Review Article

Trends in Pharmaceutical Sciences and Technologies 2025: 11(2): 127-142.

TIPS and Technol

A Glimpse into the Pathophysiology, Classification, Clinical Presentations, and Management of Psoriasis

Azin Ghaediyan[1,2];Pharm.D, Dena Firouzabadi[3];Ph.D, Mohammad M. Zarshenas[1,2*];Ph.D

[1]Medicinal Plants Processing Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Department of Clinical Pharmacy, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Skin and dermatological diseases have a considerable potential to impact a person's social conduct, self-esteem, and willingness to engage in social interactions. The burden of skin diseases includes both their high incidence and the long-term morbidity associated with them. Psoriasis is the most prevalent immune-mediated inflammatory disease worldwide and is a multifactorial skin condition that arises from the interaction of immunological, genetic, and environmental factors. Numerous comorbidities, such as psoriatic arthritis, inflammatory bowel disease, metabolic syndromes, and complications related to respiratory, cardiovascular, and mental health, are associated with chronic psoriasis. There are several forms of cutaneous psoriasis. Psoriasis vulgaris is the most common phenotype, accounting for about 85–90% of psoriasis cases. Based on the clinical severity of the lesions, patients with psoriatic disease can be categorized as having mild, moderate, or severe disease. This review highlights various psoriasis presentations, their clinical signs and symptoms, and the available treatment options.

Keywords: Psoriasis, plaque, therapy, biologic.

Please cite this article as: Ghaediyan A, Firouzabadi D, Zarshenas MM. A Glimpse into the Pathophysiology, Classification, Clinical Presentations, and Management of Psoriasis. Trends in Pharmaceutical Sciences and Technologies. 2025;11(2):127-142. doi: 10.30476/tips.2025.106092.1288

1. Introduction and Definition

Skin is an essential organ that serves primarily as a barrier. Skin diseases have the potential to impact a person's social conduct, self-esteem, and willingness to engage in social interactions (1). Although the relevance of skin diseases is frequently disregarded due to their low mortality rates and chronic nature, statistics suggest that between 21% and 87% of individuals may be suffering from a skin disorder (2). The burden of skin diseases includes both their high incidence and the long-term morbidity associated with them, such as severe itching (as in atopic dermatitis and urticaria) or deformity (as in leprosy). Psoriasis and other chronic inflammatory skin conditions are also common, and novel treatments such as biologics come at a high cost (3).

Psoriasis is a chronic, immune-mediated inflammatory skin disease. The intensity varies from a few solitary red, scaly plaques to nearly total body surface involvement. The degree of severity varies depending on genetics and environmental factors, and it may progressively worsen with age or wax and wane (4). People of all ages can be affected by psoriasis, which is not specific to any particular

Corresponding Author: Mohammad M. Zarshenas, Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
Email address: zarm@sums.ac.ir

Received: 01/03/2025; Accepted: 16/05/2025

sex. Psoriasis is linked to several comorbidities and can affect the joints, skin, and nails. The main focus of treatment is currently on managing acute symptoms. Patients who suffer from psoriasis have an increased risk of developing depression, diabetes, metabolic syndrome, and cardiovascular diseases (5). The etiology of psoriasis is uncertain; however, it may be linked to an impairment in keratinocyte proliferation and differentiation associated with inflammatory cell infiltration, primarily including T-lymphocytes, macrophages, and neutrophils (6).

2. Materials and methods

To create a review on various aspects of psoriasis, a thorough search was conducted using databases such as PubMed, Scopus, and Google Scholar. The search was done using the keywords: (psoriasis), (prevalence), (management), (etiology), and (manifestations). Data gathering was completed by August 25, 2024.

3. Epidemiology, Pathophysiology, and Possible Mechanisms

Psoriasis affects over 8 million people in the United States (7). The Multinational Assessment of Psoriasis and Psoriatic Arthritis (MAPP) survey found psoriasis prevalence ranging from 1.4% in Spain to 3.3% in Canada, for an overall prevalence of 1.9%. The incidence in the USA is slightly greater than average, at 2.2%. Prevalence varies regionally and among ethnic groups within an area, with higher rates observed in locations farther from the equator (8). With 8.5%, Norway had the highest reported prevalence of psoriasis worldwide, while Asia, with less than 0.5%, had the lowest rates (9). Psoriasis affects both men and women in equal measure. Although psoriasis has been reported to manifest at birth and as late as the ninth decade of life, the majority of patients (about 75%) begin to develop psoriasis before the age of 40 (10). A bimodal age distribution is observed between the ages of 18 to 39 and 50 to 69, although psoriasis can appear at any age (5, 9). Genetic background appears to be the primary cause of most epidemiological variations for psoriasis. Genetic factors account for over 70% of the susceptibility to psoriasis. Worldwide reports have indicated a higher occurrence of psoriasis within families. According to twin studies, monozygotic twins are 2-3 times more likely than dizygotic twins to develop psoriasis (11). Psoriasis is commonly understood to be a complex disease that results from a combination of hereditary susceptibility alleles and external factors (12).

Although the etiology of psoriasis is complicated, more knowledge about it has emerged as basic and clinical research has advanced. Psoriasis is currently recognized to be caused by immunological disorders, which are driven by hereditary and environmental factors (13). The three components of immunity are type 1 (T-helper 1 [Th1] + innate lymphoid cell [ILC] 1), type 2 (Th2 + ILC2), and type 3 (Th17 + ILC3), which are delicately balanced, with regulatory cells controlling the excess burden. Psoriasis is classified as a type 3 dominant immune disorder that is mediated by interleukin (IL)-17 (14). The pathological process originates from a complex network of cell types, such as keratinocytes, DCs (dendritic cells), and T cells, which produce cytokines that lead to a chronic inflammatory state (15). To contribute to the pathophysiology and development of psoriasis, keratinocytes and other immune cells, including T cells, myeloid dendritic cells (mDCs), plasmacytoid dendritic cells (pDCs), neutrophils, and macrophages, collaborate to establish an inflammatory circuit (13). Psoriasis lesions produce a variety of cytokines. These cytokines trigger inflammation, cause endothelial cell damage, and have different levels of involvement in the development of psoriasis. But the two most important cytokines are IL-17 and IL-23. Additionally, TNF-α plays a critical function, most likely through preserving the cells that produce these cytokines or by amplifying their

effects (14).

