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REVIEW ARTICLE

THE CURRENT TRENDS OF PSORIASIS TREATMENT IN DERMATOLOGICAL PRACTICE

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Abstract

Psoriasis is associated with many complications. The severity of the disease can range from mild or moderate to severe. Treatment for this condition should be long-term and multifaceted, and may change over time based on the condition severity. Treatment for patients with psoriasis often includes treatment of the underlying pathophysiology. Other treatments for psoriasis include topical medications, phototherapy, and medications (nonspecific/biologic and biologic). Pharmacologic therapy is generally guided by disease severity and impact on patient quality of life, ranging from topical medications to phototherapy and, when necessary, systemic medications. However, challenges remain, including side effects, poor treatment, high costs, and variability in individual responses. Recent biologics have proven effective in psoriasis; on the other hand, there are differences among these drugs such as mechanisms of action, duration of response, and side effects. Biologics are often used to treat moderate to severe psoriasis and can be the treatment of choice, particularly in patients with comorbidities such as psoriatic arthritis or in whom psoriasis treatments such as methotrexate or cyclosporine are contraindicated. Different types of therapy are often used in combination. Combined therapies may improve treatment. Clinical guidelines classify psoriasis as mild or moderate, with mild lesions managed locally and moderate to severe lesions managed systemically.

Keywords: Biologic agents, combination therapies, guidelines for psoriasis, topical corticosteroids.

INTRODUCTION

Psoriasis is a chronic, immune-mediated inflammatory skin disorder characterized by well-demarcated, erythematous plaques covered with silvery scales. It affects approximately 2-3% of the global population and can present at any age, although it commonly appears in early adulthood or middle age. The disease is driven by interplay of genetic predisposition, immune system dysfunction, and environmental triggers¹.

Psoriasis is primarily mediated by T-cells and involves complex immune responses, where cytokines such as tumor necrosis factor-alpha (TNF- α), interleukin-17 (IL-17), and interleukin-23 (IL-23) play a pivotal role. These cytokines promote the rapid proliferation of keratinocytes and the development of inflammatory plaques, which are the hallmark of the disease².

Clinical manifestations: Psoriasis most commonly affects the skin of the elbows, knees, scalp, and lower back, but it can also involve nails, joints (psoriatic

arthritis), and, less commonly, the eyes. The severity of the disease can vary from localized, mild plaques to generalized, severe involvement that significantly impacts the quality of life. The most common type is plaque psoriasis, but other forms include guttate, pustular, inverse, and erythrodermic psoriasis, each presenting distinct clinical features³.

Etiology and risk factors: The exact cause of psoriasis remains unclear, but it is believed to result from a combination of genetic, immunologic, and environmental factors. Genetic predisposition is evident, with several susceptibility genes identified, including those within the human leukocyte antigen (HLA) complex. Environmental triggers such as infections, stress, skin trauma, and certain medications can exacerbate or precipitate the disease⁴.

Impact on health: Psoriasis is not just a skin condition; it is a systemic disease associated with various comorbidities, including cardiovascular disease, metabolic syndrome, depression, and psoriatic arthritis. Patients with psoriasis have an increased risk

of developing these comorbidities, leading to a reduced quality of life and increased overall mortality⁵.

Current treatments: Management of psoriasis focuses on controlling symptoms, reducing inflammation, and improving the patient's quality of life. Treatment options range from topical therapies (e.g., corticosteroids, vitamin D analogs) and phototherapy to systemic treatments, including traditional oral medications (e.g., methotrexate, cyclosporine) and biologics that target specific immune pathways (e.g., TNF inhibitors, IL-17 inhibitors, IL-23 inhibitors)^{6,7}.

Pathology of psoriasis

Psoriasis is a complex, chronic inflammatory skin disorder primarily driven by immune system dysregulation and characterized by hyperproliferation of keratinocytes, abnormal differentiation, and angiogenesis. The pathology of psoriasis involves multiple interrelated factors, including genetic predisposition, environmental triggers, and immune system dysfunction⁸.

KEY PATHOLOGICAL FEATURES

1. Epidermal Changes:

Hyperproliferation of Keratinocytes: One of the hallmark features of psoriasis is the rapid turnover of keratinocytes in the epidermis, leading to thickened skin and the formation of plaques. The normal keratinocyte turnover time is around 28-30 days, whereas in psoriasis, it is reduced to 3-5 days.

Parakeratosis: The stratum corneum (the outermost layer of the epidermis) displays retained nuclei in keratinocytes, indicative of incomplete maturation.

Acanthosis: This refers to the thickening of the epidermal layer due to increased proliferation of keratinocytes. The rete ridges (downward projections of the epidermis) are elongated and irregular.

Munro microabscesses: Collections of neutrophils within the stratum corneum, resulting in visible pustules.

Spongiform pustules of Kogoj: Accumulations of neutrophils in the stratum spinosum, which also contribute to pustule formation¹¹.

2. Dermal changes:

Vascular abnormalities: Increased angiogenesis leads to the formation of dilated, tortuous blood vessels in the dermis, contributing to the erythematous appearance of psoriatic plaques. This is often accompanied by increased expression of vascular endothelial growth factor (VEGF).

Inflammation: The dermis contains an influx of inflammatory cells, including T-cells, dendritic cells, macrophages, and neutrophils. These immune cells release pro-inflammatory cytokines and chemokines that promote keratinocyte proliferation and further immune cell recruitment¹⁴.

3. Immunological factors:

T-cell activation: Psoriasis is driven by both innate and adaptive immune responses, particularly involving T-helper cells (Th1, Th17, and Th22 subsets). Th17 cells produce key cytokines like interleukin-17 (IL-17), IL-22, and IL-23, which are crucial in driving the

inflammatory process and keratinocyte hyperproliferation¹⁰.

Cytokines and mediators: Psoriasis is characterized by an overproduction of pro-inflammatory cytokines, such as TNF- α , IL-17, IL-23, and interferon-gamma (IFN- γ). These cytokines perpetuate the inflammatory cascade by activating various immune cells and keratinocytes, further amplifying the skin inflammation¹³.

4. Genetic factors:

Psoriasis has a strong genetic component, with several susceptibility loci identified, including the PSORS1 locus on chromosome 6, which contains the HLA-Cw6 gene, the most significant genetic risk factor. Mutations in genes involved in skin barrier function (e.g., *LCE3B/C* deletion) and immune response regulation (e.g., *IL-23R*, *IL-12B*) have also been associated with the disease⁹.

5. Environmental triggers:

Environmental factors such as infections (streptococcal pharyngitis), skin trauma (Koebner phenomenon), stress, smoking, alcohol, and certain medications (e.g., beta-blockers, lithium) can trigger or exacerbate psoriasis in genetically susceptible individuals¹⁴.

