moderate to severe psoriasis.* B[5]

- *The addition of calcipotriene to standard dose acitretin is recommended for the treatment of moderate to severe psoriasis*. A[5]

**Using biologic therapy**

- (↑↑) Offer biologic therapy to people with psoriasis requiring systemic therapy if methotrexate and ciclosporin have failed, are not tolerated or are contraindicated and the psoriasis has a large impact on physical, psychological or social functioning [for example, Dermatology Life Quality Index (DLQI) or Children's DLQI > 10 or clinically relevant depressive or anxiety symptoms] and one or more of the following disease severity criteria apply: • the psoriasis is extensive [defined as body surface area (BSA) > 10% or Psoriasis Area and Severity Index (PASI) ≥ 10] • the psoriasis is severe at localized sites and associated with significant functional impairment and/or high levels of distress (for example nail disease or involvement of high impact and difficult-to-treat sites such as the face, scalp, palms, soles, flexures and genitals).[10]

➔ Choice of biologic therapy in adults

- (↑) Consider etanercept for use in people where a TNF antagonist is indicated and other available biological agents have failed or cannot be used, or where a short half-life is important.[10]

- (↑↑) Reserve infliximab for use in people with very severe disease, or where other available biological agents have failed or cannot be used, or where weight-based dosing is a priority. [10]

➔ Choice of biologic therapy in children and young people

- (↑↑) Offer adalimumab (age ≥ 4 years), etanercept (≥ 6 years) or Ustekinumab (≥ 12 years) to children and young people who fulfil the criteria for biologic therapy.[10]

➔ Conception and pregnancy

- (↑↑) Advise women of childbearing potential, who are starting biologic therapy for psoriasis, to use effective contraception and to discuss conception plans with the consultant supervising their care. There are no known interactions between biologic therapies and contraceptive methods.[10]

➔ Cancer risk

- (↑↑) Discuss the risks and benefits of continuing vs. stopping biologic therapy in patients who develop or have completed recent treatment for cancer. Offer advice on a case-by-case basis by considering the advice from the treating oncologist, multidisciplinary team discussion and patient choice considering: the risk of severe or unstable psoriasis if the biologic therapy were stopped, the physical, psychological and social functioning if the biologic therapy were

stopped, the options for alternative treatment strategies, the impact of cancer progression/recurrence.[10]

➔ Infections

- (↑↑) Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to risk factors for infection (e.g. comorbidities, cotherapy, lifestyle and travel), known infections (past or current), signs or symptoms suggestive of infection.[10]

➔ Chronic viral infections – hepatitis B, hepatitis C and HIV

- (↑↑) Provide treatment options to people with psoriasis who are HIV seropositive on a case-by-case basis; be aware that severe psoriasis can occur in people with uncontrolled HIV infection. Involve relevant specialists and ensure HIV viral load is suppressed on antiretroviral therapy before considering biologic therapy.[10]

➔ Tuberculosis

- (↑↑) Apply local policy on the use of a plain chest radiograph for screening for TB to rule out abnormalities at baseline including granulomas indicative of prior infection and other confounding lung diseases. If positive, assess for active TB and/or management of latent TB in consultation with a TB specialist.[10]

➔ Vaccination

- (↓↓) Do not give live vaccines to people on biologic therapy or to infants (up to 6 months of age) whose mothers have received biologic therapy beyond 16 weeks' gestation. Please check individual drug SPC.[10]

➔ Kidney failure/ renal impairment

- ↑ We suggest acitretin*, apremilast, fumarates*, methotrexate* may be used in psoriasis patients with mild to moderate renal impairment (eGFR ≥30 mL/min/1.73m$^2$).[8]
- ↑ We suggest using biologics in psoriasis patients with chronic kidney disease and all stages of renal impairment.[8]

➔ Depression and/or suicidal ideation

- ↑ We suggest using alternatives to brodalumab and apremilast in patients with a history of depression and/or suicidal ideation. [8]

➔ Diabetes mellitus

- ↓ We suggest against using ciclosporin or MTX as a first line treatment in patients with diabetes and/or features of the metabolic syndrome. [8]
- ↓ We suggest against using acitretin as a first line treatment in patients with dyslipidemia.

➔ Neurological diseases

- ↑ We suggest using fumarates in psoriasis patients with multiple sclerosis.
- ↓ ↓ We recommend against using TNF antagonist therapy in psoriasis patients with a diagnosis of multiple sclerosis or other demyelinating disease.
- ↓ In psoriasis patients with a first degree relative with multiple sclerosis or other demyelinating disease, we suggest against the use of TNF antagonist therapy if other suitable treatment options are available.

## Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Psoriasis report** and aims to provide recommendations to aid in the management of Psoriasis. 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 Psoriasis. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

## Section 5.0 References


1. Psoriasis - StatPearls - NCBI Bookshelf. Accessed December 1, 2023. https://www.ncbi.nlm.nih.gov/books/NBK448194/
2. Jacquiline Habashy DMs, David T Robles MPF, William D James M, Jeffrey Meffert M. Psoriasis: Practice Essentials, Background, Pathophysiology. Published September 14, 2022. Accessed December 4, 2023. https://emedicine.medscape.com/article/1943419-overview#a1
3. Damiani G, Bragazzi NL, Karimkhani Aksut C, et al. The Global, Regional, and National Burden of Psoriasis: Results and Insights From the Global Burden of Disease 2019 Study. *Front Med (Lausanne)*. 2021;8. doi:10.3389/FMED.2021.743180/FULL
4. Faisal Alzeer, Hadil AlOtair, Abdullah Aleisa. Epidemiology and Cutaneous Manifestations of Psoriasis in Saudi Arabia: A Narrative Review - PMC. Published February 28, 2022. Accessed December 4, 2023. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8896375/
5. Elmets CA, Korman NJ, Prater EF, et al. Joint AAD–NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol*. 2021;84(2):432-470. doi:10.1016/j.jaad.2020.07.087
6. Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol*. 2020;82(6):1445-1486. doi:10.1016/j.jaad.2020.02.044
7. Nast A, Smith C, Spuls PI, et al. EuroGuiDerm Guideline on the systemic treatment of Psoriasis vulgaris – Part 1: treatment and monitoring recommendations. *Journal of the European Academy of Dermatology and Venereology*. 2020;34(11):2461-2498. doi:10.1111/jdv.16915
8. Nast A, Smith C, Spuls PI, et al. EuroGuiDerm Guideline on the systemic treatment of Psoriasis vulgaris – Part 2: specific clinical and comorbid situations. *Journal of the European Academy of Dermatology and Venereology*. 2021;35(2):281-317. doi:10.1111/jdv.16926
9. Fatani MIA, Hamadah IRA, Alajlan MA, et al. Saudi consensus statement on biologic treatment of chronic plaque psoriasis (2020).

