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REVIEW ARTICLE

Systemic Treatments for Adult Patients with Moderate-to-Severe Psoriasis: Consensus Statements for the United Arab Emirates

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Abstract:

Background:

Psoriasis is a chronic, immune-mediated disease characterized by mild localized plaques to severe plaques involving any part of the skin; it has a pronounced effect on patients' quality of life. In the United Arab Emirates (UAE), there are limited local guidelines for the management of patients with psoriasis in daily clinical practice.

Objective:

The study aimed to develop consensus statements for the evaluation and management of moderate-to-severe psoriasis in the UAE.

Methods:

To develop consensus statements, the Emirates Dermatology Society set up advisory board meetings in which local key opinion leaders (KOLs), including dermatologists from the UAE, participated. A targeted literature review was conducted to review current international and regional guidelines on the management of psoriasis, based on which the statements were formulated. A final consensus on each statement was reached based on collective agreement among the KOLs.

Results:

Consensus statements were generated with the intention of supporting physicians in clinical decision-making with respect to the classification of disease severity, treatment options including biologic and non-biologic systemic therapies, transitioning and adjusting of systemic therapies, and monitoring and management of psoriasis in special populations.

Conclusion:

These consensus statements could provide useful, practical guidance on the diagnosis and management of patients with moderate-to-severe psoriasis and would cater to the needs of physicians in the UAE.

Keywords: Psoriasis, Consensus statement, Dermatology, Medication therapy management, Non-biologic therapy, Biologic therapy.

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1. INTRODUCTION

Psoriasis is a chronic, immune-mediated disease affecting 2–3% of the global population. It is characterized by mild localized plaques to severe plaques involving any part of the skin [1, 2]. These manifestations greatly affect patients' quality of life (QoL). Based on these factors, patients with psoriasis are frequently classified into the mild, moderate, or severe category, depending on the clinical severity of the lesions, the percentage of affected body surface area (BSA), and QoL. As a disease of systemic inflammation, psoriasis is associated with multiple comorbidities, including arthritis, cardiovascular disease, diabetes, and malignancy.

Although psoriasis is incurable, there are multiple effective treatment options for its management, including topical agents, phototherapy, conventional systemic (non-biologics), and biologic therapy. The choice of therapy is mainly determined by disease severity and comorbidities. Most patients with mild-to-moderate psoriasis are able to effectively control the disease solely with topical agents or phototherapy alone or with a combination of both. However, these treatments might be insufficient in patients with moderate-to-severe disease. Hence, systemic therapies are generally prescribed to such patients, including immunosuppressive or immunomodulatory drugs such as methotrexate (MTX), ciclosporin (CSA), apremilast, and biologic agents, as well as systemic retinoids such as acitretin. Biologic agents, as monotherapy or combined with other topical or systemic medications, are also quite effective in the management of moderate-to-severe psoriasis. Most global psoriasis guidelines, including those from the American Academy of Dermatology, British Association of Dermatologists, the National Institute for Health and Care Excellence (NICE), and European S3-Guidelines, recommend biologic agents when one or more conventional systemic agents are either not tolerated or deemed unsuitable due to the presence of other comorbidities [3 - 5].

Despite the availability of sufficient information on the management of psoriasis from evidence-based treatment guidelines [3, 5, 6], there are major unmet needs in daily clinical practice, particularly in the Middle East region, including regarding treatment- and safety-related issues faced by patients and inconsistencies among physicians in clinical practice [7]. Patients often report that they do not receive optimal care to reduce their skin symptoms and are frequently left on treatments for prolonged periods, even though they are ineffective [7 - 9]. Furthermore, from the perspective of physicians, there is no consistency in clinical practice when it comes to the diagnosis and management of psoriasis [10]. In the United Arab Emirates (UAE), there are limited local guidelines for evaluating and managing patients with psoriasis in routine clinical practice. Hence, it is necessary to develop clear, definitive strategies for the management of psoriasis that cater to the needs of physicians in the region.

The aim of the advisory board meeting was to develop consensus statements for the evaluation and management of moderate-to-severe psoriasis in the UAE.

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2. METHODS

To develop consensus statements, the Emirates Dermatology Society set up two advisory board meetings. Local key opinion leaders (KOLs), including dermatologists from the UAE, were recruited to participate in these meetings. The main objective was to facilitate the selected KOLs to deep dive into the available international and local guidelines to identify gaps to be bridged, incorporate new scientific data, highlight unmet needs in current clinical practice, and agree on consensus statements for the UAE.

2.1. Targeted Literature Review

An extensive literature search was conducted to review current international and local guidelines, and treatment paradigms and gaps were assessed in local treatment algorithms for the UAE. Guidelines that were part of the literature review included regional guidelines, which were compared with the latest international guidelines (American Academy of Dermatology [AAD]—Management and Treatment of Psoriasis with Biologics Clinical Practice Guidelines, British Association of Dermatologists Guidelines for Biologic Therapy for Psoriasis, NICE—Psoriasis: Assessment and Management, European S3-Guidelines) on the systemic treatment of psoriasis vulgaris and Saudi Practical Guidelines on Biologic Treatment of Psoriasis [3 - 6, 11, 12].

Based on the review of international and regional guidelines for the management of psoriasis, consensus statements were formed and grouped into the following categories: classification of disease severity; treatment options, including biologic and non-biologic systemic therapies; efficacy and safety profiles of systemic therapies; monitoring and management of psoriasis in special populations. Finally, key findings from the review were presented to the advisory board as statements.

2.2. Voting Procedure

A total of eight KOLs participated in the first advisory board meeting. Live voting was conducted, in which each participant had to vote either in favor of (Yes) or against (No) each statement. The consensus was established based on the collective agreement of the advisory board members for each statement. Members also had the option to modify or form additional statements based on their experience and local clinical practice. After the voting was completed, consensus statements were generated. These statements were further validated at the second advisory board meeting, in which 14 KOLs participated. The final consensus statements were then approved by all the members of the advisory board.

3. RESULTS AND DISCUSSION

3.1. Classification of Disease Severity

Presently, there is inconsistency in categorizing psoriasis based on severity, as no standard definition has been accepted [13]. Based on observations from clinical practice, the experts agreed to classify patients with psoriasis into three categories according to the severity of disease, *i.e.*., mild, moderate, and severe psoriasis. This classification is in accordance with the

different metrics of screening tools used for measuring the severity of psoriasis, among which the Psoriasis Area and Severity Index (PASI), BSA, and the Dermatology Life Quality Index (DLQI) scores are the most widely accepted tools.

The BSA represents the percentage of psoriatic lesions on the body surface through the "rule of nines," which is defined as 9% coverage for the head and neck, arm, anterior and posterior legs, and each of 4 trunk quadrants, and only 1% for the genitalia. It can also be estimated by counting the number of hands that would represent the percentage affected [14]. The PASI is a validated quantitative rating score for measuring the severity of psoriatic lesions depending on the area covered and the appearance of plaques [15]. The PASI combines the assessment of the severity of lesions and the percentage of area affected into a single score ranging from 0 (no disease) to 72 (maximal disease severity) [16]. The DLQI score has also become an essential tool to evaluate the impact of psoriasis on health-related QoL. Several studies have concluded that DLQI has a reliable grading system and is easy to use [17, 18]. The DLQI uses a scoring range from 0 to 30 and is graded as follows: 0–1="no effect"; 2–5="small effect"; 6–10="moderate effect"; 11–20="very large effect"; 21–30="extremely large effect."

Most decisions related to the management of psoriasis are taken with respect to disease severity and its clinical implications. A combination of different scores, *i.e.*., BSA, PASI, and DLQI, is used to assess the severity of the disease. However, the experts suggested that patients should be classified as moderate-to-severe if the score of at least one of the severity assessment tools is more than 10. Furthermore, the experts mentioned that BSA and PASI should be assessed by physicians/specialists, while the DLQI report must be generated through a questionnaire designed for patients.