4. Risk Factors

4.1. Obesity

Research indicates that obesity both predisposes people to the onset of psoriasis and exacerbates pre-existing psoriasis through pro-inflammatory pathways (16). White adipose tissue was previously thought to be an inert energy storage tissue, but since white adipose tissue is now known to be an important endocrine organ secreting a wide range of soluble mediators involved in immunity, inflammation, and metabolic and appetite regulation, the potential link between autoimmunity and obesity has become even more relevant (17). Additionally, compared to patients with average body weight, obese or overweight patients appear to have more severe psoriasis (18).

4.2. Smoking

Based on the data that is now available, smoking cigarettes is an acknowledged environmental risk factor for psoriasis (19). Severe psoriasis risk has been linked to heavy smoking (>20 cigarettes per day) by more than a twofold margin (20). The correlations between psoriasis and smoking are probably due to a variety of pathophysiological processes. Smoking increases the risk of vascular endothelial dysfunction, leads to damage by free radicals and oxidative stress, decreases plasma antioxidant concentrations, and increases the viscosity of plasma. There are about 10^{17} free radicals in every puff of cigarette smoke. The development of psoriasis could be one of the systemic effects that could result from this increased exposure to free radicals (21). Smoking can additionally have an impact on the development of comorbidities in psoriasis and psoriatic arthritis patients. Due to the interaction of multiple variables, the relationship between smoking, psoriasis or psoriatic arthritis, and comorbidities is nevertheless complicated (19).

4.3. Infections

The connection between guttate psoriasis and streptococcal infections has been known for a century. Recently, it was found that the tonsils of psoriasis patients have higher detection rates of β-hemolytic streptococci, especially group *C. streptococci*, than the recurrently infected tonsils of patients without psoriasis (22). Guttate psoriasis is a self-limiting condition, but it may resurface if a streptococcal infection occurs. For patients with resistant psoriasis linked to tonsillitis flare-ups, tonsillectomy could be an acceptable treatment (23). In addition, throat infections can make psoriatic symptoms worse in individuals who already have plaque psoriasis. *Helicobacter pylori* and *Staphylococcus aureus* are examples of other microorganisms linked to the onset or aggravation of psoriasis. Papillomaviruses and retroviruses are among the viruses that have also been linked to psoriasis, along with fungi such as members of the genera Malassezia and Candida (24).

4.4. Medicines

Medicines have the potential to aggravate pre-existing psoriasis, induce psoriatic lesions on clinically unaffected skin in psoriasis patients, or trigger the illness in those without a family history of psoriasis or in those who are predisposed to it (25). Strong links have been found between psoriasis and certain medications. These include beta-blockers, lithium, imiquimod, terbinafine, interferons, and antimalarials such as chloroquine. (26). It has been observed that corticosteroid withdrawal may flare up pustular psoriasis. There have recently been reports that NSAIDs like indomethacin and a variety of other unrelated medications, such as tetracycline, can exacerbate psoriasis (25). NSAIDs, both systemic and topical, have been shown to aggravate psoriasis. NSAIDs slow down the metabolism of arachidonic acid by blocking the cyclooxygenase pathway, which ultimately causes leukotrienes to build up. Psoriasis aggravation is

believed to be caused by this. Synthetic antimalarials are effective inhibitors of transglutaminase. Transglutaminase has an essential role in epidermal turnover, and fluctuations in this enzyme's concentration are considered to be the cause of psoriasis induction (27).

5. Classification & Clinical Presentations

There is increasing evidence that individuals with psoriasis are more likely than the general population to suffer from other severe and chronic disorders, such as diabetes, hypertension, liver disease, Crohn's disease, arthritis, or other diseases related to metabolism. Thus, psoriasis can be divided into two categories: systemic psoriasis and cutaneous psoriasis (28). There are multiple forms of cutaneous psoriasis: plaque (psoriasis vulgaris), flexural, guttate, pustular, or erythrodermic psoriasis (29). The most prevalent phenotype, accounting for around 85-90% of psoriasis patients, is psoriasis vulgaris (28). Up to 50% of patients may develop nail psoriasis, which may present with nail pitting (an indentation in the nail), onycholysis (a separation of the nail plate from the nail bed), oil spots (discoloration of the nail bed), dystrophy, and subungual hyperkeratosis (29). Table 1 summarizes the subtypes of psoriasis (Table 1). Figure 1 and 2 demonstrates some of the presentations of psoriasis (Figure 1 and 2). Treatment lines are mentioned in Figure 3 (Figure 3).

5.1. Plaque Psoriasis (Psoriasis Vulgaris)

Psoriasis vulgaris is the most prevalent type of psoriasis, making up 90% of cases. In this type of psoriasis, papulosquamous plaques are visible from the surrounding normal skin (30). Erythematous, scaly, and well-defined plaques are the hallmark lesions of plaque psoriasis. The lesions start as erythematous papules and gradually grow into rich red plaques, which are also known as "salmon pink" (28). The knees, elbows, scalp, and lumbar area are the most common sites for lesions, which have a symmetric distribution (31). The color of the patches varies depending on the skin tone. Due to post-inflammatory hyperpigmentation, there may be transient changes in the look of color as a result of the damaged skin layer recovering, especially on brown or black skin (32).

5.2. Guttate Psoriasis

Guttate psoriasis (GP), which makes up to 25% of cases of psoriasis, can be identified by sporadic, "drop-like" papules and plaques. While GP can resolve in three to four months, up to 39% of cases have the potential to progress to chronic plaque psoriasis (33). The trunk and proximal extremities are sites of predilection for guttate psoriasis, which usually manifests as an abrupt onset of numerous, small, dispersed, teardrop-shaped, scaly, erythematous, pruritic papules and plaques (34). Guttate psoriasis is a condition that typically manifests unexpectedly after an acute infection, like streptococcal pharyngitis (35). Guttate psoriasis has been linked to both human leukocyte antigen HLA-Cw6 as well as a previous streptococcal infection (33). Guttate psoriasis is more prevalent in children (especially in adolescents) than in adults, in contrast to other types of the disease (34).