*Journal of Dermatological Treatment*. 2022;33(4):1916-1930. doi:10.1080/09546634.2021.1950601

10. Smith CH, Yiu ZZN, Bale T, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update. *British Journal of Dermatology*. 2020;183(4):628-637. doi:10.1111/bjd.19039
11. Lexicomp. Published 2023. Accessed June 6, 2023. https://online-lexi-com.ezproxy.lau.edu.lb:2443/lco/action/home
12. National Institute for Health and Care Excellence (NICE) Guidance website.
13. Canadian Agency for Drugs and Technologies in Health (CADTH) website.
14. Haute Autorite de Sante (HAS) website.
15. Institute for Quality and Efficiency in Healthcare (IQWIG) website. Institute for Quality and Efficiency in Healthcare (IQWIG) website.
16. Pharmaceutical Benefits Advisory Committee (PBAC) website.
17. SFDA Drug List J. SFDA Drug List . Published 2023. Accessed June 20, 2023. https://www.sfda.gov.sa/en/drugs-list
18. Amanda Sheldon, Eric McIntyre. FDA Approves Arcutis' ZORYVE® (roflumilast) Cream 0.3% for Treatment of Psoriasis in Children Ages 6 to 11 - Arcutis Biotherapeutics. Published October 6, 2023. Accessed December 6, 2023. https://www.arcutis.com/fda-approves-arcutis-zoryve-roflumilast-cream-0-3-for-treatment-of-psoriasis-in-children-ages-6-to-11/
19. Sheridan M. Hoy. Deucravacitinib: First Approval - PMC. Published November 19, 2022. Accessed December 6, 2023. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9676857/

# Section 6.0 Appendices

## Appendix A. Prescribing Edits Definition

**I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)**

Some covered drugs may have additional requirements, rules, or limits on coverage. These requirements and limits may include:

| Prescribing Edits Tools | Description |
|---|---|
| **AGE (Age):** | Coverage may depend on patient age |
| **CU (Concurrent Use):** | Coverage may depend upon concurrent use of another drug |
| **G (Gender):** | Coverage may depend on patient gender |
| **MD (Physician Specialty):** | Coverage may depend on prescribing physician's specialty or board certification |
| **PA (Prior Authorization):** | Requires specific physician request process |
| **QL (Quantity Limits):** | Coverage may be limited to specific quantities per prescription and/or time period |
| **ST (Step Therapy):** | Coverage may depend on previous use of another drug |
| **EU (Emergency Use only):** | This drug status on Formulary is only for emergency use |
| **PE (Protocol Edit):** | Use of drug is dependent on protocol combination, doses, and sequence of therapy |

## Appendix B. Psoriasis Scope

| Section | Rationale/updates |
|---|---|
| **Section 1.1** Clinical NICE Psoriasis: assessment and management Clinical guideline [CG153] (published 2012 last update **2017**) | **N/A** |
| **Section 1.2** Joint American Academy of Dermatology-National Psoriasis Foundation (AAD-NPF) guidelines of care for the management and treatment of psoriasis with biologics (**2019**) | **N/A** |
| **Section 1.3** Saudi practical guidelines on biologic treatment of psoriasis (**2014**) | **N/A** |
| **Section 1.4** Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients | **N/A** |

| | |
|---|---|
| (**2020**) | |
| **N/A** | Joint AADeNPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures **(2021)**<br>II. TOPICAL AGENTS<br>***Topical corticosteroids***<br>• The use of class 1, class 2, and class 3-5 topical corticosteroids for up to 4 weeks is recommended for the treatment of plaque psoriasis not involving intertriginous areas A.<br>• The use of class 1-7 topical corticosteroids for a minimum of up to 4 weeks is recommended as initial and maintenance treatment of scalp psoriasis A.<br>• The use of topical corticosteroids for [12 weeks can be considered if done under the careful supervision of a physician C<br>***Topical pimecrolimus and tacrolimus***<br>• The off-label use of 0.1% tacrolimus for psoriasis involving the face as well as inverse psoriasis for up to 8 weeks can be considered B<br>• The off-label use of pimecrolimus for inverse psoriasis for 4-8 weeks is recommended B<br>• Long-term use of tacrolimus or pimecrolimus can be considered for inverse psoriasis treatment as off-label use C<br>• The off-label combination of tacrolimus and 6% salicylic acid for 12 weeks may be used for the treatment of plaque psoriasis B<br>***Recommendations and strength of recommendation for vitamin D analogues***<br>• The long-term use of topical vitamin D analogues (up to 52 weeks), including calcipotriene/ calcipotriene, calcitriol, tacalcitol, and maxacalcitol, is recommended for the treatment of mild to moderate psoriasis A<br>• Use of calcipotriene foam and calcipotriene plus betamethasone dipropionate gel is recommended for 4-12 weeks for the treatment of mild to moderate scalp |

| | |
|---|---|
| | psoriasis A<br>• Topical tacalcitol ointment or calcipotriene combined with hydrocortisone for 8 weeks can be used for the treatment of facial psoriasis.<br>• Use of combination treatments with vitamin D analogues and potent class II and class III topical corticosteroids up to 52 weeks is recommended for the treatment of psoriasis A<br>• Use of combination products with calcipotriol and corticosteroids is recommended for the treatment of psoriasis A<br>• The application of vitamin D analogues twice daily on weekdays in conjunction with high potency topical corticosteroids twice daily on weekends can be considered for maintenance treatment for psoriasis B<br>• The application of morning high-potency topical corticosteroids and evening topical vitamin D analogues is an effective treatment regimen that can be considered for the treatment of psoriasis B<br>***Recommendations and strength of recommendation for topical tazarotene***<br>- Topical tazarotene can be used for the treatment of mild to moderate psoriasis B<br>- Topical tazarotene can be used for the treatment of nail psoriasis B<br>- The combination of topical tazarotene and NB-UVB has been shown to be effective and allow a reduction in total use of NB-UVB B<br>- The use of mid- or high-potency topical corticosteroid in combination with tazarotene for 8- 16 weeks is more effective than monotherapy with tazarotene and is recommended for the treatment of mild to moderate psoriasis A<br>- The use of topical corticosteroids along with tazarotene is recommended to decrease the duration of treatment as well as increase the length of remission A<br>***Recommendations and strength of recommendation for emollient***<br>• The use of an emollient in conjunction with topical corticosteroids for 4 to 8 weeks can be used to help reduce itching, desquamation, and total body surface area and prevent quick relapse of psoriasis when topical corticosteroids are discontinued B |