In addition, disease manifestations that may significantly affect patients' QoL should also be considered. These include major involvement of the scalp, genitals, visible areas such as the face and palms, onycholysis or onychodystrophy of at least two fingernails, pruritus, and the presence of recalcitrant plaques [4, 5, 11, 12].

Consensus statements on the classification of disease severity are presented in Table **1**.

3.2. Treatment Options

For patients with mild psoriasis, topical therapy (including corticosteroids, vitamin D_3 analogs in combination with corticosteroids) and calcineurin inhibitors are given as the first-line of treatment. For patients with plaque or guttate-pattern psoriasis that cannot be controlled with topical treatments alone, combination therapy with topical therapy and phototherapy, which includes narrowband ultraviolet B (UVB) and excimer laser (wavelength of 308 nm), should be considered. Patients with moderate-to-severe psoriasis may also benefit from phototherapy. An excimer laser is used to treat small areas of the body or difficult-to-treat sites [19].

Systemic therapies are most commonly used for the treatment of patients with moderate-to-severe psoriasis and include conventional non-biologic systemic therapies, as well as biologic therapy, which will be discussed in more detail in forthcoming sections (Fig. **1**).

3.2.1. Non-biologic Systemic Therapy

In the UAE, the most commonly used non-biologic systemic therapies include MTX, CSA, apremilast, and acitretin. According to the experts, the criteria for choosing a therapy should be individualized based on the patient profile, medical history, disease severity, and comorbidities.

There was unanimous agreement on the use of non-biologic systemic therapy, and the suggested recommendations on the indications and dosages of each therapy conform with the product label Table **2**.

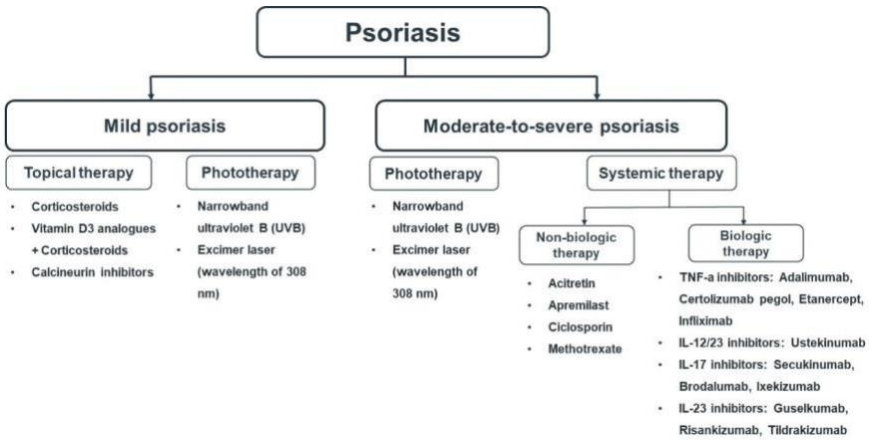

Fig. (1). Treatment pathway for psoriasis*.
UVB: Ultraviolet B; TNF: Tumor necrosis factor; IL: Interleukin.
*According to expert consensus.
Note: The treatments listed under different therapies do not depict any particular order of preference. All treatments are listed in alphabetical order.

Table 1. Consensus statements on the classification of disease severity.

• Psoriasis is classified as a mild, moderate, or severe disease based on the metrics of different screening tools used for measuring severity.
• The most common tools used for measuring severity in patients with psoriasis are BSA, PASI, and DLQI.
• Based on the BSA score, psoriasis is defined as: mild with BSA<3%, moderate with BSA 3–10%, and severe with BSA >10%.
• Based on the PASI score, psoriasis is defined as: mild with PASI <3, moderate with PASI 3–10, and severe with PASI >10.
• Based on the DLQI score, psoriasis is defined as: mild with DLQI ≤10, moderate-to-severe with DLQI >10.
• Although a combination of different scores, *i.e.*., BSA, PASI, and DLQI, is used to assess severity, when deciding on treatment initiation, psoriasis is considered moderate-to-severe if the score of at least one of the severity assessment tools is more than 10.
• Disease manifestations in high-impact sites, such as the scalp, face, palms, and genitals, should also be taken into consideration, as they significantly affect patients' QoL.

BSA: Body surface area; DLQI: Dermatology Life Quality Index; PASI: Psoriasis Area Severity Index; PDA: Psoriasis Disability Index; PGA: Physician's Global Assessment.

Table 2. Consensus statements on non-biologic systemic therapies.

• Non-biologic systemic therapies (MTX, CSA, apremilast, and acitretin) are recommended for patients with moderate-to-severe psoriasis.
MTX • MTX is generally given for 24 weeks and can be used as long-term maintenance therapy. • Recommended starting dose schedule [35]: o Weekly single oral, IM, or SC dosage schedule: 10 to 25 mg per week until adequate response is achieved. o Divided oral dose schedule of 2.5 mg at 12-hour intervals for three doses (FDA). • Higher starting doses of oral MTX (15–22.5 mg) result in a more rapid onset of response (PASI 50 within 3 to 7 weeks) [36 - 38]. • Dosages in each schedule may be gradually adjusted to achieve optimal clinical response; 30 mg/week should not ordinarily be exceeded. o Once the optimal clinical response has been achieved, each dosage schedule should be reduced to the lowest possible amount of drug and the longest possible rest period [35]. • The impact of other risk factors, such as liver disease, alcohol consumption, obesity, and type 2 diabetes, should also be considered before prescribing MTX to high-risk patients. • MTX is contraindicated during pregnancy due to its teratogenic, abortifacient, and mutagenic effects; female patients should be screened for pregnancy before initiating therapy.
CSA • CSA is generally used as an intermittent short-term therapy [39]. o CSA may be given as an alternative treatment to patients responding continuously for up to two years. • Oral CSA therapy can be initiated at 2.5 mg/kg/day as two doses of 1.25 mg/kg for at least 4 weeks, barring AEs [40]. o Higher starting doses (5 mg/kg bodyweight) lead to increased rapid onset of response (PASI 50 within 3 weeks), although this may result in increased toxicity compared to starting at a lower dose [41 - 43]. • The dose can be increased at 2-week intervals if no clinical improvement is observed; increase the dose by approximately 0.5 mg/kg/day to attain a maximum dose of 5.0 mg/kg/day [40]. • The dose should be decreased by 25%–50% at any time to control AEs. • There is a significant risk of renal toxicity, arterial hypertension, and non-melanoma skin cancer with long-term use of CSA, especially in patients who have undergone extensive phototherapy [40].
Acitretin • Acitretin is preferably reserved for palmoplantar psoriasis and pustular psoriasis *(expert consensus).* • The recommended dose is 25 to 50 mg per day [44]. • Acitretin should be prescribed based on clinical experience and the most important outcome for the individual patient [4]: o Low dose (20 to 30 mg daily): For better tolerability. o High dose (>30 mg daily): For better efficacy. • Acitretin is highly teratogenic and is contraindicated in women who might become pregnant during or within 3 years after discontinuing therapy.
Apremilast • Apremilast is indicated for the treatment of patients with moderate-to-severe plaque psoriasis who are candidates for phototherapy or systemic therapy. • Recommended dose [45]: o Initial dose: Titrated from 10 mg at Day 1 to 50 mg at Day 5. o Maintenance dose: 60 mg daily (two doses of 30 mg) from Day 6 onwards. • Apremilast should be discontinued if patients suffer from new or worsening psychiatric symptoms or if suicidal ideation or suicidal behavior is identified.

CSA: Ciclosporin; IM: Intramuscular; MTX: Methotrexate; PASI: Psoriasis Area Severity Index; PsA: Psoriatic arthritis; QoL: Quality of life; AEs: Adverse events.
Note: The treatments listed in the table do not depict any particular order of preference.