5.3. Pustular Psoriasis

Aseptic pustules are a typical feature of a heterogeneous group of skin inflammatory diseases collectively referred to as pustular psoriasis (36). Two separate subtypes of pustular psoriasis exist: palmoplantar pustulosis (PPP), a localized disease that affects the palms and soles, and generalized pustular psoriasis (GPP). Acrodermatitis continua of Hallopeau, which is described as involving the fingers, toes, and nails, is a subset of PPP. With a reported incidence of 0.05–0.12%, PPP is the most prevalent form of pustular psoriasis and is far more common in Japan than in Western countries (37). GPP prevalences in France and Japan are estimated to be 0.0002% and 0.0007%, respectively (36).

5.3.1. Generalized Pustular Psoriasis

A rare and severe type of pustular psoriasis known as generalized pustular psoriasis (GPP) is characterized by recurring, extensive episodes of neutrophil-rich pustule development in the epidermis. Fever and systemic inflammation may also accompany these episodes (38). If left untreated, GPP flares have the potential to cause major consequences like sepsis and cardiovascular failure, which can be fatal (39). It has been noted that infections, stress, corticosteroid withdrawal, and pregnancy might cause GPP to start or flare up again. GPP in pregnancy should be viewed as a dangerous, potentially fatal circumstance for the mother and the fetus (40). Based on the course of the disease and its clinical manifestation, multiple subtypes of GPP have been identified. These include the acute von Zumbusch type, GPP in pregnancy, formerly known as impetigo herpetiformis, the annular GPP clinical subphenotype, and GPP linked to psoriasis vulgaris (36).

5.3.2. Palmoplantar Pustulosis

Pustulosis palmaris et plantaris (PPP), also known as palmoplantar pustulosis, is a recurrent and chronic inflammatory skin disease characterized by erythema, scales, and pustules on the palms, soles, and medial and lateral margins of the affected areas (41). The acrosyringium, the eccrine sweat gland apparatus that is the target of inflammation in psoriasis, is thought to be the main site of inflammation in ppp. The most prevalent and well-known risk factor for PPP is smoking, with stress, hot weather, infection, dental metal allergies, and gluten sensitivity serving as additional precipitating variables (42). Nails are frequently affected, presenting with pitting, lateral grooves, longitudinal crests, nail turbidity, nail peeling, and empyema. Palmoplantar pustulosis can last for years and is typically resistant to treatment, with periods of partial or total remission disrupted by recurring exacerbations (28).

5.3.3. Acrodermatitis continua of Hallopeau

Acrodermatitis continua of Hallopeau is an uncommon form of pustular psoriasis that typically appears as a sterile pustular eruption on the tips of the fingers and toes. It affects the skin and nail bed, resulting in severe deformity of the distal phalanges (43). In most cases, the eruption follows a history of local trauma or infection; however, additional etiologies, such as infectious, neurological, inflammatory, and genetic origins, have also been reported (44). Given that ACH pustules are sterile, obtaining cultures from the afflicted skin area may aid in ruling out infection, however poor outcomes are probable. Saprophytes may be found in bacterial cultures of the afflicted area, however these bacteria are not linked to the disease's pathophysiology. Viral cultures or fluorescent antibody assays can be used to rule out viral paronychias. Histopathological analysis of a skin biopsy of the lesion, Gram stain smear, and potassium hydroxide preparation from the pustules can all be used to make a conclusive diagnosis of ACH (43). Acrodermatitis continua of hallopeau typically affects fingers rather than toes, presenting with tender pustules and underlying erythema on the tip of a digit (44). Even though histological characteristics such as hyperkeratosis, parakeratosis, and subcorneal neutrophil accumulation are consistent with a localized type of pustular psoriasis, acrodermatitis may be regarded as a distinct disease category (45). Since nails are always involved in ACH, other diseases, such as PPP, should be taken into consideration if nails are not involved (28).

5.4. Erythrodermic Psoriasis

Erythrodermic psoriasis (EP) is a severe and uncommon form of psoriasis that affects less than 3% of the patients with psoriasis. It is characterized by erythema and scaling that covers more than 90% of the body's surface area. Patients with EP may experience a number of systemic symptoms, includ-

ing tachycardia, fever, fatigue, dehydration, lymphadenopathy, and disturbances in serum electrolyte levels (46). EP has a lengthy course and is prone to recurrence (28). A variety of factors have been identified as contributing to EP, such as prior disease, infection, systemic corticosteroid treatment, drug discontinuation, and extreme emotional stress (47). Affected patients also have an increased risk of secondary infection by pathogenic skin flora due to desquamation and the ensuing disruption of the skin barrier (48).

5.5. Inverse Psoriasis

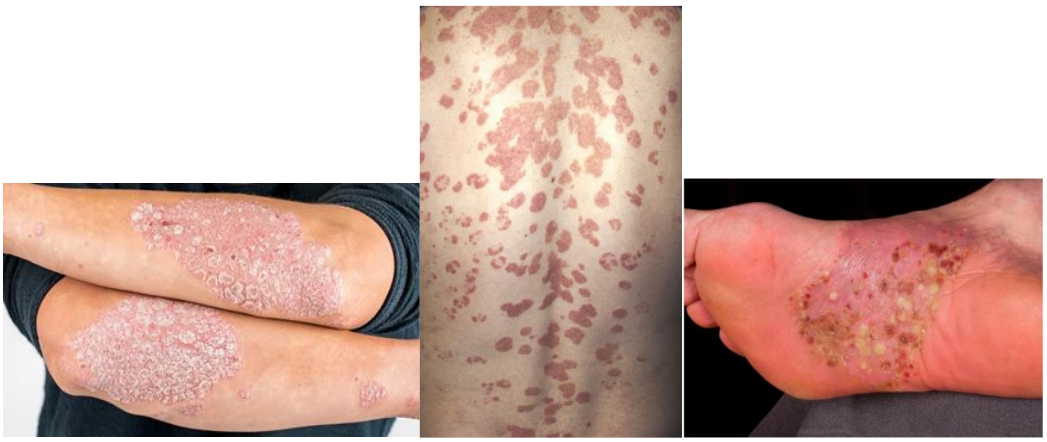
Intertriginous psoriasis, another name for inverse psoriasis, is typified by distinct, erythematous lesions that appear in the axillary, anogenital and inframammary regions of the body folds. This contrasts with the most prevalent type of psoriasis, which typically affects the scalp and extensor surfaces like the knees, elbows, and sacrum (49). The prevalence of IP varies greatly, between 3 and 36%, according to various research and demographics. This variability is attributed to the absence of clear diagnostic standards and disagreement about whether genital localization is a component of the disease. IP is common in children, particularly in newborn infants, and often it manifests as "napkin psoriasis" involving the diaper area. The quality of life may be greatly impacted by IP, particularly in relation to sexual function, embarrassment, and shame, even though it only affects just a fraction of the skin (50). Corynebacterium species, Streptococcus species, Candida spp., Malassezia spp., dermatophytes, and other microorganisms have been linked to secondary infections in inverse psoriasis and seem to be more prevalent than previously believed (51).