Clinical presentation: signs and symptoms of psoriasis

Psoriasis is a chronic inflammatory skin condition with a variety of clinical manifestations. The most common type is plaque psoriasis, but other forms include guttate, pustular, inverse, and erythrodermic psoriasis, each presenting with unique features. Below are the signs and symptoms of psoriasis, categorized by the different types¹⁵:

COMMON SIGNS AND SYMPTOMS

1. Plaque psoriasis (*Psoriasis vulgaris*)

Appearance: The most common form, characterized by well-demarcated, raised, erythematous (red) plaques covered with silvery-white scales.

Location: Typically appears on the scalp, elbows, knees, lower back, and extensor surfaces (areas where the skin stretches or extends).

Symptoms:

Itching: Frequently occurs and can range from mild to severe.

Pain or Burning Sensation: Especially in more extensive plaques or areas subject to friction or trauma.

Bleeding: Small bleeding points (Auspitz sign) may appear when the scales are removed.

Dry, cracked skin: Skin may become dry and cracked, which can lead to discomfort and bleeding¹⁶.

2. Guttate psoriasis appearance: Small, drop-shaped, salmon-pink papules (raised lesions) with fine scales.

Location: Often appears suddenly, primarily on the trunk, arms, legs, and scalp.

Symptoms:

- Frequently triggered by a streptococcal infection (e.g., strep throat).

- May cause itching or soreness, but is usually less symptomatic than plaque psoriasis¹⁷.

3. Pustular psoriasis

Appearance: Characterized by white pustules (blisters filled with non-infectious pus) surrounded by red, inflamed skin.

Types:

Localized pustular psoriasis: Limited to certain areas, such as the palms (palmar pustulosis) and soles (plantar pustulosis).

Generalized pustular psoriasis: A rare, severe form that can affect large areas of the body and may be accompanied by fever, chills, and malaise.

Symptoms:

Severe itching or burning sensation. Generalized pustular psoriasis may cause systemic symptoms, including fever and fatigue¹⁸.

4. Inverse psoriasis (Flexural Psoriasis)

Appearance: Smooth, red patches without the typical scaling, often found in skin folds.

Location: Commonly affects areas such as the armpits, groin, under the breasts, and around the genitals and buttocks.

Symptoms:

Skin is more susceptible to irritation, rubbing, and sweating. Lesions can be tender and painful due to moisture and friction in these areas¹⁹.

5. Erythrodermic psoriasis

Appearance: A rare but severe form of psoriasis characterized by widespread redness, scaling, and peeling of the skin over large areas of the body.

Location: Can affect almost the entire body surface.

Symptoms:

Intense itching, burning, and discomfort. Can lead to complications such as dehydration, infection, and electrolyte imbalances. Often associated with systemic symptoms like fever and chills, requiring urgent medical attention^{20,21}.

6. Nail psoriasis

Appearance: Affects the nails, causing pitting (small dents in the nail surface), onycholysis (separation of the nail from the nail bed), subungual hyperkeratosis (thickening under the nail), and discoloration.

Location: Nails of fingers and toes.

Symptoms:

Nails may become brittle, cracked, or crumbly. Can be painful, especially if onycholysis occurs²².

7. Psoriatic arthritis

Appearance: Occurs in about 20-30% of people with psoriasis and involves joint inflammation.

Location: Commonly affects the joints of the hands, feet, knees, ankles, and spine.

Symptoms:

Joint pain, swelling, and stiffness, particularly in the morning or after periods of inactivity.

Dactylitis ("sausage digits"): Swelling of an entire finger or toe.

Enthesitis: Inflammation at the site where tendons or ligaments insert into the bone¹⁶.

General symptoms associated with psoriasis

- **Fatigue:** Especially in cases with extensive skin involvement or psoriatic arthritis.
- **Psychological impact:** Due to visible skin lesions, psoriasis can significantly affect the

quality of life, leading to depression, anxiety, and social isolation.

- **Koebner phenomenon:** Lesions develop at the site of skin trauma (e.g., cuts, scrapes, or sunburn).

Diagnosis of psoriasis

The diagnosis of psoriasis is primarily clinical, based on the appearance and distribution of skin lesions. However, additional diagnostic tools, including biopsy and laboratory tests, may be used in specific cases to confirm the diagnosis or rule out other conditions²³.

KEY STEPS IN THE DIAGNOSIS OF PSORIASIS

1. Clinical examination:

Visual inspection: The diagnosis of psoriasis is often made by observing the characteristic lesions on the skin. Typical psoriatic plaques are well-demarcated, erythematous (red) patches covered with silvery-white scales²⁴.

Distribution of lesions: Lesions are commonly found on extensor surfaces such as the elbows, knees, and scalp, but they can appear anywhere on the body. Special sites like the scalp, nails, and intertriginous areas (skin folds) should be examined carefully.

Types of psoriasis: Identify the specific type of psoriasis based on clinical presentation:

- **Plaque psoriasis:** The most common form, presenting with thick, red plaques covered with silver-white scales.
- **Guttate psoriasis:** Small, drop-like lesions often triggered by infections such as streptococcal throat infection.
- **Pustular psoriasis:** Characterized by white pustules surrounded by red skin, which may be localized or generalized.
- **Inverse psoriasis:** Smooth, red lesions found in skin folds without the characteristic scaling.
- **Erythrodermic psoriasis:** Involves widespread redness and scaling over a large body area, often requiring urgent medical attention²⁵.
- **Nail changes:** Examine for nail psoriasis, which may present with pitting, onycholysis (separation of the nail from the nail bed), subungual hyperkeratosis, and discoloration.
- **Joint involvement:** Check for signs of psoriatic arthritis, such as joint pain, swelling, stiffness, dactylitis (sausage-like swelling of fingers or toes), and enthesitis (inflammation at tendon or ligament insertions)²⁶.

2. Patient history:

Personal and family history: Obtain a thorough medical history, including any personal or family history of psoriasis or other autoimmune conditions.

Trigger factors: Assess for factors that may trigger or exacerbate psoriasis, such as recent infections (e.g., strep throat), stress, skin trauma (Koebner phenomenon), smoking, alcohol consumption, and medications (e.g., beta-blockers, lithium, antimalarials).

Symptoms assessment: Evaluate symptoms such as itching, pain, joint discomfort, and psychological impact²⁷.

3. Skin biopsy:

Indication for biopsy: A skin biopsy may be performed in atypical cases where the clinical diagnosis is uncertain. It is particularly useful for differentiating psoriasis from other skin conditions such as eczema, lichen planus, seborrheic dermatitis, and cutaneous T-cell lymphoma.