| | |
|---|---|
| | ***Recommendation and strength of recommendation for salicylic acid***<br>• Topical salicylic acid can be used for 8-16 weeks for the treatment of mild to moderate psoriasis B<br>• The combination of salicylic acid with topical corticosteroids can be used for the treatment of moderate to severe psoriasis (body surface area ≤20%) B<br>***Recommendation and strength of recommendation for topical anthralin***<br>• Topical anthralin for 8- 12 weeks can be used for the treatment of mild to moderate psoriasis. Short contact (up to 2 hours per day) anthralin is recommended to limit adverse side effects B<br>***Recommendations and strength of recommendation for coal tar***<br>• Coal tar preparations are recommended for the treatment of mild to moderate psoriasis A<br>• According to the joint AAD-NPF phototherapy guideline, there is sufficient evidence to recommend the use of Goeckerman therapy for the treatment of psoriasis B<br>***Recommendations and strength of recommendation for the combination of topical agents with biologics***<br>• The addition of an ultrahigh potency (class 1) topical corticosteroid to standard dose etanercept for 12 weeks is recommended for the treatment of moderate to severe psoriasis. A<br>• The addition of calcipotriene/betamethasone to standard dose adalimumab for 16 weeks is recommended for the treatment of moderate to severe psoriasis to accelerate clearance of psoriatic plaques. B<br>• All topical corticosteroids can be used in combination with any biologics for the treatment of moderate to severe psoriasis C<br>***Recommendation and strength of recommendation for the combination of topical calcipotriene and methotrexate***<br>• The addition of topical calcipotriene to standard dose methotrexate therapy is |

| | |
|---|---|
| | recommended for the treatment of moderate to severe psoriasis. It may lead to lower cumulative doses of methotrexate and increased time to relapse after methotrexate discontinuation. A<br>***Recommendation and strength of recommendation for combination of topical agents and cyclosporine***<br>• *The addition of calcipotriene/ betamethasone dipropionate ointment to low dose (2 mg/kg/d) cyclosporine can be used for the treatment of moderate to severe psoriasis*. B<br>***Recommendation and strength of recommendation for the combination of calcipotriene and acitretin***<br>• *The addition of calcipotriene to standard dose acitretin is recommended for the treatment of moderate to severe psoriasis*. A<br>***Recommendation and strength of recommendation for body surface area (BSA) severity measure***<br>• BSA measurement of involved skin is recommended as an important measure of psoriasis severity to risk stratify patient for future comorbidities and to assess response to treatment. B<br>***Recommendation and strength of recommendation for Psoriasis Area and Severity Index (PASI) severity measure***<br>• PASI is a commonly used outcome measure in clinical trials. However, it is seldom used in clinical practice to assess psoriasis severity. B<br>***Recommendation and strength of recommendation for the Physician Global Assessment (PGA) severity measure***<br>• PGA measurement of psoriasis is recommended as an important measure to assess psoriasis severity. B<br>***Recommendation and strength of recommendation for Physician Global Assessment (PGA) 3 body surface area (BSA) severity measure***<br>• PGA 3 BSA is recommended as an important measure of psoriasis severity. B |

| | |
|---|---|
| | ***Recommendation and strength of recommendation for Psoriasis Symptom Inventory (PSI) severity measure***<br>• The PSI is recommended as an important patientreported measure of psoriasis severity with utility in clinical trials. PSI is a new quality of life instrument and has potential to be used in clinical practice and clinical trials. C<br>***Recommendation and strength of recommendation for the Dermatology Life Quality Index (DLQI) severity measure***<br>• DLQI measurement of psoriasis is recommended as an important measure of psoriasis severity with utility in clinical trials and is seldom used in clinical practice. B<br>***Recommendation and strength of recommendation for pruritus assessment severity measure***<br>• Pruritus is a significant symptom of psoriasis. An itch severity assessment is recommended to appropriately assess the degree of pruritus when present. B |
| **N/A** | British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update<br>Using biologic therapy:<br>- (↑↑) Initiation and supervision of biologic therapy for people with psoriasis should be undertaken by specialist physicians experienced in the diagnosis and treatment of psoriasis. Routine monitoring may be delegated to other healthcare professionals, for example clinical nurse specialists. Manage psoriatic arthritis and/or multimorbidity in consultation with the relevant healthcare professionals.<br>- (↑↑) Agree and formalize arrangements for drug administration, monitoring and follow-up between health carers and the person receiving treatment.<br>Criteria for biologic therapy<br>- (↑↑) Offer biologic therapy to people with psoriasis requiring systemic therapy if methotrexate and ciclosporin have failed, are not tolerated or are contraindicated [see National Institute for Health and Care Excellence (NICE) |

| | |
|---|---|
| | guidelines CG153]7 and the psoriasis has a large impact on physical, psychological or social functioning [for example, Dermatology Life Quality Index (DLQI) or Children's DLQI > 10 or clinically relevant depressive or anxiety symptoms] and one or more of the following disease severity criteria apply: • the psoriasis is extensive [defined as body surface area (BSA) > 10% or Psoriasis Area and Severity Index (PASI) ≥ 10] • the psoriasis is severe at localized sites and associated with significant functional impairment and/or high levels of distress (for example nail disease or involvement of high impact and difficult-to-treat sites such as the face, scalp, palms, soles, flexures and genitals).<br>- (↑) Consider biologic therapy earlier in the treatment pathway (e.g. if methotrexate has failed, is not tolerated or is contraindicated) in people with psoriasis who fulfil the disease severity criteria and who also have active psoriatic arthritis (see the NICE musculoskeletal conditions overview)8 or who have psoriasis that is persistent, i.e. that relapses rapidly (defined as > 50% baseline disease severity within 3 months of completion of any treatment) off a therapy that cannot be continued in the long term *(e.g. narrowband ultraviolet B and ciclosporin*)<br>Prescribing biologic therapy<br>- (↑↑) Be aware of the benefits of, contraindications to and adverse effects associated with biologic therapies and reference the drug specific SPCs.<br>- (↑↑) Provide high-quality, evidence-based information to people being prescribed biologic therapies. Explain the risks and benefits to people undergoing this treatment (and their families or carers where appropriate), using absolute risks and natural frequencies when possible. Explain the treatment regimen and importance of treatment adherence. Allow them adequate time to consider the information.<br>- (↑↑) Support and advice should be offered to people with psoriasis (and their families or carers where appropriate) by healthcare professionals who are trained and competent in the use of biologic therapies. |