5.6. Psoriatic Arthritis

Psoriatic arthritis (PsA) affects 20–30% of individuals with psoriasis. It primarily

Table 1. Psoriasis Subtypes.

Subtype	Clinical Characteristics
Plaque psoriasis	– Clearly defined salmon-pink plaques featuring adherent white or silvery scales(55) – Areas affected include the scalp, extensor areas such as knees and elbows, periumbilical areas, and intergluteal cleft(55)
Guttate psoriasis	– Smaller plaques involving the trunk and extremities(56) – 'Drop-like' scaly plaques(55)
Generalized pustular psoriasis	– Rapid development of diffuse sterile pustules on erythematous non-acral skin(55) – Systemic manifestations include • arthritis • fever • malaise • leukocytosis • oral and ocular issues(55)
Erythrodermic psoriasis	– Over 90% of the body's surface is affected by erythema and scale – Systemic manifestations include • hypothermia • hypoalbuminaemia • electrolyte disturbances • venous thromboembolism • high-output cardiac failure • pain(55)
Inverse (intertriginous) psoriasis	– Absence of scales; erythematous lesion on flexor surfaces, armpits, and groin (56)
Nail psoriasis	– Pitting – Onycholysis – Leukonychia – Splinter haemorrhages – Crumbling – Nail bed hyperkeratosis – Oil spots (55)



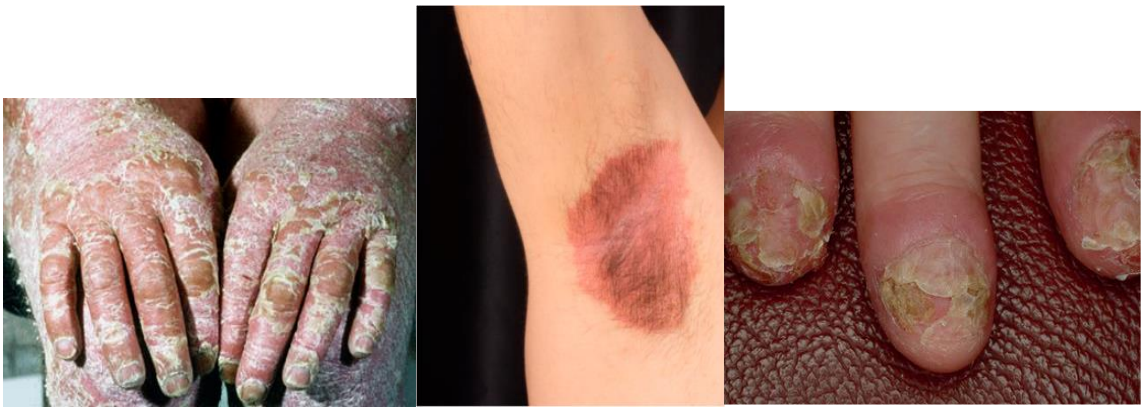
(a) (b) (c)

Figure 1. (a) Plaque psoriasis with silvery scales; (b) Guttate psoriasis presenting as numerous erythematous, scaly papules on the back; (c) Pustular psoriasis localized to the soles of the foot.

affects people between the ages of 40 and 50, impacting both men and women nearly equally (52). In addition to joint and skin symptoms, the majority of PsA patients also suffer from many concomitant conditions, including fibromyalgia, infections, inflammatory bowel disease, heart disease, and uveitis (53). Although 10%–15% of patients experience arthritis prior to psoriasis, in many cases, psoriasis and arthritis manifest simultaneously (54).

6. Treatment Lines

Psoriatic disease patients can be classified as having severe, moderate, or mild disease depending on the clinical severity of their lesions (57). The most widely used method for determining the severity of psoriasis and psoriatic arthritis is the Psoriasis Activity and Severity Index (PASI). Using measurements and evaluations of the degree of skin involvement as well as the intensity of erythema, desquamation, and plaque induration (thickness) in each area, the PASI generates an overall score ranging from 0 (no psoriasis) to 72 (severe psoriasis) (58). Mild to moderate cases can be treated topically with a combination of glucocorticoids, vitamin D analogues, and phototherapy. For moderate to severe cases of psoriasis, systemic treatment is often necessary; the presence of comorbidities like psoriasis arthritis plays a significant role in treatment selection (59). BSA (Body Surface Area) is



(a) (b) (c)

Figure 2. (a) Erythrodermic psoriasis; (b) Inverse psoriasis affecting the axillary area; (c) nail yellowing, onycholysis, and subungual hyperkeratosis due to psoriasis.

typically used in the clinical setting to classify disease severity. When there is no involvement of the face, genitalia, hands, or feet and the BSA is less than 5%, the condition is considered mild and can be cleared with topical medications alone. Moderate illness applies to patients with 5 to <10% BSA involvement or those who may require escalation of therapy to phototherapy or nonbiologic systemic medicines. Severe disease is often defined as >10% BSA affected or as requiring escalation to biologic therapy (60, 61). The PASI75 response is the proportion of individuals whose initial score has improved by 75%. For the majority of psoriasis clinical trials, PASI75 serves as the benchmark for primary endpoints. However, the ultimate objective of therapy—the PASI90 response—is now seen as the most important result of treatment, particularly for patients with severe cases (62).