Histopathological findings: Common histological features of psoriasis include:

- Acanthosis (thickening of the epidermis).
- Parakeratosis (retention of nuclei in the stratum corneum).
- Munro microabscesses (collections of neutrophils in the stratum corneum).
- Dilated blood vessels in the dermal papillae.
- Reduced or absent granular cell layer²⁹.

4. Laboratory tests:

- **Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP):** These markers may be elevated in severe psoriasis or psoriatic arthritis, indicating systemic inflammation.
- **Anti-Streptolysin O (ASO) Titer:** May be checked in cases of guttate psoriasis to identify a recent streptococcal infection.
- **Rheumatoid Factor (RF) and Anti-Cyclic Citrullinated Peptide (anti-CCP) Antibodies:** To differentiate psoriatic arthritis from rheumatoid arthritis.
- **Uric Acid Levels:** May be elevated in psoriasis due to increased turnover of skin cells²⁸.

5. Imaging Studies:

- **X-rays and MRI:** Used to assess joint involvement in suspected psoriatic arthritis, particularly if joint symptoms are present. Typical findings may include joint erosions, new bone formation, and enthesitis.
- **Ultrasound:** Can be useful for detecting early signs of enthesitis and synovitis in psoriatic arthritis³⁰.

6. Differential diagnosis:

- **Conditions to rule out:** Differentiate psoriasis from other dermatological conditions that can present with similar symptoms, such as eczema, seborrheic dermatitis, lichen planus, pityriasis rosea, and fungal infections.
- **Psoriasis mimickers:** Consider skin conditions like cutaneous T-cell lymphoma or systemic lupus erythematosus (SLE) if the presentation is atypical²³.

Target goals in the management of psoriasis

The target goals in the management of psoriasis are designed to achieve optimal patient outcomes, including symptom relief, improved quality of life, and minimization of disease impact. These goals are based on clinical, patient-reported outcomes, and tailored to individual needs³¹.

1. Clinical goals:

Clearance or Significant Reduction of Skin Lesions:

- **Aim for complete or near-complete clearance:** The primary clinical target is to achieve complete or near-complete clearance of psoriatic skin lesions, typically defined as a Psoriasis Area and

Severity Index (PASI) score of 1 or less or a Body Surface Area (BSA) involvement of 1% or less.

- **PASI 75/90/100 response:** Achieving a 75%, 90%, or 100% reduction in PASI score from baseline is commonly used to define success in clinical trials and practice. PASI 90 or 100 is increasingly viewed as the preferred target, indicating almost complete to complete clearance of psoriasis.
- **Improvement in Static Physician's Global Assessment (sPGA):** sPGA scores aim for 0 (clear) or 1 (almost clear).

Long-term disease control and remission:

- **Sustained response:** Maintain the achieved clinical response over time, aiming for prolonged periods without flares or exacerbations.
- **Minimize relapse and flare-ups:** Target to reduce the frequency and severity of psoriasis flare-ups, ideally achieving long-term remission³².

2. Patient-centered goals:

Improved Quality of Life:

- **Patient satisfaction and well-being:** Minimize the physical discomfort (itching, pain, scaling) and psychological impact (anxiety, depression, social stigma) of psoriasis.
- **Dermatology Life Quality Index (DLQI):** Achieve a DLQI score of 0 or 1, indicating no impact of psoriasis on the patient's quality of life.
- **Patient-Reported Outcome Measures (PROMs):** Regularly assess PROMs to understand the patient's experience of symptoms, treatment satisfaction, and functional outcomes.

Reduced impact on daily activities:

- **Functional improvement:** Enable the patient to perform daily activities without restriction caused by the disease.
- **Minimized impact on employment and social life:** Support patients to maintain their social and professional lives without psoriasis-related hindrances³³.

3. Safety and tolerability goals:

Minimization of adverse effects:

- **Monitor for side effects:** Ensure that treatment regimens are safe and well-tolerated, with regular monitoring for potential side effects, especially for systemic therapies and biologics.
- **Adjust treatment as needed:** Modify or switch treatments to balance efficacy with safety concerns, particularly in patients with comorbid conditions or risk factors³⁴.

4. Management of comorbidities:

- **Address psoriatic arthritis and other comorbidities:**
 - **Early detection and treatment of psoriatic arthritis:** Screen for joint involvement and treat psoriatic arthritis to prevent joint damage and maintain mobility.
 - **Manage cardiovascular and metabolic comorbidities:** Actively manage cardiovascular risks (hypertension, hyperlipidemia), metabolic

syndrome, diabetes, and obesity, which are more prevalent in psoriasis patients.

Holistic approach to comorbid conditions:

- **Integrated care:** Collaborate with other healthcare professionals to provide comprehensive care for all aspects of the patient's health³⁵.

5. Optimized treatment strategy:

Personalized Treatment Approach:

- **Tailored therapy based on disease severity and patient preferences:** Select and adjust therapies (topical treatments, phototherapy, systemic agents, biologics) according to disease severity, patient preferences, and response to treatment.
- **Treatment adherence:** Promote adherence to therapy by minimizing side effects, simplifying regimens, and providing patient education.

Cost-effective management:

- **Economic Considerations:** Ensure that the treatment plan is cost-effective, considering both the direct costs (medications, consultations) and indirect costs (impact on work, need for long-term care)³⁶.

6. Preventing progression and damage:

- **Prevent disease progression:**
 - **Early intervention:** Implement early and aggressive treatment to prevent disease progression, particularly in cases of moderate to severe psoriasis.
 - **Protect against long-term complications:** Aim to reduce the risk of complications like joint damage, cardiovascular diseases, and mental health issues^{37,38}.

The current strategies of psoriasis treatment

Management of psoriasis is based on controlling psoriasis related complications. Treatment selection should always be patient-specific, taking into account the severity of the disease, the patient's response, and their tolerance to various regimens. Other medical conditions, if present, should also be considered and treated as soon as possible. Other treatments for psoriasis include topical medications, phototherapy, and systemic therapies such as biologics drugs. Topical treatments are the first line of care for localized disease or mild to moderate pain. Phototherapy and photochemotherapy for moderate to severe cases³⁹. Treatment with or without topical medications is the usual standard of care for patients with moderate to severe or severe disease. Newer therapies (e.g., biologics) may be the preferred treatment modality, particularly in patients with concurrent diseases such as psoriatic arthritis (PsA) or if treatment as methotrexate or cyclosporine is required⁴⁰. The European consensus classifies psoriasis to mild psoriasis or moderate to severe psoriasis, as mild disease requiring topical treatment and moderate to severe disease requiring treatment⁴¹.