| | |
|---|---|
| | Reviewing biologic therapy<br>- (↑↑) Assess initial response to biologic therapy in people with psoriasis at time points appropriate for the drug in question, and then on a regular basis during therapy (e.g. every 6 months)<br>- (↑↑) Review the response to biologic therapy by considering:<br>  o psoriasis disease severity compared with baseline (e.g. PASI baseline to endpoint score)<br>  o the agreed treatment goal<br>  o control of psoriatic arthritis disease activity and/or inflammatory bowel disease (in consultation with a rheumatologist and/or gastroenterologist)<br>  o the impact of psoriasis on the person's physical, psychological and social functioning<br>  o the benefits vs. the risks of continued treatment<br>  o the views of the person undergoing treatment (and their family or carers, where appropriate)<br>  o adherence to the treatment<br>• (↑↑) Assess whether the minimal response criteria have been met, as defined by:<br>  o a 50% or greater reduction in baseline disease severity (e.g. PASI 50 response, or percentage BSA where PASI is not applicable) and<br>  o clinically relevant improvement in physical, psychological or social functioning (e.g. ≥ 4-point improvement in DLQI or resolution of low mood).<br>• (↑) Consider changing to an alternative therapy, including another biologic therapy, if any of the following applies:<br>  o the psoriasis does not achieve the minimum response criteria.<br>  o the psoriasis initially responds but subsequently loses this response (secondary failure)<br>  o the current biologic therapy cannot be tolerated or becomes contraindicated. |

| | |
|---|---|
| | Choice of biologic therapy: general considerations<br>- (↑↑) Before initiating or making changes to biologic therapy, consider both psoriasis and psoriatic arthritis and manage treatment in consultation with a rheumatologist or pediatric rheumatologist. Be aware that the presence of and phenotype of psoriatic arthritis (e.g. peripheral vs. axial disease) may influence access to, choice of and dose of biologic therapy. Actively screen for psoriatic arthritis (in people without this diagnosis), using a validated tool, e.g. Psoriasis Epidemiology Screening Tool (PEST), and be aware that the PEST may not detect axial arthritis/inflammatory back pain.<br>- (↑↑) Tailor the choice of agent to the needs of the person.<br>*Psoriasis factors:* • the goal of therapy [for example, Physician's Global Assessment of clear or nearly clear], disease phenotype and pattern of activity, disease severity and impact, the presence of psoriatic arthritis (in consultation with an adult or pediatric rheumatologist), the outcomes of previous treatments for psoriasis.<br>*Other individual factors:* person's age, past or current comorbid conditions (e.g. inflammatory bowel disease, heart failure), conception plans, body weight, the person's views and any stated preference on administration route or frequency, likelihood of adherence to treatment.<br>*Drug costs:* including administration costs, dosage, price per dose and commercial arrangements.<br>Choice of biologic therapy in adults<br>When to consider dose escalation/interval reduction<br>• (↑) Consider escalating the dose of or reducing the interval for biologic therapy in adults and when an inadequate primary response might be due to insufficient drug exposure (e.g. in people who are obese and/or whose psoriasis relapses during the treatment cycle and/or if the drug level is known to be subtherapeutic). Consider that this may be associated with an increased risk of infection/adverse events and, depending on the drug, off-licence and may not be approved by NICE and therefore not funded. |

| Biological agent | Suggested dose-escalation/interval-reduction strategy |
|---|---|
| Adalimumab 40 mg every other week | Adalimumab 40 mg weekly |
| Certolizumab pegol 200 mg every 2 weeks | Certolizumab pegol 400 mg every 2 weeks |
| Etanercept 50 mg once weekly | Etanercept 50 mg twice weekly |
| Infliximab 5 mg $kg^{-1}$ every 8 weeks | [a]Infliximab 5 mg $kg^{-1}$ every 6 weeks |
| Ixekizumab 80 mg every 4 weeks | [a]Ixekizumab 80 mg every 2 weeks |
| Tildrakizumab 100 mg every 12 weeks | Tildrakizumab 200 mg every 12 weeks (high disease burden or ≥ 90 kg) |
| Ustekinumab 45 mg every 12 weeks (≤ 100 kg) | [a]Ustekinumab 90 mg every 8 or 12 weeks (≤ 100 kg) |
| Ustekinumab 90 mg every 12 weeks (> 100 kg) | [a]Ustekinumab 90 mg every 8 weeks (> 100 kg) |

[a]Off-license use.

What to do when a second or subsequent biologic therapy fails in adults

- (↑↑) When a person's psoriasis responds inadequately to a second or subsequent biological agent, review treatment goals, seek advice from a dermatologist with expertise in biologic therapy and consider any of the following strategies: reiterate advice about modifiable factors contributing to poor response such as obesity and poor adherence (intentional or nonintentional), consider whether drug exposure is adequate, optimize adjunctive therapy (e.g. switch from oral to subcutaneous methotrexate), switch to an alternative biological agent, alternative or supplementary nonbiologic therapy approaches (e.g. inpatient topical therapy, phototherapy or systemic therapies).

Choice of biologic therapy in children and young people

- (↑↑) Offer adalimumab (age ≥ 4 years), etanercept (≥ 6 years) or Ustekinumab (≥ 12 years) to children and young people who fulfil the criteria for biologic therapy.
- (↑↑) When a child's or young person's psoriasis responds inadequately to a first or subsequent biological agent seek advice from a dermatologist with expertise in biologic therapy in this age group and consider any of the following strategies: reiterate advice about modifiable factors contributing to poor response (e.g. obesity and poor adherence), optimize adjunctive therapy (e.g. switch from oral to subcutaneous methotrexate), switch to an alternative biological agent, alternative or supplementary nonbiologic therapy approaches (e.g. inpatient topical therapy or systemic therapies).

| | |
|---|---|
| | Transitioning to or between biologic therapies<br>• (↑↑) When choosing the transitioning strategy from one drug therapy to another and whether a therapy washout (or no washout) should be used, take into consideration: the pharmacology of the drugs that are being stopped and started, the person's clinical circumstances, the person's views on the risks and benefits of transitioning option(s)<br>• (↑) When transitioning from standard systemic therapy to biologic therapy consider these:<br>  • In stable disease, aim to allow 1 month to elapse between the last dose of any current standard systemic immunosuppressant psoriasis therapy (except methotrexate) and the planned date of biologic initiation.<br>  • Start a biologic therapy with no drug washout period in people taking methotrexate, or in people on other therapies where this would lead to unstable disease.<br>  • When standard, systemic immunosuppressant therapy cannot be stopped (e.g. in people for whom a disease flare would be severe or hazardous), rationalize use of therapy and stop as soon as possible (e.g. when a minimum response has been achieved).<br>• (↑) When transitioning to a new biologic therapy (from a previous biologic therapy) consider using a 1-month washout period, or the length of the treatment cycle (whichever is longer), between the last dose of the current biologic therapy and the planned date of biologic initiation.<br>Conception and pregnancy<br>Biologic therapy and cancer risk<br>• (↑↑) Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to:<br>  ○ their past or current history of cancer and/or<br>  ○ any future risk of cancer |