6.1. Treatments for Mild Psoriasis

ALess than 3% to 5% of the body's surface area is typically affected by mild psoriasis. Mild psoriasis can be treated with a variety of drugs, such as calcineurin inhibitors, topical corticosteroids, vitamin D analogs, keratolytics, and targeted phototherapy (63-65). The main treatment for individuals with localized or mild psoriasis is often topical corticosteroids. Through the downregulation of inflammatory pathways, corticosteroids minimize inflammation, prevent cell division, and constrict blood vessels. Formulations that combine corticosteroids with keratolytic drugs or vitamin D analogs, including tazarotene and halobetasol propionate, are less likely to cause adverse effects and more effective than when taken separately (66). Analogs of vitamin D3 were first made commercially available in the early 1990s as a topical psoriasis treatment. The first-line treatments for psoriasis are calcipotriol, calcitriol, and tacalcitol due to their therapeutic efficacy and low toxicity (67). The topical calcineurin inhibitors tacrolimus and Pimecrolimus are frequently used to treat psoriasis, despite not having FDA approval for this purpose. For extended use (> 4 weeks), they act as steroid-sparing agents and are especially beneficial on thinner skin, such as the skin on the face and intertriginous areas (64). Phototherapy is an option for inflammatory skin disorders like vitiligo, eczema, and psoriasis that involves repeatedly exposing the skin to ultraviolet (UV) radiation. For the treatment of psoriasis, phototherapy comes in three primary forms: psoralen plus ultraviolet A (PUVA), narrowband ultraviolet B (NB-UVB), and broadband ultraviolet B (BB-UVB) (68). Nuclear DNA is the main molecular target of ultraviolet B (UVB) radiation. When light is absorbed, it produces pyrimidine dimers and other photoproducts, which ultimately prevent DNA synthesis (69). The UVB spectrum of the sun spans a wide range of wavelengths, from 290 to 320 nm. Originally, artificial UVB emitters radiated all of this wavelength range. Currently, UVB therapy is most often administered using narrowband sources, which emit UV light within the precise wavelength range of 311–312 nm. This more focused range has proven to be the most effective component of natural sunlight for treating psoriasis and other skin problems (70). Psoralen-UV-A (PUVA; 320–400 nm) therapy was first presented in the 1970s. Psoralens are photosensitizers derived from plants that can be ingested or applied topically. A therapeutically advantageous phototoxic response in the skin is brought on by further UVA irradiation. With response rates ranging from 74% to 100%, PUVA therapy effectively treats psoriasis and has anti-inflammatory and antiproliferative properties. Thus, PUVA is among the best options for treating psoriasis; nevertheless, it is not as well tolerated as UV-B phototherapy, and there is more evidence of its possible carcinogenicity (71).

6.2. Treatments for Moderate-to-Severe Psoriasis

AIt is generally accepted that moderate psoriasis is characterized by a body surface

area coverage of 3~5% to 10%, whereas severe psoriasis is commonly described as 10% or above. For these patients, a combination of oral medications, phototherapy, and biologics is advised by both American and European guidelines (66). Topical drugs are useful in treating moderate to severe psoriasis, but they should not be used as monotherapy. Methotrexate, apremilast, acitretin, and cyclosporine are among the oral options for psoriasis. Oral drugs, with the exception of cyclosporine, are typically less effective than biologics in the treatment of psoriasis (72). The development of biological agents has significantly increased the safety and effectiveness of psoriasis therapies in recent years. Currently recommended biological agents to treat moderate-to-severe psoriasis include tumor necrosis factor-α inhibitors, interleukin-17 inhibitors, interleukin-12/23 inhibitors, and interleukin-23 inhibitors (73). Overall, using biologics to treat psoriasis does not increase the risk of serious infections or internal malignancies. Common side effects of all biologics include injection site reactions, nasopharyngitis, and upper respiratory tract infections; these side effects occur at slightly higher rates than placebo (72).

6.2.1. TNF-α inhibitors

ATumor necrosis factor-alpha (TNF-α), a cytokine involved in inflammation, is the target of a class of drugs known as TNF-α inhibitors (66). There are currently five TNF-α inhibitors approved to treat psoriasis. Monoclonal antibodies include Infliximab, Adalimumab, and Golimumab; fusion proteins like Etanercept; and monoclonal antibody (mAb) fragments linked to polyethylene glycol known as Certolizumab Pegol (74). For patients with advanced congestive heart failure, hepatitis B infection, demyelinating illnesses including multiple sclerosis, or active tuberculosis, TNF-α inhibitors are contraindicated. Individuals who are being treated for latent tuberculosis can also be treated simultaneously with a TNF-α inhibitor (72). In terms of PASI, a meta-analysis has established that infliximab is the most effective medication in this class, with adalimumab coming in second. Nonetheless, there is a chance of significant infection when using infliximab, and infusion reactions might happen (75).

6.2.2. IL-17 inhibitors

AThe etiopathogenesis of immunological and inflammatory illnesses, such as psoriasis, psoriatic arthritis, and ankylosing spondylitis (AS), involves a series of inflammatory transformations in which interleukin 17 plays a role. Human interleukin 17 is a glycoprotein consisting of 155 amino acids. This family currently consists of five receptors (IL-17RA to IL-17RE) and six ligands (IL-17A to IL-17F). The etiopathogenesis of psoriasis is primarily linked with the keratinocyte-affecting IL-17A, IL-17F, and IL-17A/F subtypes (76). IL-17 inhibitors target either the IL-17 ligand or its receptor; ixekizumab and secukinumab inhibit the IL-17A ligand, while bimekizumab inhibits both the IL-17A and IL-17F ligands, and brodalumab inhibits the IL-17 receptor (72). IL-17 inhibitors ought to be taken into consideration as first-line treatment in circumstances when a prompt therapy response is required. Inhibiting IL-17 may also be beneficial for patients with cardiovascular problems (77).