In terms of efficacy and safety profiles, the experts agreed that clinicians should adhere to the prescription label and follow local guidelines if any. MTX has been shown to be effective in psoriasis and is associated with successful treatment response, as defined by an improvement in the PASI score by 50% to 75% and in absolute DLQI value [20 - 22]. However, MTX is associated with risk factors, including liver disease, obesity, alcohol intake, and type 2 diabetes, and is also

contraindicated in pregnancy due to its teratogenic, abortifacient, and mutagenic effects [23 - 28]. The use of CSA has shown promising results in achieving treatment response as a short-term therapy; however, there is a significant risk of renal toxicity, arterial hypertension, and non-melanoma skin cancer [29 - 31]. Acitretin is generally considered for palmoplantar or pustular forms of psoriasis and is prescribed at either low doses for better tolerability or high doses for better efficacy [4]. In terms of safety, acitretin is classified by the Food and Drug Administration (FDA) as a class X drug due to its teratogenic effects and is contraindicated in pregnancy [27, 28]. Recent randomized controlled trials of apremilast have indicated that around 33.1% of patients show PASI 75 response by Week 16; apremilast was found to be effective in palmoplantar, scalp psoriasis, and nail psoriasis [32 - 34]. Its common side effects include nausea, diarrhea, and upper respiratory tract infections that resolve over time; however, it should be discontinued if patients suffer from any psychiatric symptoms or if suicidal ideation or suicidal behavior is identified [4].

Overall consensus statements on the management of moderate-to-severe psoriasis using non-biologic systemic therapies are presented in Table **2** [35 - 45].

3.2.2. Biologic Systemic Therapy

In the UAE, the most commonly used biologic systemic therapies include tumor necrosis factor (TNF) inhibitors (adalimumab, certolizumab pegol, etanercept, infliximab), interleukin (IL)-12/23 inhibitors (ustekinumab), IL-17 (brodalumab, ixekizumab, and secukinumab), and recently approved IL-23 inhibitors (guselkumab, risankizumab, and tildrakizumab). According to the experts, biologics can be prescribed early in the treatment paradigm as the first-line treatment on a case-by-case basis, depending on the severity of disease, presence of comorbidities, and location of lesions Table **3**.

The panel has also suggested that the criteria for choosing biologic therapy should be individualized based on the patient profile and medical history, and other factors—including the availability of drugs and treatment costs.

There was unanimous agreement among the experts on the indications and dosage of different biologic therapies. This was in line with the product labels, as well as international guidelines, which specified that biologic agents are routinely used in case of failure of non-biologic therapy due to inadequate response, safety concerns, or the presence of comorbidities. The experts also reached a consensus on the use of biologics based on disease location and subtypes in patients with moderate-to-severe psoriasis [3].

The TNF-α inhibitors are considered first-generation biologics. Evidence on the positive efficacy of anti-TNF therapies for plaque psoriasis is well established. Different PASI 75 response rates have been reported in clinical studies in the context of treatment for psoriasis with anti-TNF therapies of varied doses: 33% (50 mg weekly) and 49% (50 mg twice weekly) for etanercept at Week 12 [46], 71% for adalimumab at Week 16 [47, 48], 75.5% (5 mg/kg) and 70.3% (3 mg/kg) for infliximab at Week 10 [49], and 75% (200 mg every 2 weeks) and 83% (400 mg every 2 weeks) for certolizumab pegol [50]. Local injection-site reactions, infections, and autoimmune phenomena are common adverse events (AEs) associated with anti-TNF therapies. Ustekinumab, an IL-12/23 inhibitor, has been shown to have a PASI 75 response of 72.4% and 61.2% at 90 mg and 45 mg, respectively, at Week 76 [51 - 53]. Common AEs listed for ustekinumab include nasopharyngitis and upper respiratory tract infections. Several studies have also assessed the efficacy of IL-17 inhibitors, including secukinumab, in psoriasis with 81.6% and 28.6% of patients reaching PASI 75 and PASI 100 response at Week 12 [54]. Secukinumab showed a rapid onset of action and was found to be superior to ustekinumab [55, 56]. Both ixekizumab and brodalumab also showed a more promising response when compared to placebo with 89.1% and 83.3% PASI 75 response, respectively, at Week 12 [57, 58]. Frequent AEs of IL-17 inhibitors include nasopharyngitis, headache, upper respiratory tract infection, and arthralgia [54].

Of note, IL-23 inhibitors are the newest class of biologics approved for patients with moderate-to-severe psoriasis who are candidates for systemic therapy or phototherapy or have failed response to other systemic therapies. They are being used by physicians in their local practice for the treatment of psoriasis in the UAE. IL-23 inhibitors have shown positive results in terms of efficacy. With risankizumab, PASI 75 and PASI 90 response was observed in 88% and 81% at Week 12 [59]. Guselkumab has been reported to be clinically more advantageous than adalimumab, with 85.1% of patients reaching PASI 75 response and 73.3% receiving PASI 90 response at Week 16 [60, 61]. Furthermore, results from the phase 3 ECLIPSE trial indicate that the proportion of patients with a PASI 90 response at Week 48 was greater for guselkumab in comparison to secukinumab (84% *versus* 70%) [62]. In the case of tildrakizumab, clinical studies showed 74% PASI 75 and 52% PASI 90 at Week 16, and patients on tildrakizumab were more likely to reach PASI 75 at Weeks 16 and 28 as compared to patients on etanercept [63, 64]. Safety studies also reported IL-23 inhibitors to be associated with upper respiratory infections, headache, fatigue, injection-site reactions, diarrhea, gastroenteritis, arthralgia, herpes simplex infections, and tinea infections.

Table 3. Consensus statements on biologic systemic therapy.

Biologic systemic therapies for the management of moderate-to-severe psoriasis include:
• TNF-α inhibitors: Adalimumab, infliximab, etanercept, certolizumab pegol
• IL-12/23 inhibitor: Ustekinumab
• IL-17 inhibitors: Brodalumab, ixekizumab, and secukinumab
• IL-23 inhibitors: Guselkumab, risankizumab, and tildrakizumab

Biologics can be prescribed early in the treatment paradigm as first-line treatment in the following cases:
• Moderate-to-severe patients (>10% BSA, PASI, and/or DLQI).
• In case of comorbidities such as PsA.
• Affected high-impact sites (DLQI >10), including hands and feet, face and scalp, genital area, and significant nail disease (regardless of BSA or PASI score).

Biologics should be prescribed in correct form and dosage, as indicated in the product label:

Biologic agent	Starting dose	Maintenance dose
Adalimumab	80-mg subcutaneous injection (taken as two 40-mg doses), followed by a 40-mg subcutaneous injection 1 week later	40-mg subcutaneous injection every 2 weeks
Etanercept	50-mg subcutaneous injection twice weekly for 12 weeks	50-mg subcutaneous injection once per week
Infliximab	5-mg/kg IV infusion administered at Week 0, Week 2, and Week 6	5-mg/kg IV infusion administered every 8 weeks*
Certolizumab	(a) 400 mg	a) 400 mg every other week (b) Alternative regime for patients who weigh <90 kg: 400 mg initially and at Week 2 and Week 4	b) 200 mg every other week
Ustekinumab	(a) For patients weighing ≤100 kg: 45 mg administered subcutaneously initially and 4 weeks later (b) For patients weighing >100 kg: 90 mg administered subcutaneously initially and 4 weeks later	(a) Patients ≤100 kg: 45 mg administered subcutaneously every 12 weeks (b) Patients >100 kg: 90 mg administered subcutaneously every 12 weeks
Secukinumab	300-mg subcutaneous injection at Week 0, Week 1, Week 2, Week 3, and Week 4	300-mg subcutaneous injection every 4 weeks
Brodalumab	210-mg subcutaneous injection at Week 0, Week 1, Week 2	210-mg subcutaneous injection every 2 weeks
Ixekizumab	160-mg subcutaneous injection followed by 80 mg at Week 2, Week 4, Week 6, Week 8, Week 10, and Week 12	80-mg subcutaneous injection every 4 weeks
Guselkumab	100-mg subcutaneous injection at Week 0 and Week 4 and every 8 weeks thereafter	100-mg subcutaneous injection every 8 weeks
Risankizumab	150 mg (2 × 75-mg injections) administered subcutaneously initially and at Week 4	150 mg administered subcutaneously every 12 weeks
Tildrakizumab**	100 mg administered subcutaneously initially and 4 weeks later	100 mg administered subcutaneously every 12 weeks

*Time interval can be modified or dose per kg can be increased according to the patient's response.
**Not registered in UAE (December 2020 update).