| | |
|---|---|
| | • (↑↑) Provide information to people with psoriasis about the importance of participating in national cancer screening programs.<br>• (↑↑) Exercise caution and discuss with the relevant cancer specialist when prescribing biologics in people with psoriasis and:<br>  ○ a history of cancer, particularly if this has been diagnosed and treated less than 5 years previously and/or<br>  ○ where the baseline risk of skin cancer is increased<br>• (↑↑) Discuss the risks and benefits of continuing vs. stopping biologic therapy in patients who develop or have completed recent treatment for cancer. Offer advice on a case-by-case basis by considering the advice from the treating oncologist, multidisciplinary team discussion and patient choice considering: the risk of severe or unstable psoriasis if the biologic therapy were stopped, the physical, psychological and social functioning if the biologic therapy were stopped, the options for alternative treatment strategies, the impact of cancer progression/recurrence.<br>Biologic therapy and infections<br>• (↑↑) Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to risk factors for infection (e.g. comorbidities, cotherapy, lifestyle and travel), known infections (past or current), signs or symptoms suggestive of infection.<br>Biologic therapy and chronic viral infections – hepatitis B, hepatitis C and HIV<br>• (↑↑) Test for hepatitis B (surface antigen and core antibody), hepatitis C (IgG) and HIV (HIV-1 and HIV-2 antibodies and HIV-1 antigen) infection in people starting biologic therapy.<br>• (↑) Consider ongoing screening (e.g. annually) for hepatitis B, hepatitis C and HIV, particularly in people who are at increased risk of infection.<br>• (↑↑) Retest for viral hepatitis in any person who develops unexplained transaminitis (raised alanine aminotransferase and/or aspartate aminotransferase); retest for HIV |

| | |
|---|---|
| | infection in any person who has symptoms or other conditions that might represent HIV seroconversion/infection.<br>• (↑↑) Consult a hepatitis specialist when treating all people with biologic therapy who have hepatitis B or C infection, whether newly diagnosed or previously known.<br>• (↑↑) Provide treatment options to people with psoriasis who are HIV seropositive on a case-by-case basis; be aware that severe psoriasis can occur in people with uncontrolled HIV infection. Involve relevant specialists and ensure HIV viral load is suppressed on antiretroviral therapy before considering biologic therapy.<br>• (GPP) Test for varicella zoster (VZ) virus antibody in people with a negative or uncertain history for chickenpox before starting biologic therapy. Consider varicella vaccination before initiating biologic therapy in those who are not varicella immune and seek expert advice. Be aware of the indications for postexposure prophylaxis in VZ-susceptible individuals taking biologics, with VZ immunoglobulin or oral acyclovir/valaciclovir.<br>Use of biologic therapy and tuberculosis |
| **N/A** | EuroGuiDerm – Part 1: Treatment goals and treatment recommendations **(2021)**<br><u>General recommendations</u><br>• ↑↑ We recommend taking account of efficacy and safety, time until onset of treatment response, comorbidities and individual patient factors when choosing a systemic treatment for moderate to severe psoriasis. Consensus, evidence- and consensus-based<br>• ↑↑ We recommend initiating a systemic treatment in patients with moderate to severe. Strong consensus, consensus-based<br>• ↑↑ For patients who require systemic treatment, we generally recommend initiating a “conventional” systemic agent. Strong consensus, evidence- and consensus-based<br>• ↑↑ We recommend initiating a biologic if conventional systemic agents were inadequate in response or if they are contraindicated or not tolerated. Strong |

| | |
|---|---|
| | consensus, evidence- and consensus-based<br>• ↑ In cases of psoriasis where conventional treatments are not expected to lead to a sufficient response*, we suggest initiating a biologic agent that has a "first-line label".** *e.g., particularly severe disease (e.g., PASI ≥ 20) or rapid worsening of disease; severe involvement of the nails, the genital area or the scalp; or a particularly strong impact on quality of life (e.g., DLQI ≥ 15) **"First line label" refers to the therapeutic indication as approved by the EMA (European Medicines Agency). Strong consensus, consensus-based<br>• ↑ We suggest using apremilast if an oral treatment is desired and "conventional" systemic agents led to an inadequate response or are contraindicated or not tolerated. Strong consensus, consensus based.<br><u>Specific recommendations</u><br>➔ *Conventional systemic therapy with Acitretin, Ciclosporin, Dimethyl fumarate/fumaric acid esters,* Methotrexate, Adalimumab, Apremilast, Brodalumab, Certolizumab pegol, Etanercept, Guselkumab, Infliximab, Ixekizumab, Risankizumab, Secukinumab, Tildrakizumab, Ustekinumab |
| **N/A** | EuroGuiDerm Guideline on the systemic treatment of Psoriasis vulgaris – Part 2: specific clinical and comorbid situations 2021[8]<br>• ↑↑ We recommend interdisciplinary cooperation with a rheumatologist for the confirmation of the diagnosis of psoriatic arthritis and the selection of a suitable treatment whenever needed. Strong consensus (Due to personal–financial conflict of interest 4 abstentions) EXPERT CONSENSUS 100% agreement.<br>• ↓↓ We recommend starting a conventional synthetic DMARD (MTX) early to prevent progression of disease and erosive destruction of joints for patients with moderate to severe psoriasis and peripheral active joint involvement (PsA) despite the usage of NSAIDs, or glucocorticoid site injections if applicable and/or potential poor prognosis due to polyarthritis, increased inflammatory markers and erosive changes, and extra-articular musculoskeletal manifestations. Strong consensus EVIDENCE AND EXPERT CONSENSUS Table 3 100% agreement |

| | |
|---|---|
| | • ↑↑ For inadequately responding patients after at least one synthetic DMARD, we recommend the use of biological DMARDs as monotherapy or in combination with synthetic DMARDs. Strong consensus 100% agreement EVIDENCE AND EXPERT CONSENSUS Table 3<br>• ↑↑ For the selection of a bDMARD for patients with moderate to severe psoriasis of the skin and active joint involvement (PsA), we recommend taking aspects of efficacy with regard to skin and the joints, comorbidity, practicability and safety into account. Strong consensus EXPERT CONSENSUS 100% agreement<br>*Inflammatory bowel disease: How should psoriasis patients be managed with concomitant inflammatory bowel disease?*<br>All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.<br>• ↑↑ We recommend working in collaboration with the treating gastroenterologist when prescribing a systemic therapy in psoriasis patients with concomitant chronic inflammatory bowel disease. Strong consensus1 EXPERT CONSENSUS<br>• ↑↑ In patients with psoriasis and active IBD or a history of IBD, we recommend to preferentially use approved targeted therapies with a documented efficacy in these conditions: Crohn's disease: anti-TNF (infliximab, adalimumab, certolizumab) and anti-IL-12/23p40 (ustekinumab). Ulcerative colitis: anti-TNF (infliximab, adalimumab) and anti-IL-12/23p40 (ustekinumab).<br>• ↑ If these first-choice treatments cannot be used, we suggest the following treatments to be considered as second choice targeted treatment options in patients with psoriasis and IBD: Crohn's disease: Anti-IL-23p19 (preferred risankizumab, guselkumab; also possible: tildrakizumab) Ulcerative colitis: Anti-IL-23p19 (preferred risankizumab, guselkumab; also possible: tildrakizumab)<br>• ↑ If these first-choice treatments cannot be used, we suggest the following treatments to be considered as second choice oral treatment options in patients with psoriasis and IBD Crohn's disease: Methotrexate Active ulcerative colitis: Ciclosporine (preferred), apremilast (also possible) |