6.2.3. IL-23 inhibitors

ARisankizumab, tildrakizumab, and guselkumab are the IL-23 inhibitors that the US Food and Drug Administration has approved for the treatment of adult plaque psoriasis (72). In two separate trials comparing risankizumab and ustekinumab, 75% of patients treated with risankizumab and less than 50% of patients treated with ustekinumab attained PASI90. There have been no reports of increased incidences of cancer, significant and opportunistic infections, or major cardiovascular events. The reduced administration frequency of anti-IL-23 drugs—generally every 12 weeks as opposed to every 4 weeks with

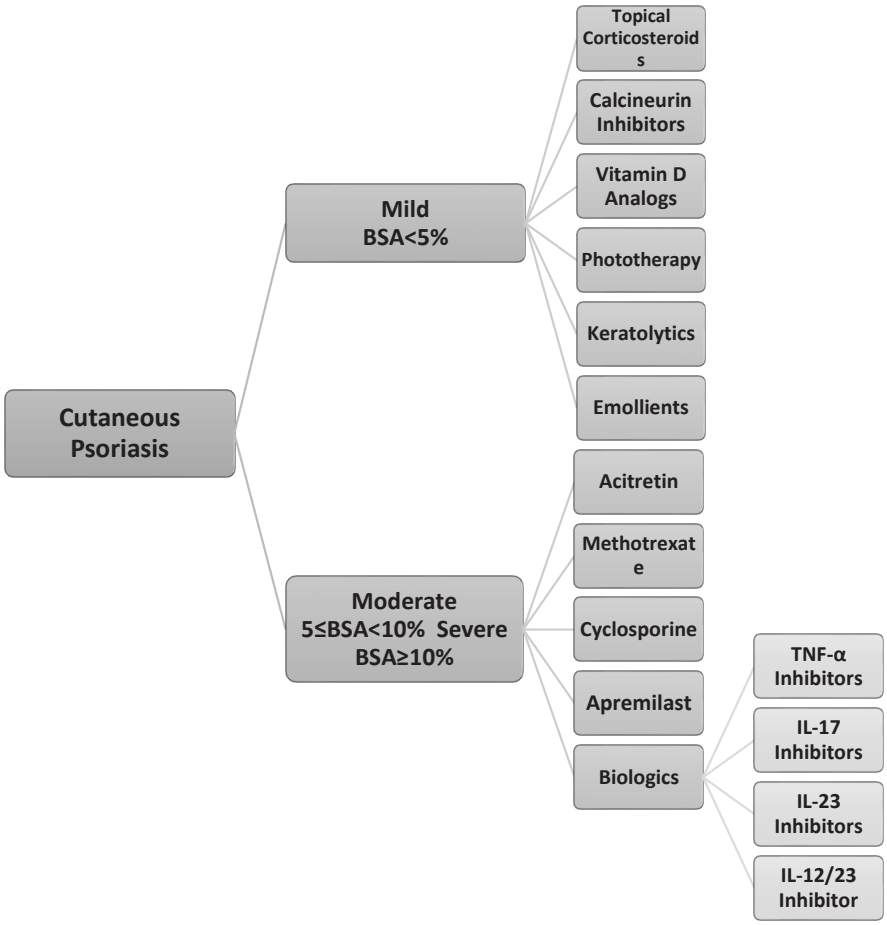


Figure 3. Treatments for cutaneous psoriasis – BSA: body surface area.

secukinumab—is another advantage of these drugs (78).

6.2.4. IL-12/23 inhibitor

AUstekinumab is the only biologic that inhibits both IL-12 and IL-23 by inhibiting their shared p40 subunit and has been approved by the US Food and Drug Administration to treat psoriasis and psoriatic arthritis (72). Regarding ustekinumab's safety profile, findings from Phase II and III trials, both short- and long-term, are positive and do not show any dose-dependent side effects (79).

6.2.5. Challenges of Treating Psoriasis with Biologics

APatients with moderate-to-severe psoriasis can benefit greatly from biologics. Biologics are great options for patients who don't respond to UVB phototherapy in terms of safety and effectiveness. Nevertheless, there are challenges that restrict their use in the management of psoriasis. Psoriasis treatment is expensive for patients as well as the healthcare system. Biologics are more costly than oral medications such as cyclosporine and methotrexate. The requirement for injection or infusion is also one of the advantages and drawbacks of all biologics. Some patients require at-home assistance or office administration because they are uncomfortable self-injecting (80). One major factor contributing to the failure of psoriasis treatments is the development of anti-drug antibodies (ADAs) against biologics. Both drug-related and patient-related factors influence the risk of developing ADAs. The ADAs that are found can either have temporary or neutralizing effects, the latter of which totally stops biological activity by attaching to the drug's active site

(81).

6.3. Emerging Therapies

AJanus kinase (JAK) inhibitors are a new drug class that are now considered as one of the new treatment options for psoriasis. These inhibitors are currently available for the treatment of ulcerative colitis, psoriatic arthritis, and rheumatoid arthritis. They suppress the gene transcription of proinflammatory cytokines by blocking the intracellular signal pathway that is regulated by JAK and signal transducer and activator of transcription (STAT) proteins (82). Tofacitinib (JAK3 inhibitor), baricitinib (JAK1 and JAK2 inhibitor) for plaque psoriasis, and filgotinib and upadacitinib (JAK1 inhibitors) are among the oral small molecule medications being researched to target this pathway in psoriasis (83).

7. Conclusion

In conclusion, psoriasis is a skin disease that has major medical and psychosocial comorbidities. It manifests itself in multiple ways, such as plaque, pustular, and more. The etiology of psoriasis is complex; however, growing therapy options that could significantly enhance the quality of life for psoriasis patients have been made possible by advances in our understanding of the disease's etiology.