Adalimumab (ADA)
• Recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy:
o Associated or not associated with psoriatic arthritis
• The recommended dose is:
o Starting dose: 80 mg taken as two 40-mg SC injections of the initial dose, followed by a 40 mg SC 1 week later, then 40 mg SC every 2 weeks thereafter.
o Maintenance dose: 40 mg once weekly.
• In case of inadequate response, the dosage can be increased from 40 mg every other week to 40 mg weekly.

Etanercept
• Recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis affecting the nails, scalp, and other subtypes (including pustular or erythrodermic).
• The recommended dose of etanercept is:
o Starting dose: 50 mg as SC injection twice weekly for 12 consecutive weeks.
o Maintenance dose: 50 mg once weekly.
• In case of inadequate response, the dosage can be increased from 50 mg per week to 2 × 50 mg per week.

Infliximab
• Recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy.
• The recommended dose is:
o Starting dose: 5 mg/kg as IV injection administered at Weeks 0, 2, and 6, and thereafter every 8 weeks.
o Maintenance dose: 5 mg/kg every 8 weeks.
o Dosing intervals with infliximab monotherapy should not be increased; however, the dose may be decreased from 5 mg/kg to a minimum of 3 mg/kg.
• If there is an inadequate response, decreasing the dosing intervals from every 8 weeks to every 6 weeks with 5 mg/kg can be considered in secondary non-responders.

Certolizumab pegol
• Recommended (within its marketing authorization) for adults with plaque psoriasis who are candidates for systemic treatments or who have not responded to standard systemic therapies, including CSA, MTX, and psoralen and ultraviolet A (PUVA); or the person is intolerant of or has a contraindication to these treatments. Certolizumab pegol is also recommended for pregnant women due to its low teratogenic risk.
• The recommended dose is:
o Starting dose: 400 mg (given as two subcutaneous injections of 200 mg each) at Weeks 0, 2, and 4.
o Maintenance dose: 200 mg every 2 weeks.
o A dose of 400 mg every 2 weeks can be considered in patients with insufficient response.

Ustekinumab • Recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy. • Dosing of ustekinumab is based on the weight of the patient: o Patients weighing ≤100 kg: 45 mg at Week 0, and 4, then 45 mg every 12 weeks. o Patients weighing >100 kg: 90 mg at Week 0, and 4, then 90 mg every 12 weeks. • In case of inadequate response, the dose can be increased from 45 mg to 90 mg with 12-week dosing intervals (with primary partial responders). If this is unsuccessful, the dose can be further increased to 90 mg every 8 weeks.
Secukinumab • Recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy. • The recommended dosage is 300 mg by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 followed by 300 mg every 4 weeks.
Brodalumab • Brodalumab is recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis and patients with generalized pustular psoriasis. • The recommended dose of brodalumab is 210 mg by self-administered subcutaneous injection at Week 0, Week 1, and Week 2 followed by 210 mg every 2 weeks.
Ixekizumab • Ixekizumab is recommended as a monotherapy treatment option for use in adult patients with moderate-to-severe plaque psoriasis affecting the scalp, nails; and in erythrodermic and pustular psoriasis. • The recommended starting dose of ixekizumab is 160 mg (two 80-mg injections) by self-administered subcutaneous injection at Week 0 followed by 80 mg at Week 2, Week 4, Week 6, Week 8, Week 10, and Week 12 and then every 4 weeks thereafter. o Some patients may require 80-mg dose every 2 weeks to maintain response to treatment.
Guselkumab • Guselkumab is recommended as a monotherapy treatment option for use in adult patients with moderate-to-severe plaque psoriasis: o Associated or not associated with psoriatic arthritis. • The recommended dose is 100 mg administered as subcutaneous injection at Week 0, Week 4 and every 8 weeks thereafter.
Risankizumab • Risankizumab is recommended for patients with moderate-to-severe disease who are eligible for systemic therapy or phototherapy or have failed response to other systemic therapies. • The recommended dose is 150 mg (two 75-mg injections) administered as a subcutaneous injection at Week 0, Week 4, and every 12 weeks thereafter.
*Tildrakizumab** • Tildrakizumab is recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis. • The recommended dose is 100 mg given by physician-administered subcutaneous injection at Week 0 and Week 4 and every 12 weeks thereafter.
Combination therapy • MTX and acitretin can be added to anti-TNF therapy with the intention of improving efficacy, optimizing the risk/benefit profile, reducing the risk of immunogenicity (with MTX), and enhancing long-term disease management. o Consider adding the lowest recommended dosage for conventional systemic therapy at the beginning (*e.g.*., 5–10 mg/week for MTX). • Treatment with a combination of MTX with IL-12/IL-23, IL-17, and IL-23 inhibitors cannot yet be recommended in the management of psoriasis because of limited data on safety and efficacy. • Because of the lack of evidence and increased toxicity (*e.g.*., an increased skin cancer risk), a combination of anti-TNF therapies or ustekinumab with CSA is not recommended.

ADA: Adalimumab; CSA: Ciclosporin; IL: Interleukin; MTX: Methotrexate; PUVA: Psoralen and ultraviolet A; SC: Subcutaneous; TNF: Tumor necrosis factor; PsA: Psoriatic arthritis. Note: The treatments listed in the table do not depict any particular order of preference. *Not registered in UAE (December 2020 update).

3.2.3. Treatment Response

Attaining complete clearance of skin lesions and avoiding suboptimal or unnecessary treatment are the key goals in treating psoriasis. The expert panel agreed that therapeutic goals should be defined based on the criteria recommended in the recent French guidelines (2019) [65]:

- Absolute PASI ≤3: Reflects clear or almost clear status (or a physician global assessment [PGA] score of 0–1) of the patient.
- DLQI 0 or 1: Indicates the absence of impact of psoriasis on QoL.
- PASI 90 and PASI 100 responses: This criterion has emerged because of the high efficacy of some of the most recent biological agents (Fig. **2**).

3.2.4. Combination Therapy

Due to limited efficacy studies, there are no approved indications and doses for the combination of biologic therapy with conventional systemic therapy for the treatment of psoriasis. However, a literature review by Heffernan indicated the potential benefits of combination therapy, including additive or synergistic improvement in efficacy and minimized cost and toxicity, by using lower doses of the drug [66]. As such, most recent global guidelines recommend adding low-dose MTX or acitretin to anti-TNF therapy with the aim of improving efficacy, optimizing the risk/benefit profile, lowering the risk of immunogenicity (with MTX), and enhancing long-term disease management. Some trials have shown beneficial treatment effects using a combination of MTX and anti-TNF therapies [67, 68].