| | |
|---|---|
| | • ↑ In combination with other treatments, we suggest acitretin as an adjunct therapy for patients with IBD and psoriasis, especially in cases with mild paradoxical psoriasis.<br>• ↓ We suggest against the use of anti-IL 17 antibodies in patients with inflammatory bowel disease.<br>*Cancer: How should psoriasis patients with a history of malignancies be managed?*<br>All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.<br>• ↑↑ We recommend taking the burden of psoriasis, and the risk of cancer worsening or recurrence (pre-cancer vs low risk vs high risk) into account for shared therapeutic decision making.<br>• ↑↑ For patients with recent malignancy we recommend topical therapies, phototherapy (narrow band UVB) * and/ or acitretin. *except patients with a recent, and/or high risk of cutaneous malignancy<br>• ↑↑ We recommend discussing the decision to initiate immunosuppressive therapies, in psoriasis patients with a current or recent diagnosis of cancer in the previous five years case-by-case with cancer specialists and to reach an informed decision, respecting the patient's preference.<br>• ↑ In case of inadequate response to topical therapies, phototherapy, (narrow band UVB) and/or acitretin we suggest using MTX in psoriasis patients with a previous history of cancer. * (*for patients with history of non-melanoma skin cancer, see background text)<br>• ↓ We suggest apremilast can be used in psoriasis patients with a previous history of cancer despite the lack of long-term experience based on pathophysiological considerations on a case-by-case basis including discussion with cancer specialist.<br>• ↓ We suggested against using ciclosporin in psoriasis patients with a previous history of cancer.<br>• ↑ We suggest anti-TNF, Ustekinumab can be used based on existing safety data on |

| | |
|---|---|
| | a case-by-case basis including discussion with cancer specialist. We suggest anti-IL17, anti IL23, can be used in psoriasis patients with a previous history of cancer despite the lack of long-term experience based on pathophysiological considerations on a case-by-case basis including discussion with a cancer specialist.<br>*<u>Depression: How should psoriasis patients with a history of depression and/or suicidal ideation be managed?</u>*<br>All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.<br>• ↑↑ We recommend being aware of signs and symptoms of anxiety and depression in patients with psoriasis and monitor for symptoms of depression and/or suicidal ideation or anxiety during systemic treatments for psoriasis especially in those with a history of any of the above.<br>• ↑ We suggest using alternatives to brodalumab and apremilast in patients with a history of depression and/or suicidal ideation.<br>*<u>Diabetes: How should psoriasis patients with diabetes mellitus be managed?</u>*<br>• ↓ We suggest against using ciclosporin or MTX as a first line treatment in patients with diabetes and/or features of the metabolic syndrome. Consensus 89% agreement EXPERT CONSENSUS<br>• ↓ We suggest against using acitretin as a first line treatment in patients with dyslipidemia. Strong Consensus 100% agreement EXPERT CONSENSUS<br>*<u>Heart disease: How should psoriasis patients with ischemic heart disease and/or congestive heart failure be managed?</u>*<br>All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.<br>• ↓ We suggest cyclosporine or acitretin as preferred treatments in patients with psoriasis and ischemic heart disease.<br>• ↑ We suggest methotrexate as preferred first-line therapy in patients with psoriasis |

| | |
|---|---|
| | and ischemic heart disease* if other patient characteristics do not preclude its use.<br>• ↑ We suggest anti-TNFs, Ustekinumab, and IL-17 inhibitors as preferred targeted therapies in patients with psoriasis and ischemic heart disease* (*In case of concomitant congestive heart failure, also note the recommendations from the respective section)<br>➔ ***Heart failure***<br>All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.<br>• ↓ We suggest against using cyclosporine in patients with psoriasis and advanced congestive heart failure.<br>• ↑ We suggest that methotrexate, acitretin and apremilast are considered as treatment in patients with psoriasis and advanced congestive heart failure.<br>• ↑ We suggest that ustekinumab, inhibitors of IL-17 and of IL-23 are considered as treatment in patients with psoriasis and advanced congestive heart failure.<br>• ↓ ↓ We recommend against using anti-TNFs in patients with psoriasis and advanced congestive heart failure.<br>• ↑↑ We recommend discussing the choice of a systemic therapy in psoriasis patients with advanced congestive heart failure with a cardiologist.<br>*Kidney disease: How should psoriasis patients with kidney failure/ renal impairment be managed?*<br>All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.<br>• ↑↑ We recommend ensuring an accurate assessment of renal function in any psoriasis patient with known or suspected chronic kidney disease prior to therapy.<br>• ↑↑ We recommend working in collaboration with the nephrologist when prescribing systemic therapy in any psoriasis patient with chronic kidney disease of stage 3 (Egfr (eGFR <60 mL/min/1.73 $m^2$) or more.<br>• ↑ We suggest acitretin*, apremilast, fumarates*, methotrexate* may be used in |

| | |
|---|---|
| | psoriasis patients with mild to moderate renal impairment (eGFR ≥30 mL/min/1.73m²). *(careful dosing/dose adjustment may be needed)<br>• ↑ We suggest using biologics in psoriasis patients with chronic kidney disease and all stages of renal impairment.<br>• ↓ ↓ We recommend against using ciclosporin, fumarates, or methotrexate in psoriasis patients with chronic kidney disease and severe renal impairment (eGFR <30 mL/min/1.73m²).<br>*Neurological diseases: Which treatments are appropriate for psoriasis patients with neurological diseases?*<br>All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement<br>• ↑ We suggest using fumarates in psoriasis patients with multiple sclerosis.<br>• ↓ ↓ We recommend against using TNF antagonist therapy in psoriasis patients with a diagnosis of multiple sclerosis or other demyelinating disease.<br>• ↓ In psoriasis patients with a first degree relative with multiple sclerosis or other demyelinating disease, we suggest against the use of TNF antagonist therapy if other suitable treatment options are available.<br>*Viral hepatitis: How should patients who test positive be managed?*<br>All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.<br>• ↑↑ We recommend that treatment decision for patients with positive test result for HBsAg or positive HBV DNA should always be taken together with a hepatologist.<br>• ↑ Depending on the individual health care setting and personal experience and training, we suggest consulting with a hepatologist to choose a systemic treatment for patients that have a positive anti-HBc with a neg. HBsAG/HBV-DNA test. We suggest, based on the common practice within the guideline group, acitretin, apremilast, fumarates, MTX, ustekinumab and the anti-IL 17 and anti-IL 23 antibodies as preferred systemic treatment options for this patient group. Strong |