Topical treatment

Most patients with psoriasis have mild-to-moderate symptoms should be managed with topical treatment alone⁴². Traditional topical treatment consists of corticosteroids, retinoids, vitamin D₃ analogs, anthralin, and coal tar. Moreover, topical calcineurin

inhibitors can be used in difficult clinical settings including the face or intertriginous locations. Topical biologic drugs are being marketed. These drugs are used as combination treatment for patients with more severe disease, who are on phototherapy or systemic therapies. In USA, the recent (2021) treatment guidelines indicated TCS as the mainstay of treatment for limited psoriasis as monotherapy or add-on with nonsteroidal topical drugs⁴³.

Corticosteroids

For more than half a century, topical corticosteroids (TCS) have been the first-line treatment for most people with psoriasis. Most of these agents are well tolerated. A comparison of effective classification methods was recently published. More potent TCS works quickly but has the biggest risk of side effects. Their indication should be determined in size of body area and course duration (2–4 weeks)⁴⁴. The lowest strength TCS can be indicated on the face and skin folds. Combination of TCS with other agents may lead to steroid sparing, which may result in a positive effect. The rational therapy of TCS should consist of an assessment of the severity and location of disease, an understanding of patient preferences, and age. The highest strength TCS is usually restricted for patients with extensive plaques or refractory disease⁴². The continued TCS use carries a risk of cutaneous infection and systemic adverse effects⁴¹. It has been reported that not only super-strong corticosteroids but moreover long-term use or use of stronger medications can cause side effects⁴².

Vitamin D₃ analogs

Vitamin D analogues are defined as safe and effective agents in treating psoriasis in adults and young patients⁴⁵. Calcitriol can be used topically as an initial drug or in combination in patients with mild plaques. Calcipotriol has been shown to be as effective as all but the most effective TCS⁴¹. Add-on therapy with TCS is especially effective⁴⁶. They are recognised as the safest for maintenance treatment⁴⁷. The most common side effects on the skin include a mild inflammation called dermatitis and symptoms such as burning, itching, edema, peeling, dryness, and erythema. Side effects such as hypercalcemia and parathyroid hormone suppression are rare unless patients use higher than recommended doses or have kidney disease or calcium metabolism deficiencies⁴². Calcipotriol is neutralized by acids and therefore should not be used with salicylic acid to treat psoriasis. The combination of betamethasone dipropionate and calcipotriol ointment or foam may be more effective than either drug alone⁴⁵.

Retinoids

The retinoid used on the skin to treat psoriasis is tazarotene. Therapeutic effects were maintained for 12 weeks after discontinuation of treatment⁴⁸. A combination is available (halobetasol propionate and tazarotene lotion) and was approved by the FDA in April 2019. Tazarotene side effects are concentration-dependent effect such as irritations at the site of application site⁴¹. Tazarotene has photosensitizing adverse effect because prolonged use may cause skin irritation. Tazarotene is avoided during pregnancy and

should not be used by women of childbearing potential unless they are taking birth control pills⁴².

Coal tar

Coal tar was from the first drugs of psoriasis treatment. Due to strength limitations and problems with patient acceptance and compliance, coal tar preparations are less commonly prescribed recently, particularly in North America and European countries⁴⁹.

Coal tar has similar effects to calcipotriol, but its onset is slower. Coal tar has odor and clothes staining properties. Coal tar side effects are folliculitis, local irritation, acne, and phototoxicity⁴¹. It has carcinogenic effect in animals, but there are no reliable data on carcinogenicity in humans from topical application⁴². The FDA considers coal tar concentrations (0.5–5%) to be safe for use in the treatment of psoriasis⁵⁰. However, occupational exposure to coal tar, particularly at pressures such as those used in the paving industry, has been reported to increase the risk of pneumonia, scrotal and skin conditions⁴².

Salicylic acid

Salicylic acid increases steroid penetration when combined with TCS, thus improving performance. It should not be used with ultraviolet B (UVB) phototherapy, as the filtering effect reduces UVB efficacy. It should not be used with calcipotriol, as it deactivates calcipotriol on contact. Absorption and toxicity may report, particularly when used for >20% BSA⁵⁷ or in patients with renal insufficiency. Do not use salicylic acid in young individuals, but it can be indicated during pregnancy for plaque psoriasis⁴².

Calcineurin inhibitors

They have not approval by FDA to treat psoriasis. Pimecrolimus has been shown to be effective in plaque psoriasis⁵¹ and also in patients with moderate to severe relapsing psoriasis⁵². This cream would be of great benefit to patients with cuts or wounds on the face because the irritating adverse effect is less in related to the use of calcipotriene and also avoids the steroids side effects including skin atrophy⁴⁵.

Skin atrophy is an adverse effect of topical corticosteroids (TCs)

Janus Kinase (JAK) inhibitors

Tofacitinib (topical and oral) and ruxolitinib (topical) are nonbiologic JAK inhibitors. Tofacitinib is currently used off-label for plaque psoriasis (topical and oral) but is indicated for psoriatic arthritis (oral use), rheumatoid arthritis, ankylosing spondylitis, and ulcerative colitis. If used systemically, the dosage must be adjusted for moderate-to-severe renal impairment and moderate hepatic impairment, Tofacitinib is not indicated in severe hepatic diseases⁵³.

Phototherapies and photochemotherapy

Phototherapy has been indicated to psoriasis treatment for many decades and continues to be an important treatment option today. Some skin conditions can be improved by exposure to sunlight. Phototherapy combined with photochemotherapy (PUVA), involves the local or topical application of psoralen, followed by increasing doses of ultraviolet light after an appropriate period of time⁴².

Side effects related to the phototherapy treatment such as erythema, pruritus, hyperpigmentation, xerosis, and

blistering, particularly at higher doses. It should be prescribed with caution in patients with photosensitivity problems, and drug interactions as photosensitizing drugs including tetracyclines. Individuals with psoriasis should wear 24-hour eye protection during PUVA treatment⁵⁴. The UVA dose may be decreased by one-third for patients receiving oral retinoids plus PUVA combination⁴². The phototherapy or photochemotherapy use is avoided in people with previous skin cancers such as melanoma or multiple nonmelanoma⁵⁴. Focused phototherapy by delivery of ultraviolet radiation directly focused on psoriasis lesions that do not affect normal skin is an option being investigated with early support despite blistering and heat burns in a more medically safe location in the long term⁴².

Systemic treatment

Systemic treatment is the first choice for patients' therapy with moderate-to-severe psoriasis. However, under add-on therapies, Local use of calcipotriol and betamethasone dipropionate ointment can improve disease symptoms for certain psoriasis patients. the systemic treatment includes: acitretin, methotrexate, cyclosporine, mycophenolate mofetil (MMF), and hydroxyurea; and the biologic agents⁴¹.