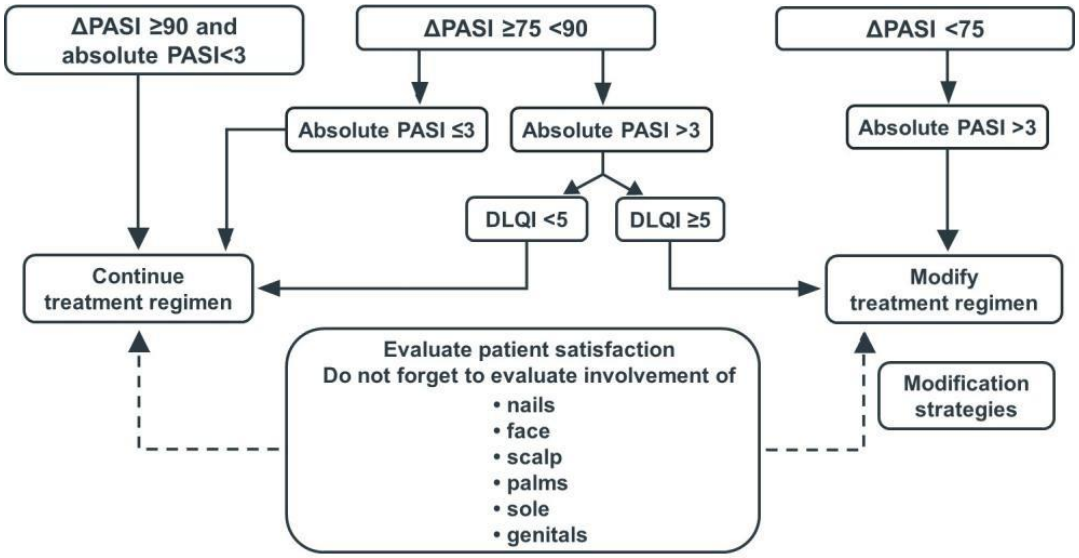

Fig. (2). Treatment response in plaque psoriasis based on PASI and DLQI scores.
DLQI: Dermatology Life Quality Index; PASI: Psoriasis Area Severity Index.
Source: Amatore F, Villani AP, Tauber M, Viguier M, Guillot B. French guidelines on the use of systemic treatments for moderate-to-severe psoriasis in adults. Journal of the European Academy of Dermatology and Venereology: JEADV. 2019;33(3):464-483. (Accessed May 07, 2020)

Conversely, potential complications exist when combining non-biologic systemic therapy and biologic therapy, including issues with drug metabolism and additive AEs [66]. There is a potentially increased risk of nephrotoxicity, hypertension, and non-melanoma skin cancer with the combination of CSA and anti-TNF therapies or ustekinumab [69]. Further, there is a dearth of evidence on the use of MTX with IL-12/IL-23, IL-17, and IL-23 antagonists, although a combination of MTX with IL-12/IL-23 is suggested for psoriatic arthritis (PsA). According to the consensus report by Mrowietz *et al*., optimal safety monitoring for combination therapy has not been established and may involve parameters that require more frequent monitoring [70].

Consensus statements on the management of moderate-to-severe psoriasis using biologic systemic therapies are presented in Table **3**.

3.2.5. Transitioning and Adjusting Therapy

Emphasis on dose escalation, switching or stopping of therapy, and resuming treatment after stopping in case there is an inadequate response were also considered by the experts. Dose escalation strategies for individual drugs are presented in Table **3**.

The expert panel also agreed that switching to alternative therapy should be considered in case treatment response is not achieved even after the optimum dose and duration of treatment. Based on the reviewed international guidelines, strategies to transition from non-biologic systemic to biologic therapy and between different classes of biologic therapy were suggested [3, 5]. Although there is little evidence, stopping systemic therapy can be considered in patients with well-controlled psoriasis on a case-by-case basis [70].

In addition, the panel also agreed that restarting or resuming biologic treatment after discontinuation should be done on an individual basis, taking into account the severity of the disease and the number of doses missed [3].

Consensus statements for transitioning and adjusting therapy are shown in Table **4**.

Table 4. Consensus statements on transitioning and adjusting therapy.

• Dose escalation should be considered in case of inadequate primary response with recommended dosing (such as in obese patients or relapse of psoriasis during treatment cycle) [5].
Biologic agent Suggested dose escalation strategy
Adalimumab 40 mg every other week Adalimumab 40 mg weekly
Etanercept 50 mg once weekly Etanercept 50 mg twice weekly
Infliximab 5 mg/kg every 8 weeks Infliximab 5 mg/kg every 6 weeks
Certolizumab pegol 200 mg every 2 weeks Certolizumab pegol 400 mg every 2 weeks
Ustekinumab 45 mg every 12 weeks (<100 kg) Ustekinumab 90 mg every 12 weeks (<100 kg)
Ustekinumab 90 mg every 12 weeks (>100 kg) Ustekinumab 90 mg every 8 weeks (>100 kg)

(Table 4) contd.....

• Consider switching to alternative therapy in case treatment response is not achieved even after optimum dose and duration of treatment *(expert consensus).* • When transitioning from non-biologic systemic to biologic therapy [5]: o For stable disease, allow one month between the last dose of the previous standard non-biologic systemic therapy and the initial dose of biologic therapy. o Treatment transition from MTX to biologic therapy can be performed with no drug washout period in people taking or in people on other therapies where this would lead to unstable disease. o Start biologic therapy with no drug washout period in people on other therapies where this would lead to unstable disease. o Take into account special considerations for patients for whom a disease flare would be severe or hazardous and discontinue therapy as soon as the minimum response has been achieved. • If clinically indicated, switching of biologics should be considered with the possibility of improved efficacy, safety, and/or tolerability [3]. • The duration of the transition period (ie, interval between discontinuation of previous treatment and initiation of the new treatment) should be assessed on a case-by-case basis, depending on: o Treatment that is being discontinued. o Disease severity. o Response to prior treatment [3].
• Consideration of stopping therapy in patients with well-controlled psoriasis should be based on [70]: o Patient preference. o Presence of individual risk factors with an impact on the long-term benefit/risk profile. o Prior course of disease including pattern of flares/rebound. o Presence of comorbidity. o Presence of PsA. o Disease phenotype, severity, and impact on QoL. o Type of treatment. • Stopping systemic therapies can be considered in patients with [70]: o Clinical response of clear or almost clear with good QoL for a prolonged period (eg, a minimum of 1 year). o History of disease-free intervals or previously stable plaque-type psoriasis. o Absence of significant comorbidities, including PsA. o Mild-to-moderate disease course. o Low impact on QoL. o No worsening of disease after previous treatment withdrawal. o Patient preference. • Caution must be taken when considering stopping biologics, as the risk of antibody formation against biological therapies increases with intermittent therapy.
• Resuming biologic therapy in patients who have discontinued should be based on: o Disease severity. o Number of doses missed. • In case of severe disease flares or if more than three to four half-lives have passed since the previous dose, it is recommended to repeat the administration of the starting dose. A small percentage of patients restarting treatment after discontinuation may not be able to reach the same response levels attained previously [3].

MTX: Methotrexate; PsA: Psoriatic arthritis; QoL: Quality of life.

3.3. Monitoring

3.3.1. Non-biologic Systemic Therapy

Before starting any systemic therapy, there must be a practical approach in place to monitor patients on the basis of their medical history, physical examination, and laboratory tests in order to maximize the benefits and minimize the risks associated with these drugs. Based on the European S3-Guidelines and local practice, there was an agreement among the experts with regard to the appropriate laboratory tests required for monitoring of patients with moderate-to-severe psoriasis who are eligible for non-biologic systemic therapy [4, 6]. These include periodic blood count and liver function tests, along with screening for hepatotoxicity, renal toxicity, malignancies, and serious infections—including hepatitis and human immunodeficiency virus (HIV).

Screening and laboratory controls required for monitoring at baseline and during treatment in patients taking non-biologic systemic therapy are presented in Table **5**. Overall consensus statements on monitoring requirements for non-biologic systemic therapy are presented in Table **6**.

Table 5. Monitoring requirements for non-biologic systemic therapy.