| | |
|---|---|
| | consensus EVIDENCE AND CONSENSUS BASED, see METHODS & EVIDENCE REPORT<br>• ↑↑ We recommend regular testing for HBsAG/HBV-DNA (e.g. every three months) during systemic treatment.<br>• ↑↑ We recommend recording all treatment initiations and follow up visits of psoriasis patients with concomitant hepatitis B or C cases in drug registries.<br><u>Tuberculosis: How to manage psoriasis in patients with positive tuberculosis test results?</u><br>All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.<br>• ↓ ↓ We recommend against TNF alpha antagonists as a treatment for patients with latent TB unless there are no other suitable treatment options.<br>• ↑↑ We recommend remaining alert to signs and symptoms of tuberculosis activation or re-infection during therapy.<br>• ↑ We suggest acitretin, apremilast or fumarates or a treatment from the anti-IL 17 and anti-IL 23 group for patients with latent TB that require a systemic antisporiatic treatment.<br><u>Wish for child/pregnancy: How should psoriasis patients with a wish for pregnancy in the near future or who are pregnant be managed?</u><br>All the recommendations mentioned below are Strong consensus EXPERT CONSENSUS 100% agreement.<br>• ↑ We suggest ciclosporin as a first line convention agent in women planning conception and when it is necessary to start systemic therapy during the 2nd and 3rd trimester of pregnancy.<br>• ↓ ↓ Methotrexate and acitretin are contra-indicated in women planning conception. We recommend using these.<br>• ↓ Fumarates and apremilast are contra-indicated in women planning conception. We suggest against using these. |

| | |
|---|---|
| | • ↑↑ We recommend consultation and information sharing across specialties, including with an obstetrician with expertise in caring for pregnant women with medical problems.<br>• ↑↑ We recommend the collection of maternal exposure to medications and pregnancy outcome data in national safety registries where available.<br>• ↑ We suggest certolizumab pegol as a first line choice when starting biologic therapy in women planning conception (when a biologic is considered essential to use in pregnancy) and when it is necessary to start a systemic therapy during the second or third trimester.<br>• ↑ We suggest stopping biologic therapy in the second and third trimester (except certolizumab pegol) to minimise fetal exposure and limit potential infection risk to the neonate.<br>• ↓ We suggest against using live or live attenuated vaccines in infants (up to 6 months of age) whose mothers received biologic therapy beyond 16 weeks gestation, unless the benefit of the vaccination clearly outweighs the theoretical risk of administration.<br>• ↑↑ We recommend consultation and information sharing across specialties, including with an obstetrician with expertise in caring for pregnant women with medical problems.<br>• ↑↑ We recommend the collection of maternal exposure to medications and pregnancy outcome data in national safety registries where available.<br>• ↑↑ It is recommended that men discontinue methotrexate 3 months before attempting conception. * *EMA recommends 6 months as a means of precaution; the practice of the guideline group differs from this.<br>• ↑ As a precaution, it is suggested that men receiving acitretin use barrier forms of contraception post-conception to limit exposure via direct contact with semen during pregnancy.<br>• ↑↑ We recommend the collection of paternal exposure to medications during |

| | |
|---|---|
| | conception and pregnancy outcome data in national safety registries where available. |
| **N/A** | Saudi consensus statement on biologic treatment of chronic plaque psoriasis **(2020)**<br>Therapeutic use of biologics for the management of psoriasis Overview of biologic agents available for psoriasis in Saudi Arabia:<br>**Transitioning**<br>*Benefits of transitioning*<br>Switching psoriasis treatment is a common, accepted practice for improving patient outcomes (e.g. when patients are experiencing suboptimal efficacy and/or intolerability with a given therapy). There are no evidence-based studies on the duration of the interval between discontinuation of the previous medication and initiation of biologic therapy. This may depend on the treatment that is being discontinued, disease severity, and response to prior treatment, as well as on expert opinion, and it should be assessed on a case-by-case basis. Therefore, whereas some experts will start administration of a new biologic as soon as it is available for the patient, others may wait for a period of 3 or 4 half-lives of the previous therapy before the transition.<br>*Transitioning from conventional systemic therapy to biologic therapy*<br>• General considerations: Recommendations for transitioning from conventional systemic therapy to biologic therapy will differ depending on the reason for transition. For example:<br>- When transitioning due to safety reasons (development of medication-related side effects), a treatment-free interval may be necessary until the safety parameter has normalized or stabilized.<br>- When transitioning due to lack of efficacy, which could be primary or secondary inefficacy, or due to suboptimal response; transitioning directly or with an overlap period can be considered.<br>- Additionally, if a patient develops psoriatic arthritis, transitioning to a therapy that |

| | |
|---|---|
| | is efficacious in both psoriasis and psoriatic arthritis is required.<br>- Irrespective of the reason for transitioning, approved induction dosages should be used for the new drug.<br>• *Transitioning from cyclosporine to biologic therapy, transitioning from one biologic therapy to another,* Adjusting biologic therapy<br>• Use of biologics in special patient populations: *Pregnancy and lactation, p*ediatric and adolescent patients, Malignancy, Patients undergoing surgery, Patients with hepatitis, Tuberculosis<br>Patients with demyelinating diseases/multiple sclerosis (MS)<br>• Do not use TNF-a antagonists in patients with demyelinating diseases and review alternative interventions in patients who have an affected first-degree relative with the demyelinating disease. Stop treatment and seek specialist advice if neurological symptoms suggestive of the demyelinating disease develop during TNF-a antagonist therapy.<br>• IL 12/23 inhibitors may be used in patients with MS as it does not improve or worsen MS. IL-17 inhibitors can be used with some benefit in MS symptoms. Data are limited for the IL-23 inhibitors, but there are no reports of MS worsening with these drugs.<br>Patients at elevated cardiovascular risk<br>- TNF-α inhibitors are preferred systemic agents for the treatment of psoriasis in patients with coexisting cardiovascular risk factors. IL-12/23 inhibitor has some potential cardioprotective benefit, but more long-term data are needed. More data is needed for the use of IL-17 and IL-23 inhibitors.<br>Congestive heart failure (CHF)<br>• Avoid TNF-a antagonist therapy in people with severe cardiac failure (New York Health Association [NYHA] class III and IV) and discontinue TNF-a antagonist therapy in the event of new or worsening preexisting heart failure and seek specialist advice. IL 12/23, IL-17, and IL-23 inhibitors appear to be safe to use in |