Acitretin

Acitretin was indicated as the initial oral retinoid or tretinoin derivative available for the psoriasis therapy in the 1980s. Since its active metabolite has replaced by acitretin. When used as monotherapy, retinoids may be no better than methotrexate or cyclosporine, but in patients with severe psoriasis, the initial response may be quicker than methotrexate. Acitretin is often used in combination with topical calcipotriol or phototherapy⁴¹. The most common side effects of acitretin include hypertriglyceridemia and skin and mucosal side effects such as dry eyes, nasal and oral mucosa, chapped lips, cheilitis, epistaxis, dryness, brittle nails, and hot or clammy skin⁵⁵. Eye adverse effects such as photosensitivity, discoloration vision, and defect night vision. Gastrointestinal changes such as hepatitis and jaundice are rare, and elevations in liver enzymes are usually transient⁵⁶. Peritubal pyogenic granulomas occasionally occur after chronic acitretin use⁵⁵.

Excess intake of retinoids by pregnancy has teratogenic effects and is strictly avoided such as topical preparation of retinoids. Blood donation (male and female) is not allowed during treatment and one year after these drugs use. Female individuals should abstain from ethanol consumption during therapy and for minimum 2 months after discontinuing treatment because it causes acitretin to convert to acitretin ester, which has a longer elimination half-life⁵⁶.

Cyclosporine

Cyclosporine was FDA approval in 1997 for the psoriasis therapy and rheumatoid arthritis⁵⁷. Cyclosporine is effective in remission and maintenance treatment in individuals with moderate to severe state of plaque psoriasis. It can also be used to treat impetigo, erythroderma, and nail psoriasis. The 2009 Canadian guidelines recommend that most patients with psoriasis use cyclosporine continuously for up to

12 weeks for treatment failure, flare management, and as a bridge to other therapies such as biologics⁴¹.

In patients stopping cyclosporine, reducing the weekly dose by 1 mg/kg/day can increase the time to relapse in relation to abrupt withdrawal⁵⁷. In some cases, abrupt stopping of the drug has resulted in significant improvement in psoriasis. Side effects of cyclosporine include nephrotoxicity, hypertriglyceridemia, and hypertension. The nephrotoxicity and hypertension are especially important in individuals with preexisting diastolic blood pressure or high triglycerides. Baseline blood creatinine, complete blood count, blood pressure, blood urea nitrogen, triglycerides, uric acid, magnesium, and potassium needed to evaluate before starting treatment, per 2 weeks during the first three months of treatment, and every month subsequently⁴¹.

If the patient's serum creatinine level rises 25% of the individual's baseline value every 2 weeks, the cyclosporine dose should be reduced by 25% to 50% and the serum creatinine level should be retested weekly. Patients should have dental checkups at least annually because of the risk of gum disease. Cyclosporine, a cytochrome P450 isoenzyme 3A4 (CYP3A4) substrate, has significant drug interactions. Blood pressure monitoring is generally not necessary in patients with psoriasis because the doses used are lower than in those receiving transplants, although monitoring may be recommended in patients receiving drug interactions⁵⁷.

Methotrexate

Methotrexate has been the cornerstone of treatment for individuals with severe psoriasis for many years. It is highly effective than acitretin and as well as or slightly effective than cyclosporine⁴¹.

Methotrexate is usually reported a safer alternative to cyclosporine unless there are patient history of contraindications such as hepatic toxicity. In some previous studies, many patients stopped the cyclosporine treatment because of side effects. Although biologics are not believed to be more effective, they are more expensive, and some insurance companies require poor response or resistance to methotrexate (the gold standard) before their use is approved⁵⁸. The starting methotrexate dose is 7.5 to 15 mg once per week may be elevate to 20 to 25 mg once per week if the response is sub-optimal at 8 to 12 weeks, with appropriate safety monitoring. Low-dose methotrexate (7.5 to 10 mg once weekly in combination with a biologic agent is also recommended⁵⁶.

Methotrexate has been used for decades with good results⁴¹. Folic acid deficiency is thought to be a risk factor for liver toxicity with methotrexate administration⁵⁸. The pancytopenia can report during weekly maintenance dose as well as after a single dose of methotrexate⁵⁵. Educating individuals regarding the early pancytopenia symptoms may be helpful in the early stages⁵⁶.

Methotrexate is a teratogenic abortifacient and is absolutely contraindicated during pregnancy. After stopping methotrexate therapy, it is advised that men continue effective contraception for 3 months (since the spermatogenesis cycle lasts 74 days) and women

use effective birth control for at least 1 ovulatory cycle. Agents that decrease the renal clearance of methotrexate (e.g. salicylates or acidic agents such as vitamin C) may also elevate blood levels of methotrexate and lead to toxicity. The risk of hepatotoxicity may also be increased with methotrexate use⁴¹.

Janus Kinase (JAK) inhibitors:

JAK inhibitors are a recent class of drugs used to treat moderate to severe psoriasis and psoriatic arthritis (PsA). The recommended dose of tofacitinib is 5 mg twice daily (or 11 mg tofacitinib XR once daily)⁵⁹. Drugs such as CYP3A4 inhibitors (e.g., ketoconazole), CYP3A4 and CYP2C19 inhibitors (e.g., fluconazole) may increase tofacitinib levels, while CYP3A4 inhibitors such as rifampin may decrease tofacitinib levels⁴⁵.

Oral phosphodiesterase inhibitors:

It is effective for psoriasis, particularly for palmar-plantar or scalp psoriasis, and also for PsA. The safety profile of apremilast is good with gastrointestinal symptoms being most common. Depression occurs in about 1% of patients, and it is recommended that patients receive appropriate discussion and counseling before apremilast is initiated to prevent worsening of depression or suicidality⁵⁵.

Systemic therapy with biologic agents

Biologic drugs are indicated as the first of choice therapies in conjunction with systemic drugs for moderate-to-severe disease. British Association of Dermatologists (BAD) recommends using biologics instead of methotrexate and cyclosporine failure/intolerance/contraindications where psoriasis has another physical, psychological or work-related impact and (a) psoriasis is widespread or (b) psoriasis is severe and associated with poor function and/or high stress (e.g. cell disease) or affecting hard and difficult-to-patch areas such as the face, scalp, palms, feet, folds and genitals). BAD released some switching approaches in their 2017 guidelines: in stable condition, the target is 1 month between the last dose of the recent immunosuppressive regimen (excluding MTX) and the planned start date of the biologic. In patients receiving MTX or other drugs for which a washout period may result in unstable disease, begin biologic therapy without a washout period. When it is no longer possible to stop preventive measures such as systemic immunosuppressant agent (e.g. if the disease flare is severe or dangerous), use appropriate therapy and discontinue treatment as soon as possible (e.g. when the response is minimal)⁶⁰. If there are comorbidities, biologics may be indicated as the first of choice treatment. Infliximab or adalimumab may be rational treatments for patients with plaque psoriasis and psoriatic arthritis. Biologics are now available to treat psoriasis and/or PsA⁶¹.