-	MTX	CSA	Acitretin	Apremilast
Baseline screening, monitoring, and laboratory investigations				
CBC	X	X	X	X
Liver function tests	X	X	X	Optional***
Serum creatinine	X	X	X	X
Pregnancy test	X	X	X	X
Urine status	X	X		
Uric acid		X		

(Table 5) contd.....

-	MTX	CSA	Acitretin	Apremilast
Fasting blood glucose test			X	
Triglycerides, cholesterol, and HDL		X	X	
Hepatitis B and C and HIV infection	X	X		Optional
Serum albumin test*	X			
Type III procollagen (PIIINP)	X			
Electrolyte levels[1]		X		
Magnesium levels[2]		X		
Ongoing monitoring				
CBC	X	X	X	X
Liver function tests	X	X	X	Optional***
Serum creatinine	X	X		X
Pregnancy test			X**	X
Urine status	X	X		
Uric acid		X		
Fasting blood glucose test				
Triglycerides, cholesterol, and HDL		X[2]	X	
Serum albumin test*	X			
Type III procollagen (PIIINP)	X			
Electrolyte levels[1]		X		
Magnesium levels[2]		X		

eGFR: Estimated glomerular filtration rate; HDL: High-density lipoprotein; HIV: Human immunodeficiency virus; CBC: Complete blood count; PIIINP: Type III procollagen, MTX: Methotrexate; CSA: Ciclosporin.

*To be considered in special cases with suspected hypoalbuminemia or in patients using other drugs with high binding affinity for serum albumin.

**Monthly up to 2 years after therapy.

***Based on physician's discretion.

[1]Includes sodium and potassium.

[2]Only with indication (muscle cramps).

Table 6. Consensus statements on monitoring requirements for non-biologic systemic therapy.

• CBC with differential should be done pre-treatment and periodically during any non-biologic systemic treatment (from once every 2 weeks to every 2–3 months), as per medical history, risk exposure, and patient characteristics.
• Liver function tests should be done pre-treatment and periodically during any non-biologic systemic treatment (from once every 2 weeks to every 2–3 months), as per medical history, risk exposure, and patient characteristics.
• Testing for serum creatinine should be done prior to initiation of any non-biologic systemic treatment, followed by periodic testing from once every 2 weeks to every 2–3 months.
• Pregnancy test should be performed prior to initiation of any non-biologic systemic treatment.
• In patients treated with apremilast, liver function tests are optional, as apremilast does not require dose adjustment, except in patients with severe hepatic impairment.
• For patients taking acitretin or CSA, triglyceride and cholesterol tests should be done pre-treatment and once every two months thereafter.
• For patients taking MTX or CSA, urine status and uric acid test should be done pre-treatment and periodically during treatment.
• In female patients in the childbearing period taking acitretin, pregnancy tests should be considered pre-treatment and monthly, during and post-treatment, for 3 years.
• Hepatitis B, hepatitis C, and HIV infection should be tested in patients with psoriasis starting MTX. • For patients taking MTX, serum albumin test should be considered only in special cases* pre-treatment, then once every 2 weeks for the first 2 months and once every 3 months thereafter. • Type III procollagen (PIIINP) test should be done in patients taking MTX pre-treatment and every 3 months thereafter.
• In patients taking CSA, electrolyte (sodium and potassium) levels should be tested pre-treatment, once every two weeks for the first month and once every month thereafter. • For CSA, magnesium levels should be tested prior to treatment initiation and once every 2 months thereafter**. • Kidney toxicity for patients on CSA therapy should be monitored monthly by measurement of serum creatinine levels and eGFR assessment.

CBC: Complete blood count; CSA: Ciclosporin; eGFR: Estimated glomerular filtration rate; HIV: Human immunodeficiency virus; MTX: Methotrexate; PIIINP: Type III procollagen.

*Cases with suspected hypoalbuminemia or in patients using other drugs with high binding affinity for serum albumin.

**Only with indication (muscle cramps).

3.3.2. Biologic Systemic Therapy

Although several guidelines and reviews offer recommendations on screening and monitoring tests for biologics, there are no definitive recommendations, given widespread variations in prescriber practices, the prevalence rates of risks associated with therapy, availability of tests, etc.

Based on the available guidelines, the experts agreed that prior to initiating biologic therapy, it is important to obtain a baseline evaluation of the patient, including hematology and biochemistry, screening for severe infections—including tuberculosis (TB), hepatitis B virus (HBV)/hepatitis C virus (HCV), and HIV, and case-by-case assessment for malignancy and inflammatory bowel disease (IBD) [3, 4, 6].

Screening and laboratory controls required for monitoring at baseline and during treatment in patients taking biologic systemic therapy are presented in Table **7**. Consensus statements on monitoring requirements for biologic systemic therapy are presented in Table **8**.

3.4. Special Populations

3.4.1. Pregnancy and Nursing Mothers

For pregnant women with milder forms of psoriasis, topical corticosteroids and UVB are considered the safest options for treatment. For those who require systemic therapy, CSA is a reasonable choice, although it is associated with an increased risk of hypertension [27], low birth weight, intrauterine growth retardation, and premature delivery. Acitretin and MTX are contraindicated in pregnancy due to their teratogenic effects [27] [28].

Table 7. Monitoring requirements for biologic systemic therapy.

-	TNA-α inhibitor	IL-12/23 inhibitor	IL-17 inhibitor	IL-23 inhibitor
Baseline screening, monitoring, and laboratory investigations				
CBC	X	X	X	X
Complete metabolic profile	X	X	X	X
Pregnancy test	X	X	X	X
Tuberculosis	X	X	X	X
Hepatitis B and C virus	X	X	X	X
HIV	X	X	X	X
Infectious disease	X	X	X	X
Non-melanoma skin cancer	X	X	X	X
Chronic heart failure	X			
History of IBD			X	
Ongoing monitoring				
Infectious disease	X	X	X	X
Non-melanoma skin cancer	X	X	X	X
Latent tuberculosis	X	X	X	X
Hepatitis B and C virus				X
IBD			X	

HIV: Human immunodeficiency virus; IBD: Inflammatory bowel disease; IL: Interleukin; CBC: Complete blood count; TNF: Tumor necrosis factor.
*In high-risk patients (with a history of cutaneous malignancy or ultraviolet [UV] phototherapy).

Table 8. Consensus statements on monitoring requirements for biologic systemic therapy.

• CBC with differential should be done pre-treatment and periodically during treatment at the discretion of each physician, indicated by patient history, clinical signs, or other laboratory test results. • In patients treated with infliximab, CBC should be done before treatment and before every further infusion.
• Liver function tests should be done pre-treatment and periodically during treatment at the discretion of each physician, indicated by patient history, clinical signs, or other laboratory test results. • In patients treated with infliximab, liver function tests should be done before treatment and before every further infusion.
• Pregnancy test should be performed prior to initiation of biologic treatment.
• Testing for TB infection (purified protein derivative and QuantiFERON-TB Gold) should be done prior to initiation of biologic treatment, followed by annual testing for latent TB in high-risk patients.
• Testing for HBV (surface antigen and core antibody) and HCV (IgG) infection should be done in patients with psoriasis starting biologic therapy. • Testing for HBV and HCV should be considered during treatment with IL-23 inhibitors.
• Pre-treatment testing for HIV is considered at the treating practitioner's discretion and depends on patient-specific risk factors.
• Patients should be monitored for early signs and symptoms of infection prior to and during treatment with biologic therapies. • Specific assessment for infections (*e.g.*., tuberculosis, histoplasmosis) should be considered, especially in patients using anti-TNF therapies plus MTX.
• Assessment of malignancy (including skin cancer), especially in high-risk patients (with a history of cutaneous malignancy or UV phototherapy), should be considered prior to and during treatment with biologic therapy. • Yearly skin examinations to check for non-melanoma skin cancer should be routinely practiced for patients taking CSA.
• The history of IBD should be considered prior to and during treatment with an IL-17 inhibitor.