Authors' Contributions

DF and MMZ designed the study. AGH gathered the data and prepared the draft of the paper. DF and MMZ revised the manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Chen WY, Chen SC, Hsu SY, Lin YA, Shih CM, Huang CY, Wang KH, Lee AW. Annoying Psoriasis and Atopic Dermatitis: A Narrative Review. *Int J Mol Sci*. 2022 Apr 28;23(9):4898. doi: 10.3390/ijms23094898. PMID: 35563285; PMCID: PMC9104570.
2. Sanclemente G, Burgos C, Nova J, Hernández F, González C, Reyes MI, et al. The impact of skin diseases on quality of life: A multicenter study. *Actas Dermosifiliogr.* 2017 Apr;108(3):244-252. English, Spanish. doi: 10.1016/j.ad.2016.11.008. Epub 2017 Jan 4. PMID: 28063525.
3. Flohr C, Hay R. Putting the burden of skin diseases on the global map. *Br J Dermatol.* 2021 Feb;184(2):189-190. doi: 10.1111/bjd.19704. PMID: 33544440.
4. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM; Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. *J Invest Dermatol*. 2013 Feb;133(2):377-85. doi: 10.1038/jid.2012.339. Epub 2012 Sep 27. PMID: 23014338.
5. Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. *J Eur Acad Dermatol Venereol.* 2017 Feb;31(2):205-212. doi: 10.1111/jdv.13854. Epub 2016 Aug 30. PMID: 27573025.
6. Rajguru JP, Maya D, Kumar D, Suri P, Bhardwaj S, Patel ND. Update on psoriasis: A review. *J Family Med Prim Care.* 2020 Jan 28;9(1):20-24. doi: 10.4103/jfmpc.jfmpc_689_19. PMID: 32110559; PMCID: PMC7014874.
7. Armstrong AW, Mehta MD, Schupp CW, Gondo GC, Bell SJ, Griffiths CEM. Psoriasis Prevalence in Adults in the United States. *JAMA Dermatol*. 2021 Aug 1;157(8):940-946. doi: 10.1001/jamadermatol.2021.2007. PMID: 34190957; PMCID: PMC8246333.
8. Kimmel GW, Lebwohl M. Psoriasis: Overview and Diagnosis. *Evidence-Based Psoriasis.* 2018 Jul 1:1–16. doi: 10.1007/978-3-319-90107-7_1. PMCID: PMC7122924.
9. Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. *J Am Acad Dermatol.* 2014 Mar;70(3):512-6. doi: 10.1016/j.jaad.2013.11.013. Epub 2014 Jan 2. PMID: 24388724.
10. Garshick MK, Kimball AB. Psoriasis and the life cycle of persistent life effects. *Dermatol Clin*. 2015 Jan;33(1):25-39. doi: 10.1016/j.det.2014.09.003. PMID: 25412781.
11. Ogawa K, Okada Y. The current landscape of psoriasis genetics in 2020. *J Dermatol*

Sci. 2020 Jul;99(1):2-8. doi: 10.1016/j.jdermsci.2020.05.008. Epub 2020 May 28. PMID: 32536600.
12. Capon F. The Genetic Basis of Psoriasis. *Int J Mol Sci*. 2017 Nov 25;18(12):2526. doi: 10.3390/ijms18122526. PMID: 29186830; PMCID: PMC5751129.
13. Wu M, Dai C, Zeng F. Cellular Mechanisms of Psoriasis Pathogenesis: A Systemic Review. *Clin Cosmet Investig Dermatol.* 2023 Sep 14;16:2503-2515. doi: 10.2147/CCID.S420850. PMID: 37727872; PMCID: PMC10506593.
14. Yamanaka K, Yamamoto O, Honda T. Pathophysiology of psoriasis: A review. *J Dermatol.* 2021 Jun;48(6):722-731. doi: 10.1111/1346-8138.15913. Epub 2021 Apr 22. PMID: 33886133.
15. Hugh JM, Weinberg JM. Update on the pathophysiology of psoriasis. *Cutis.* 2018 Nov;102(5S):6-12. PMID: 30566550.
16. Zachariae C, Skov L. Obesity as a risk factor for psoriasis. *J Eur Acad Dermatol Venereol.* 2020 May;34(5):915-916. doi: 10.1111/jdv.16434. PMID: 32441426.
17. Jensen P, Skov L. Psoriasis and Obesity. *Dermatology*. 2016;232(6):633-639. doi: 10.1159/000455840. Epub 2017 Feb 23. PMID: 28226326.
18. Fleming P, Kraft J, Gulliver WP, Lynde C. The Relationship of Obesity With the Severity of Psoriasis: A Systematic Review. *J Cutan Med Surg.* 2015 Sep-Oct;19(5):450-6. doi: 10.1177/1203475415586332. Epub 2015 May 7. PMID: 26271963.
19. Pezzolo E, Naldi L. The relationship between smoking, psoriasis and psoriatic arthritis. *Expert Rev Clin Immunol*. 2019 Jan;15(1):41-48. doi: 10.1080/1744666X.2019.1543591. Epub 2018 Nov 6. PMID: 30380949.
20. Fortes C, Mastroeni S, Leffondré K, Sampogna F, Melchi F, Mazzotti E, et al. Relationship between smoking and the clinical severity of psoriasis. *Arch Dermatol.* 2005 Dec;141(12):1580-4. doi: 10.1001/archderm.141.12.1580. PMID: 16365261.
21. Armstrong AW, Harskamp CT, Dhillon JS, Armstrong EJ. Psoriasis and smoking: a systematic review and meta-analysis. *Br J Dermatol.* 2014 Feb;170(2):304-14. doi: 10.1111/bjd.12670. PMID: 24117435.
22. Thorleifsdottir RH, Eysteinsdóttir JH, Olafsson JH, Sigurdsson MI, Johnston A, Valdimarsson H, et al. Throat Infections are Associated with Exacerbation in a Substantial Proportion of Patients with Chronic Plaque Psoriasis. *Acta Derm Venereol.* 2016 Aug 23;96(6):788-91. doi: 10.2340/00015555-2408. PMID: 26984718; PMCID: PMC4995120.
23. Kamiya K, Kishimoto M, Sugai J, Komine M, Ohtsuki M. Risk Factors for the Development of Psoriasis. *Int J Mol Sci.* 2019 Sep 5;20(18):4347. doi: 10.3390/ijms20184347. PMID: 31491865; PMCID: PMC6769762.
24. Lee EB, Wu KK, Lee MP, Bhutani T, Wu JJ. Psoriasis risk factors and triggers. *Cutis*. 2018 Nov;102(5S):18-20. PMID: 30566552.
25. Basavaraj KH, Ashok NM, Rashmi R, Praveen TK. The role of drugs in the induction and/or exacerbation of psoriasis. *Int J Dermatol.* 2010 Dec;49(12):1351-61. doi: 10.1111/j.1365-4632.2010.04570.x. PMID: 21091671.
26. Balak DM, Hajdarbegovic E. Drug-induced psoriasis: clinical perspectives. *Psoriasis (Auckl)*. 2017 Dec 7;7:87-94. doi: 10.2147/PTT.S126727. PMID: 29387611; PMCID: PMC5774610.
27. Alharbi NS, Almami IS. Activation and upregulation of keratinocyte and epidermal transglutaminases are associated with depletion of their substrates in psoriatic lesions. *Eur Rev Med Pharmacol Sci.* 2023 Dec 1;27(23). doi: 10.26355/eurrev_202312_34567.
28. Yan BX, Chen XY, Ye LR, Chen JQ, Zheng M, Man XY. Cutaneous and Systemic Psoriasis: Classifications and Classification for the Distinction. *Front Med (Lausanne)*. 2021 Oct 13;8:649408. doi: 10.3389/fmed.2021.649408. PMID: 34722555; PMCID: PMC8548430.
29. Raharja A, Mahil SK, Barker JN. Psoriasis: a brief overview. *Clin Med (Lond).* 2021 May;21(3):170-173. doi: 10.7861/clinmed.2021-0257. PMID: 34001566; PMCID: PMC8140694.
30. Griffiths CE, Christophers E, Barker JN, Chalmers RJ, Chimenti S, Krueger GG, Leonardi C, Menter A, Ortonne JP, Fry L. A classification of psoriasis vulgaris according to phenotype. *Br J Dermatol.* 2007 Feb;156(2):258-62. doi: 10.1111/j.1365-2133.2006.07675.x. PMID: 17223864.
31. Sarac G, Koca TT, Baglan T. A brief sum-