Anti-Tumor Necrosis Factor- α agents (Anti-TNF- α agents):

One safety concern with TNF-alpha inhibitors is the increased risk for infection⁶². A second safety consideration is the peripheral and central demyelinating diseases development or exacerbation as well as autoimmune diseases such as multiple sclerosis

and a lupus-like syndrome. A third safety concern is the probability to cause cancers⁶³. A fourth safety concern is the possibility of vasculitis, granulomatous reactions, skin infections, psoriasis-like swellings, and other adverse skin reactions to infusions or injections⁶⁴. A fifth safety concern is the hematologic toxicity risk⁶². The sixth safety concern regarding congestive heart failure (CHF). Anti-TNF- α agents are avoided in patients with HF stage C & D⁵⁶ and should be discontinued in patients with mild CHF due to the development of new respiratory symptoms of CHF⁶⁵. Despite the above mentioned are safety concerns for adalimumab, certolizumab, etanercept, and infliximab, their safety issues are inconsistent. For instance, the risk of tuberculosis (TB) is with minimum for etanercept and with maximum for infliximab⁴¹. However, these agents are avoided in individuals with tuberculosis⁵⁶.

Adalimumab is FDA approval on January 22, 2008. It is recently indicated for more indications. The recommended dosing for psoriasis is 80 mg given subcutaneously at starting, then 40 mg subcutaneous injection administered the next week and at 2-week intervals subsequently⁶⁶.

Etanercept has FDA approval in America for use in PsA in June 2002 and indicated in 2004 for use in patients with moderate-to-severe psoriasis. Etanercept is recently indicated for management of moderate-to-severe adult and young individuals with plaque psoriasis, PsA, rheumatoid arthritis, juvenile rheumatoid arthritis, and ankylosing spondylitis. The recommended etanercept dose in psoriasis patients is 50 mg administered subcutaneously bid per week for the first 3 months then 50 mg once per week subsequently⁶⁶.

Infliximab was approved by FDA on September 27, 2006. This agent also has been approval for rheumatologic arthritis before psoriasis. It is more effective than etanercept⁶⁸. Methotrexate may decrease the infliximab immunogenicity, thereby reducing the risk of developing antibodies to infliximab and causing loss of response to treatment. Therefore, the joint AAD-NPF guidelines recommend that infliximab should be added to methotrexate and indicated this combination for all patients needed infliximab³¹. Moreover, developing antibodies and infusion reactions, adverse events such as fatal cases of hepatosplenic T-cell lymphoma, have occurred rarely with infliximab⁶⁵.

Certolizumab was FDA approved on May 27, 2018 for the management of plaque psoriasis, psoriasis arthritis, ankylosing spondylitis, Crohn's disease, and rheumatoid arthritis. The recommended dosing for psoriasis of moderate-to-severe status is 400 mg per another week. Another recommended dosing option may be indicated for patients of 90 kg or less: 400 mg at starting and at week 2 and week 4, then a dose of 200 mg per other week.

Certolizumab may have similar properties to other anti-TNF- α agents, such as combination therapy, efficacy in refractory areas, and potential resistance. However, no evidence on this topic is available and these statements are based on data from other anti-TNF- α agents⁴².

IL-12/23, IL-17 and IL-23 inhibitors for moderate to severe plaque psoriasis: *Ustekinumab* (IL-12/23 inhibitors) was FDA approved on September 25, 2009 for the treatment of plaque psoriasis and/or active PsA with moderate-to-severe status as alone or with methotrexate in patients 18 years or older⁶⁹. This agent has a more drug survival rate than anti-TNF- α agents in longer duration of efficacy with continued treatment³¹. Ustekinumab has reported sustained efficacy and safety for about 5 years⁴¹. Moreover, it is effective in treating difficult-to-treat locations including hand and foot, nail, and scalp psoriasis³¹. According to the manufacturer labeling, ustekinumab showed higher ACR20 responses in active psoriatic arthritis at week 24 in elderly patients compared to placebo. Serum ustekinumab levels are affected by body weight⁷⁰. The manufacturer's recommended dose is 45 mg for patients of 100 kg or less and 90 mg for patients weighing more. The use of this drug is similar in PsA, alone or in combination with methotrexate. If the patient has an inadequate response, the dose may be elevated from 45 mg every 12 weeks to 90 mg per 8 weeks to improve outcomes⁴¹.

Serious side effects of ustekinumab similar to those seen with other biologics such as serious infections, fungal infections, infections, and cancer⁷¹. Reversible leukoencephalopathy syndrome has also been demonstrated⁶⁴. Recommended monitoring tests include complete blood count, liver enzymes, serum creatinine, and renal function (before treatment and every 3–6 months after treatment). Pretreatment CRP testing and testing for hepatitis B and C and human immunodeficiency virus are also recommended. Contraindications for ustekinumab include treated and untreated latent tuberculosis and hypersensitivity to the ustekinumab or its excipients⁵⁶.

IL-17 inhibitors (secukinumab, ixekizumab, brodalumab, and bimekizumab) are useful in blocking IL-17, the essential cytokine in the psoriasis pathogenesis. These drugs have similar effects and some similar side effects, such as increased risk of infection, particularly mucocutaneous candidiasis. Patients with a history of inflammatory bowel disease (IBD) or active inflammatory bowel disease (IBD) who may have flare-ups or reactivations should avoid IL-17 inhibitors in this patient. Anti-IL-17 inhibitors antibodies have been reported and their presence may be related to lower serum levels and reduced efficacy of biologics³¹. Secukinumab was approved in USA and Canada in 2015 for the management of moderate to severe plaque psoriasis in adult individuals who are indicated for systemic therapy or phototherapy. The initial dose of secukinumab is 300 mg by self-administered subcutaneous injection at weeks 0, 1, 2, 3, and 4 then by 300 mg per 4 weeks. Drug toxicities from previous studies generally included headache, nasopharyngitis, URTIs, diarrhea, and rarely included neutropenia and detection of neutralizing antibodies for secukinumab⁷². Ixekizumab was approved by the FDA on March 22, 2016, for the treatment of psoriasis of moderate-to-severe. It is also effective against palmoplantar (nonpustular), nail, scalp, erythrodermic, reversible, and pustular psoriasis³¹. The starting dose is