CBC: Complete blood count; CSA: Ciclosporin; HBV: Hepatitis B virus; HCV: Hepatitis C virus; HIV: Human immunodeficiency virus; IBD: Inflammatory bowel disease; IgG: Immunoglobin G; IL: Interleukins; MTX: Methotrexate; TB: Tuberculosis; TNF: Tumor necrosis factor; UV: Ultraviolet.

Biologics should be used with more caution in women of childbearing potential or those who become pregnant. In such patients, the benefits and risks of continuing *versus* stopping biologic treatment should also be discussed [5]. Studies have shown that any risks of biologic use, particularly with anti-TNF therapies and IL-12/23 inhibitors in pregnancy, are not related to teratogenesis and congenital malformations but to immunosuppression of the neonate [28, 71]. Moreover, it is likely that most immunoglobulins can be excreted in human milk, although data are limited. Hence, there is a potential for adverse reactions in nursing infants from mothers undergoing biologic therapy. However, certolizumab pegol has shown minimal to no placental transfer and is safer for use in breastfeeding women compared to other biologics [72]. In the case of IL-17 and IL-23 inhibitors, there are insufficient data on their use in pregnant and breastfeeding women to inform any drug-associated risk of adverse developmental outcomes. Thus, no recommendations on using IL-17 and IL-23 inhibitors were provided in any guideline for this population. The experts' recommendations are, therefore, in line with current evidence and prescription labels, suggesting that both certolizumab pegol and adalimumab can be prescribed (with caution) during pregnancy and breastfeeding if the benefits outweigh the risks.

3.4.2. Geriatric Use

In elderly patients starting treatment with MTX, dose reduction should be considered due to reduced hepatic and renal function, as well as lower folate reserves, which occur more frequently with increased age [35]. Similarly, dose adjustment is also required in elderly patients being treated with CSA, along with regular monitoring of renal function during the course of treatment [40]. In the case of acitretin and apremilast, no dose adjustment is required for elderly patients [44, 45]. Anti-TNF therapies, on the other hand, are a safer option in elderly patients with moderate-to-severe disease, although side effects are more likely to occur with adalimumab [4]. In the case of IL-12/23, IL-17, and IL-23 inhibitors, safety or efficacy outcomes were consistent between older and younger subjects, and, hence, no dose adjustments are required [73 - 79].

3.4.3. Malignancies

Long-term use of certain psoriasis treatments such as PUVA, UVB irradiation, and CSA is associated with an increased risk of developing non-melanoma skin cancer and lymphomas [31, 80, 81]. Patients with psoriasis taking CSA should avoid concomitant UVB or PUVA photochemotherapy and should be monitored for non-melanoma skin cancers (NMSC) prior to and during treatment [40].

In the case of biologics, studies have suggested that there is no risk of solid tumor or lymphoreticular malignancy when using anti-TNF therapies and IL-12/23 inhibitors as monotherapy in patients with moderate-to-severe psoriasis [82, 83]. Likewise, both anti-TNF therapies and IL-12/23 inhibitors can be prescribed to patients with a history of solid tumor malignancy who have failed ultraviolet phototherapy, MTX, and/or acitretin without expecting any risk of tumor recurrence [84, 85]. However, caution should be exercised in such patients if cancer has been diagnosed and treated less than five years previously and/or where the baseline risk of skin cancer (such as in patients previously treated for NMSC) is increased [4, 5]. Additionally, there is no conclusive evidence that other biologics, such as IL-17 and IL-23, have any associated risk of malignancy, as more long-term safety studies are required to evaluate their safety profiles. However, findings from clinical studies show that the incidence of malignant or unspecified tumors in patients receiving secukinumab was consistent with expected rates for patients with psoriasis [86]. Considering the available data, the experts agreed that biologics could be considered in the treatment paradigm, given that their benefits outweigh the negligible risk of solid organ malignancy.

3.4.4. Tuberculosis (TB)

Biologics, especially anti-TNF therapies, are associated with an increased risk of activating latent tuberculosis infection, leading to severe morbidity and mortality in some cases [87, 88]. However, in the case of IL-12/23 inhibitors, the occurrence of tuberculosis has been rarely observed [89]. Similarly, the risk of TB reactivation is relatively lower in patients taking IL-17 and IL-23 inhibitors as compared to patients taking anti-TNF therapies [86, 90]. However, as most biologics are immunosuppressive, it is important that all patients are screened for latent TB using purified protein derivative (PPD) skin test or QuantiFERON-TB Gold prior to initiating treatment. If active TB is suspected, treatment with biologics should be deferred, and patients should be treated with rifampicin, isoniazid, pyrazinamide, or ethambutol [91]. In case latent tuberculosis is detected, patients should begin prophylaxis for TB with rifamycin-based treatment regimens or isoniazid [92]. When anti-tuberculous therapy is indicated, patients should aim to complete one month of treatment before initiating any biologic therapy [12].

3.4.5. Hepatitis Virus Reactivation

MTX is relatively contraindicated in patients with active or recurrent HBV, considering MTX is significantly associated with hepatotoxicity [93, 94]. Similarly, the occurrence of hepatitis has also been reported in patients taking acitretin. Hence, prior to initiating therapy with acitretin, it is necessary that patients undergo liver function tests [44]. For active HBV, the experts agreed that patients with psoriasis should not be prescribed immunosuppressive therapies till it is controlled by antiviral treatment [3, 4]. Consecutively, reactivation of HBV can occur due to a compromised immune system as a result of using biologics in patients identified as carriers of HBV or in those who were previously infected with the virus [95]. Such patients may require antiviral prophylaxis 2–4 weeks before starting immunosuppressive therapy [95]. It is also necessary that these patients are monitored periodically for any clinical signs and symptoms of active infection and undergo liver function tests prior to and during treatment with biologics for psoriasis [96]. In the case of HCV, patients with a history of or currently active infection may receive biologics for the management of psoriasis [96 - 98]. The occurrence of HCV reactivation with regard to the administration of biologics is rare. However, periodic monitoring of patients through measuring HCV RNA load, as well as standard liver function

tests, is required in order to exclude the likelihood of such events.

Overall, although HBV or HCV infection is not considered a barrier to the administration of immunosuppressive therapy in patients with moderate-to-severe psoriasis, it is important to take necessary precautions due to the risk of reactivation in patients with a history and/or those who are inactive carriers of the virus. Therefore, the experts agreed that there must be a multidisciplinary approach involving gastroenterologists/hepatologists for the treatment of hepatitis virus among patients with psoriasis [3 - 5].

3.4.6. Infections

The infection risk in psoriasis patients taking biologics therapy does not seem to be higher during the first year of use; however, the occurrence of serious infections is still plausible [99]. As per product labels, the use of anti-TNF therapy can lead to serious infections, such as histoplasmosis, bacterial sepsis, and infections caused by other opportunistic pathogens [72, 100 - 102]. Serious infections associated with IL-12/23 inhibitor include pneumonia, appendicitis, cellulitis, cholecystitis, diverticulitis, osteomyelitis, sepsis, gastroenteritis, viral and urinary tract infections [73]. Similarly, for patients taking IL-17 inhibitors, there is an increased risk of nasopharyngitis, upper respiratory tract infection, and arthralgia; *Candida* infections occur more frequently with secukinumab and ixekizumab [74 - 76]. Clinical studies for IL-23 inhibitors reported diarrhea, gastroenteritis, arthralgia, upper respiratory infections, tinea infections, and herpes simplex infections as the most common infections [77 - 79]. Overall, the risk of serious infection varies across treatments, although there is a higher risk of serious infections with anti-TNF therapies as compared to IL-23 and IL-17 inhibitors [86, 103, 104]. Based on recommendations from international guidelines, the experts agreed that in order to manage the risk of serious infections in patients on biologics, regular monitoring of early signs and symptoms of infection should be done prior to and during treatment in high-risk patients [105].