| | |
|---|---|
| | patients with CHF.<br>Inflammatory bowel disease (IBD)<br>• Patients with a history of concomitant IBD might benefit from TNF-a inhibitor therapy. In fact, adalimumab, infliximab, and certolizumab are approved by the US FDA for the treatment of IBD. Etanercept is not as effective as other TNF-a inhibitors for Crohn's Disease.<br>• IL 12/23 inhibitor is also approved for Crohn's disease but not ulcerative colitis. IL-23 inhibitor use in Crohn's disease has promising results in preliminary studies, but more data are needed to draw definite conclusions (104). Exercise caution and consult a gastroenterology specialist before using IL-17 inhibitors in patients with IBD, or those with first-degree relatives with IBD.<br>Lupus erythematosus<br>• There is a concern for the development of de novo lupus or flare-up of lupus during treatment with TNF- a blockers, also known as anti TNF- a induced lupus (ATIL). IL-12/23 inhibitor is the safest treatment option for concomitant lupus and psoriasis as it reportedly improves SLE symptoms, specifically oral ulcerations, anemia or thrombocytopenia, and lupus arthritis. There are not enough data regarding the use of IL-17 and IL-23 inhibitors in patients with SLE, but no new cases of lupus induction or flare have been reported yet |

## Appendix C. MeSH Terms PubMed

**C.1 PubMed Search for Psoriasis:**

| Query | Filters | Search Details | Results |
|---|---|---|---|
| **((((((psoriasis[MeSH Terms]) OR (Psoriasis[Title/Abstract])) OR (Psoriases[Title/Abstract])) OR (Pustulosis of Palms[Title/Abstract] AND Soles[Title/Abstract])) OR (Pustulosis Palmaris et Plantaris[Title/Abstract])) OR (Palmoplantaris Pustulosis[Title/Abstract])) OR (Pustular Psoriasis of Palms[Title/Abstract] AND Soles[Title/Abstract])** | Guideline, in the last 5 years | ("Psoriasis"[MeSH Terms] OR "Psoriasis"[Title/Abstract] OR "Psoriases"[Title/Abstract] OR ("Pustulosis"[All Fields] AND "of palms"[Title/Abstract] AND "Soles"[Title/Abstract]) OR "pustulosis palmaris et plantaris"[Title/Abstract] OR "palmoplantaris pustulosis"[Title/Abstract] OR ("pustular psoriasis of palms"[Title/Abstract] AND "Soles"[Title/Abstract])) AND ((y_5[Filter]) AND (guideline[Filter])) | 48 |

## Appendix D. Treatment Algorithm

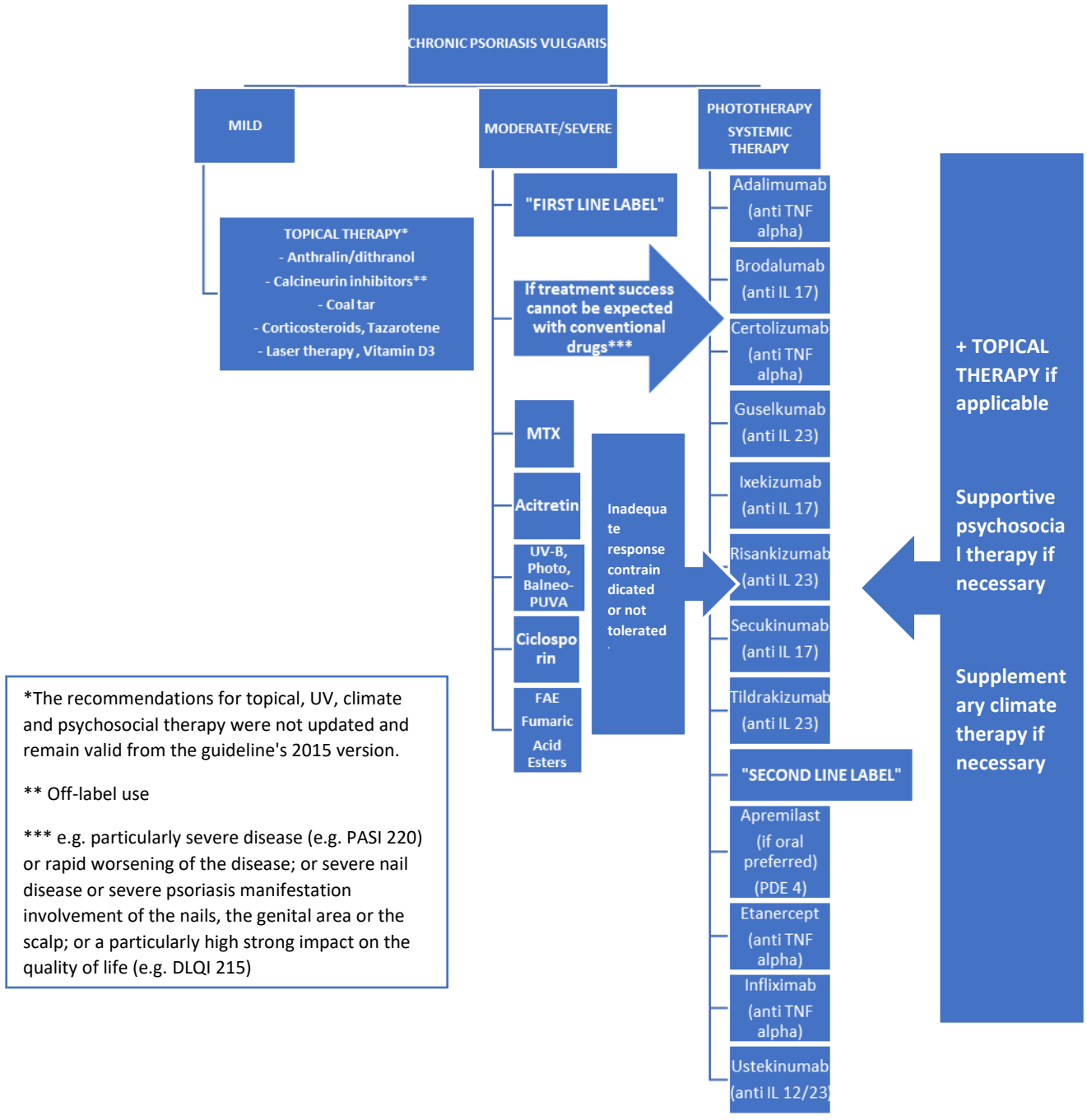


***Figure 4.*** *Overview of therapeutic options for the management of psoriasis*