160 mg administered subcutaneously, then 80 mg at weeks 2, 4, 6, 8, 10, and 12. However, some patients may require doses of 80 mg every 2 weeks to maintain response⁷³. Neutralizing anti-ixekizumab antibodies emerge over time and are associated with under dosage and lack of efficacy³¹. Brodalumab was FDA approved on February 15, 2017 as a recommended dosing 210 mg subcutaneous injection by self-administered subcutaneous at weeks 0, 1, and 2, then by 210 mg per 2 weeks⁷⁴. Black box warning and contraindicated in patients with suicidal attempt, new suicidal behavior, or history of suicidal attempt are reported. Additionally, brodalumab is only found through the Review of Risk and Effectiveness (REMS) program³¹. Bimekizumab was approved for plaque psoriasis of moderate-to-severe by Health Canada in February 2022 but had failed FDA preapproval inspection at the time of this writing. Bimekizumab has also received approval for use in psoriasis from other countries such as Japan. Bimekizumab dosing is weight dependent, since adult individuals of 120 kg or more are estimated to have at least 30% lower drug plasma concentrations than those weighing 90 kg. Bimekizumab is administered as 160 mg subcutaneous injections (320 mg dose) twice per 4 weeks for 16 weeks, followed by differential dosing based on weight: every 8 weeks thereafter except in patients of 120 kg or more, for whom 320 mg per 4 weeks may be considered after week 16 if complete skin response has not been achieved. Significant adverse reactions to bimekizumab include infections and antibody development (45%; neutralizing 16%). Recently, the two-year safety profile for bimekizumab based on large data suggests that bimekizumab is well tolerated⁷⁵. In patients on IL-23 Inhibitors (Guselkumab, Tildrakizumab, or Risankizumab,) who do not respond adequately may need to increase their dose or switch to another medication. Such as TCS, vitamin D analogs, methotrexate, or UVB may be added. The recommended guselkumab dose for active PsA and plaque psoriasis is 100 mg subcutaneously at weeks 0 and 4, and per 8 weeks subsequently. The drug has also been shown to be effective against scalp, nail, and plaque palmoplantar psoriasis. The recommended dose of Tildrakizumab is 100 mg by subcutaneous injection administered by a physician only at Weeks 0 and 4 and then per 12 weeks subsequently³¹. Risankizumab was FDA and Health Canada approved in April 2019 for treatment of moderate-to-severe plaque psoriasis⁷⁶. The recommended dosing for risankizumab is 75 mg for 2 doses (150 mg subcutaneous totally) at weeks 0 and 4, then 150 mg as two injections every 12 weeks thereafter.

Transitioning among biologics

Transitioning between biologics to potentially improve efficacy and safety with tolerability is highly desirable. Biologics that produce neutralizing antibodies may lose efficacy over and the current goal of treating biologics is to continue for more than three years, which is not a very duration for chronic diseases such as psoriasis. Transitioning to another biologic, even within the same class of biologic, may be beneficial. However, not all changes lead to improvement, and there are no

recommendations in the US guidelines for specific changes or suspension and resumption of discontinuation³¹. The BAD provides some general suggestions in its 2020 guidelines: Consider a one-month washout interval between the end of the current biologic dose and the determined date of the next biologic, otherwise the treatment period (whichever is longer) will apply. The BAD also recommends considering the drug properties, the clinical condition of patients, and the patient's perception of the safety and effectiveness issues of the change⁷⁷.

Combination therapies

Combinations may be useful in the treatment of plaque psoriasis: increasing overall efficacy or decreasing toxicity. The combination consists of two topical drugs, a topical drug + phototherapy, a systemic drug + a topical drug, a systemic drug + phototherapy, a biologic agent with either a systemic drug or a topical drug, or two systemic drugs used in rotation. Biologic agents have been investigated and approved in combination with nonbiologic therapies, sometimes only theoretically. Due to reduce the development of neutralizing biologic antibodies, recent biologics agents associated with neutralizing antibodies are often used in combination with an immunosuppressive drug such as MTX³¹.

General issues and safety

Many of these biologic agents carry the risk of infection. The live or live attenuated vaccines use during treatment is generally not recommended. Since biological products are new to the market, the risk of rare but serious side effects or side effects with a long latency period not being noticed or not being noticed has been announced. Moreover, clinical trial experience is limited for some biologics, and adequate post-marketing or long-term data are not available. Likewise, safety information for specialized groups such as children or women planning to become pregnant is generally not available⁷⁸. In 2020, a Canadian panel of experts considered safety and efficacy of biologics and provided indications for three biologics in children with plaque psoriasis of moderate-to-severe⁷⁹. A recent concern with the use of biologics is that their effectiveness does not last more than three years, meaning that their effects wane over time. Recent data also concluded that failure of one biologic drug can affect the outcomes of the next, as seen in psoriasis reports. Based on biologic data in rheumatoid arthritis, other agents appear to be less effective after our biologics have been used; a similar effect may occur in psoriasis⁷⁸.

Other drugs used

PDE4 inhibitors:

A new approach to the treatment of skin diseases such as psoriasis. This agent aims to inhibit phosphodiesterase 4 (PDE4) which has multiple effects such as reducing the efficacy of proinflammatory therapies. Apremilast is used orally as a tablet and has the approval in USA and Canada for individuals with active PsA or moderate to severe psoriasis^{80,81}. The apremilast concentration and effect may be reduced by bosentan, CYP3A4 inducers, dabrafenib, deferiasirox,

ivosidenib, lorlatinib, pitolisant, sarilumab, siltuximab, tocilizumab, and St. John's wort⁸².

Mycophenolate Mofetil:

Mycophenolate mofetil (MMF) is a drug sometimes used in the management of moderate to severe drug-resistant psoriasis⁴¹. One small study investigated eight severe psoriasis patients who were transferred from cyclosporine to MMF after a 2- to 4-week washout period. Seven of these patients developed renal dysfunction and hypertension after receiving cyclosporine, and one patient developed functional impairment. After switching to MMF, 5 of 8 patients experienced a decrease in psoriasis control, but 6 patients also had significant improvement in renal function^{83,84}. In contrast, another small study evaluated cyclosporine after MMF in 8 patients with severe psoriasis. All patients improved significantly with MMF, and all improved further after switching to cyclosporine⁸⁵. MMF has some rare but serious side effects such as an increased incidence of infectious diseases such as cytomegalovirus, cryptococcosis, candidiasis, and pneumocystis jiroveci⁸³.