Overall consensus statements on the management of psoriasis in special populations are presented in Table **9**.

Table 9. Consensus statements on special populations.

Pregnancy and nursing mothers
• Risks and benefits of continuing *versus* stopping psoriasis treatment with women who are of childbearing potential or who become pregnant should be based on the safety profile of the treatment.
• CSA is a reasonable option for patients requiring systemic therapy during pregnancy.
• MTX is contraindicated in pregnant women due to its teratogenic, abortifacient, and mutagenic effects, and female patients should be screened for pregnancy before initiating MTX therapy.
• Acitretin is contraindicated in pregnant women due to its teratogenic effects, and female patients should completely avoid getting pregnant during the treatment with acitretin and for a further period of three years after discontinuing therapy.
• The safety of biologics is not absolute in pregnant women.
• Certolizumab pegol is suggested for pregnant women with moderate-to-severe psoriasis requiring biologics if the benefits outweigh the risks. • Certolizumab pegol has shown minimal to no placental transfer and is safe for use in nursing mothers.
• The safety of biologicals has been shown during the first and second trimesters of pregnancy [106 - 108].
Geriatric use
• Dose adjustment is required in elderly patients when treated with MTX due to the reduced liver and kidney function, as well as lower folate reserves, which occur with increased age. • Caution should be taken when treating elderly patients with CSA due to the increased risk of developing renal failure; the dosage should be adjusted, and patients regularly monitored for renal function. ▲ No dose adjustment is required for elderly patients when treated with apremilast and acitretin.
• Anti-TNF therapies are considered safe for use in the elderly population, although adalimumab should be prescribed with caution in elderly patients due to the high risk of infections and malignancies. • No dose adjustment is required for elderly patients when treated with IL-12/23, IL-17, or IL-23 inhibitors.
Malignancies
• Patients on CSA should not receive concomitant ultraviolet B irradiation or PUVA photochemotherapy due to the increased risk of malignancies, especially non-melanoma skin cancer.
• Biologics used as monotherapy in patients with moderate-to-severe psoriasis are almost never associated with a high risk of solid tumors or lymphoreticular malignancy.
• Caution should be exercised when considering biologic therapy for patients with a history of solid tumor malignancy, particularly in patients with psoriasis with a current or recent diagnosis of cancer in the previous five years.
• The benefits of biologic therapy, in relation to QoL, often outweigh the negligible risk of solid organ malignancy.
Tuberculosis (TB)
• Biologics should not be used in patients with active TB infection, and patients must be treated with recommended regimens (*e.g.*., rifampicin, isoniazid, pyrazinamide, ethambutol) for 6 months prior to initiating any biologic therapy.
• All patients should be screened for latent TB using a PPD skin test or QuantiFERON-TB Gold prior to initiating biologics. • If active TB is suspected, treatment with biologics should be deferred, and patients should be treated with rifampicin, isoniazid, pyrazinamide, or ethambutol. • If latent TB is diagnosed, patients must receive anti-tuberculous prophylaxis with rifamycin-based treatment regimens or isoniazid. • When anti-tuberculosis therapy is indicated, patients should complete one month of treatment before commencing biologic therapy.

(Table 9) contd.....

Pregnancy and nursing mothers
• The risk of TB reactivation must be taken into account when a patient is treated with anti-TNF therapy. • There is a relatively lower risk of TB reactivation with IL-12/23 IL-17 and IL-23 inhibitors compared to anti-TNF therapies.
Hepatitis virus reactivation
• MTX is relatively contraindicated in patients with active or recurrent HBV due to the increased risk of hepatotoxicity. • Patients should undergo liver function tests prior to initiating therapy with acitretin, as it is associated with elevations in liver function test results or triglyceride levels and with hepatitis.
• Systemic immunosuppressive anti-psoriatic therapies must be ceased in patients with active HBV infection until the infection is controlled with adequate antiviral treatment.
• Due to a compromised immune system as a result of using biologics, it is quite likely that reactivation of HBV can occur; hence caution should be exercised while prescribing biologics to patients identified as carriers of HBV or those previously infected with hepatitis B virus. • Inactive carriers of HBV need to receive antiviral prophylaxis 2–4 weeks before starting immunosuppressive therapy and is discontinued after 6-12 months. • Patients who are carriers of HBV or those previously infected with the virus should be closely monitored periodically for any clinical signs and symptoms of active infection and undergo liver function testing prior to and during treatment with biologics for psoriasis.
• Biologics are considered safe in patients with psoriasis with concomitant HCV infection. • Periodic monitoring of patients through measuring HCV RNA load and standard liver function tests is recommended to prevent reactivation of HCV.
• Consult a gastroenterologist or hepatologist when treating patients with biologic therapy who have newly diagnosed or previously known hepatitis B or C infection.
Infections
• Patients taking anti-TNF therapies are at risk of histoplasmosis, bacterial sepsis, and infections due to other opportunistic pathogens. • There is an increased risk of diverticulitis, cellulitis, pneumonia, appendicitis, cholecystitis, sepsis, osteomyelitis, viral infections, gastroenteritis, and urinary tract infections in patients prescribed IL-12/23 inhibitors. • There is an increased risk of nasopharyngitis, headache, upper respiratory tract infection, *Candida* infections, and arthralgia in patients prescribed IL-17 inhibitors. • IL-23 inhibitors are commonly associated with upper respiratory infections, arthralgia, diarrhea, gastroenteritis, tinea infections, and herpes simplex infections.

CSA: Ciclosporin; FDA: Food and Drug Administration; HBV: Hepatitis B virus; HCV: Hepatitis C virus; TNF: Tumor necrosis factor; PPD: Purified protein derivative.

3.4.7. COVID-19

Coronavirus disease (COVID-19) is a highly contagious respiratory infection that has become a serious public health concern. At present, there are no conclusive data to determine its impact on patients with psoriasis receiving systemic treatment. However, several international guidelines have come up with recommendations on the management of psoriasis during the pandemic. For patients with psoriasis diagnosed with COVID-19, the National Psoriasis Foundation recommends that the decision to start or stop a biologic or oral systemic therapy should be made on a case-by-case basis, in consultation with the health care provider [109]. In addition, the International Psoriasis Council (IPC) recommends that physicians should either discontinue or delay the use of immunosuppressant medications [110]. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis and NICE have also advised patients to temporarily stop their medications if they are COVID-19 positive and to follow the advice of the doctor on temporarily stopping, reducing, or delaying taking medications in specific circumstances [111, 112]. Furthermore, the British Association of Dermatologists guidelines offer a grid for health care professionals that can aid in identifying patients who are at a higher risk of COVID-19 due to their disease and treatment [113].

Recent evidence suggests that older patients (>60 years) and/or patients with certain underlying health conditions, including chronic obstructive pulmonary disease, diabetes, cardiovascular diseases, chronic kidney diseases, and cancer, are more likely to develop severe illness. Therefore, the guidelines also recommend considering the risks and benefits of any immunosuppressive therapy in patients with comorbidities on a case-by-case basis [109, 110, 112].

According to the IPC, and as of September 2020, it is still uncertain whether psoriasis is a risk factor for COVID-19 or whether it may lead to poor outcomes associated with COVID-19. Comorbidities associated with psoriasis have been found to be important risk factors (especially obesity) for adverse COVID-19 outcomes. Moreover, as vaccines are being developed and population vaccination schedules are already planned, it is important to consider the impact of psoriasis treatments—particularly systemic therapy—on the effectiveness and safety of these vaccines [110].

CONCLUSION

The experts' recommendations are based on local practice and their experience, particularly in areas where evidence is lacking. These consensus statements will enable psoriasis experts to provide useful and practical advice on the diagnosis and management of patients with moderate-to-severe psoriasis in the UAE. Further clinical investigations are needed to enhance these expert-based recommendations.

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

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