Hydroxyurea

Hydroxyurea has been used in treatment of psoriasis for over 30 years⁴¹. Although biologic drugs may be the best choice for these individuals, there are occasional attempts to manage severe psoriasis. Once weekly of hydroxyurea may be an alternative to MTX in patients who have had adverse reactions to MTX or who have reached the recommended MTX dose⁸⁶. Side effects of hydroxyurea include marked myelosuppression, focal erythema, local tenderness, and reversible hyperpigmentation⁴¹.

Considerations for special populations

Psoriasis treatment of young patients

One third of patients with psoriasis had onset of symptoms during the pediatric years with the most common onset during adolescence⁸⁷. Plaque lesions in younger patients are generally smaller, thinner, and less scaly than in adults' patients, making diagnosis difficult. The face and flexural area are usually affected more than in adults. In psoriasis, the diaper rash can appear for up to 2 years and PsA is very rare⁴¹.

The 2020 AAD-NPF guidelines of psoriasis care in young patients state that BSA should not be the essential criteria of disease severity, and that the impact on the child's QoL should be taken into consideration. A 2020 Canadian consensus concurs that young patients with psoriasis may experience stigmatization, social isolation, negative impacts on emotional and/or social development, and changes in school performance⁷⁹.

Psoriasis in young patients is related to increase risk factors of cardiovascular and metabolic diseases. Risk factors of cardiovascular diseases include obesity, hyperlipidemia, hypertension, hyperglycemia, and diabetes. The first choice of treatment for psoriasis in young patients is topical treatment⁴¹. Vitamin D3 analogues such as calcipotriene, calcipotriol, and calcitriol have a corticosteroid-sparing function; this is an important advantage for pediatric patients. Calcipotriol in combination with TCS or as a monotherapy has been recommended as the preferred

treatment because of its low risk⁸⁸. If TCS is necessary, the lowest intensity TCS required to control should be provided and should be as tight as possible to provide better pain relief⁴¹. The calcipotriol and betamethasone dipropionate in a combined preparation are safe and have FDA approval for use in children 12 years and older. To minimize corticosteroid use, combination therapy can be transitioned to topical vitamin D monotherapy when the condition improves. For psoriasis of the face, genitalia, and genitals, calcineurin inhibitors are the preferred initial treatments. Alternative therapy with topical vitamin D analogs, topical calcineurin inhibitors, emollients, coal tar therapy, and topical corticosteroids should be considered as a steroid-sparing regimen for young patients⁸⁷. Generally, the systemic therapies are indicated in young patients to manage or cure the disease, provide maintenance disease stability for a few months, then tapering to a minimum and finally stopping treatment if possible. MTX can clear the disease and has been indicated as a treatment of choice by the Canadian guidelines and recommended as a rational systemic treatment in the AAD-NPF guidelines. Folate supplementation and a rational monitoring for hepatotoxicity is required⁴¹. Other nonbiologic systemic agents (cyclosporine and acitretin) may also be used in young patients. Biologic agents recommended in the 2020 AAD-NPF guidelines for use in young patients such as etanercept, adalimumab, infliximab, and Ustekinumab⁸⁷. A previous trial in 211 young individuals with moderate-to-severe plaque psoriasis reported that etanercept substantially decreased the severity of disease and about 4 serious adverse events reported as ovarian cyst removal, gastroenteritis, intestinal dehydration, and left basilar pneumonia⁸⁹.

Biologics may be combined with topical corticosteroids with or without vitamin D analogs and these three combinations can be used with highly safety and efficacy in treating severe plaque in young patients⁸⁷. Phototherapy is recommended to use with caution, particularly for younger pediatrics, due to carcinogenic risks and phototoxicities with long-term use. UVB may be a treatment of choice for adolescences and older pediatrics with extensive, serious, or resistant disease for treatment⁴¹.

Psoriasis treatment during pregnancy

Hormonal fluctuations during pregnancy may improve outcomes in female with plaque psoriasis⁴¹. It is related with more estrogen concentrations but not progesterone⁹⁰. So, some pregnant patients may need minimal intervention for psoriasis treatment. Some psoriasis medications have teratogenic effects in animal investigations or have restricted data in human pregnancy. UVB is considered the best psoriasis therapy during pregnancy. It is indicated for individuals with severe disease that cannot be controlled with topical medications. One concern with this treatment is the high chance of herpes simplex reactivation, which can be transmitted to the baby at birth. A 2009 Canadian guideline provides recommendations for topical, phototherapy, and orally agents medications during pregnancy⁴¹. The 2015

European S3 guideline also discusses the most appropriate treatments for women hoping to become pregnant in the future, as well as treatments to avoid⁵⁶.

Psoriasis in elderly

The physiologic changes related to age, drug elimination, and drug sensitivity may increase the potentiality of adverse drug reactions in older individuals with psoriasis. MTX is hepatotoxic and used with caution in the older patients. Cyclosporine may be nephrotoxic and may cause hypertension. Significant drug interactions and polypharmacy are present in elderly patients. Adalimumab can also be used in patients aged 65 years and older with hypertension, hyperlipidemia, depression, obesity, and diabetes⁹¹. Ustekinumab does not require dose adjustments for renal or hepatic impairment, and dosages for adults are the same as for adults <65 years of age and are determined by body weight. Secukinumab also does not require dose adjustments for the elderly or those with renal/hepatic disease. Topical treatment of psoriasis is generally used as first-line therapy in adults⁴¹.

Psoriasis treatment in patients with solid tumors

Systemic therapies (cyclosporine), PUVA, and some biologics are related to an increased risk of neoplastic disease. PUVA is related to an increased risk of malignant melanoma and cutaneous squamous cell carcinoma (CSCC); UVB is a more safe treatment than PUVA; cyclosporine increases lymphoma risks and skin cancers; MMF may be related to lymphoproliferative diseases, and the risk of malignancy for biologic agents may be increased particularly TNF- α inhibitors⁹². In 2009, Canadian guidelines recommend caution in the use of anti-TNF- α agents in psoriasis patients with a history of malignancy or active malignancy⁶³.

CONCLUSIONS

The current trends in psoriasis treatment reflect a dynamic and rapidly advancing field, with a strong focus on personalized care, enhanced efficacy, and improved safety. The integration of novel therapies, patient-centered approaches, and comprehensive management of comorbidities represents a significant shift towards more effective and holistic treatment strategies. Ongoing research and innovations continue to drive progress, offering hope for further improvements in the management of psoriasis and overall patient well-being.

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AUTHOR'S CONTRIBUTIONS

Abuarij M: manuscript writing, literature survey. **Alyahawi A:** conceived the idea, writing the manuscript. **Alkaf A:** literature survey, formal

analysis, critical review. Final manuscript was checked and approved by all authors.

DATA AVAILABILITY

This article is available to anyone upon request from the corresponding authors.

CONFLICT OF INTEREST

None to declare.

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