mary of clinical types of psoriasis. *North Clin Istanb*. 2016 Jun 14;3(1):79-82. doi: 10.14744/nci.2016.16023. PMID: 28058392; PMCID: PMC5175084.

32. Dhabale A, Nagpure S. Types of Psoriasis and Their Effects on the Immune System. *Cureus*. 2022 Sep 24;14(9):e29536. doi: 10.7759/cureus.29536. PMID: 36312680; PMCID: PMC9592057.

33. Zhou T, Koussiouris J, Kim L, Vender R. Management of Guttate Psoriasis: A Systematic Review. *J Cutan Med Surg*. 2024 Nov-Dec;28(6):577-584. doi: 10.1177/12034754241266187. Epub 2024 Jul 30. PMID: 39080843; PMCID: PMC11619194.

34. Leung AK, Barankin B, Lam JM, Leong KF. Childhood guttate psoriasis: an updated review. *Drugs Context.* 2023 Oct 23;12:2023-8-2. doi: 10.7573/dic.2023-8-2. PMID: 37908643; PMCID: PMC10615329.

35. Pfingstler LF, Maroon M, Mowad C. Guttate psoriasis outcomes. *Cutis*. 2016 Feb;97(2):140-4. PMID: 26919501.

36. Bachelez H. Pustular Psoriasis: The Dawn of a New Era. *Acta Derm Venereol.* 2020 Jan 30;100(3):adv00034. doi: 10.2340/00015555-3388. PMID: 31971600; PMCID: PMC9128889.

37. Menter A, Van Voorhees AS, Hsu S. Pustular Psoriasis: A Narrative Review of Recent Developments in Pathophysiology and Therapeutic Options. *Dermatol Ther (Heidelb)*. 2021 Dec;11(6):1917-1929. doi: 10.1007/s13555-021-00612-x. Epub 2021 Oct 9. PMID: 34626330; PMCID: PMC8611132.

38. Marrakchi S, Puig L. Pathophysiology of Generalized Pustular Psoriasis. *Am J Clin Dermatol*. 2022 Jan;23(Suppl 1):13-19. doi: 10.1007/s40257-021-00655-y. Epub 2022 Jan 21. PMID: 35061228; PMCID: PMC8801405.

39. Rivera-Díaz R, Daudén E, Carrascosa JM, Cueva P, Puig L. Generalized Pustular Psoriasis: A Review on Clinical Characteristics, Diagnosis, and Treatment. *Dermatol Ther (Heidelb).* 2023 Mar;13(3):673-688. doi: 10.1007/s13555-022-00881-0. Epub 2023 Jan 13. PMID: 36635445; PMCID: PMC9836924.

40. Bachelez H. Pustular psoriasis and related pustular skin diseases. *Br J Dermatol*. 2018 Mar;178(3):614-618. doi: 10.1111/bjd.16232. Epub 2018 Jan 15. PMID: 29333670.

41. Murakami M, Terui T. Palmoplantar pustulosis: Current understanding of disease definition and pathomechanism. *J Dermatol Sci.* 2020 Apr;98(1):13-19. doi: 10.1016/j.jdermsci.2020.03.003. Epub 2020 Mar 14. PMID: 32201085.

42. Kharawala S, Golembesky AK, Bohn RL, Esser D. The clinical, humanistic, and economic burden of palmoplantar pustulosis: a structured review. *Expert Rev Clin Immunol*. 2020 Mar;16(3):253-266. doi: 10.1080/1744666X.2019.1708194. Epub 2020 Feb 19. PMID: 32073337.

43. Maliyar K, Crowley EL, Rodriguez-Bolanos F, O'Toole A, Gooderham MJ. The Use of Biologic Therapy in the Treatment of Acrodermatitis Continua of Hallopeau: A Review. *J Cutan Med Surg.* 2019 Jul/Aug;23(4):428-435. doi: 10.1177/1203475419836435. Epub 2019 Apr 2. PMID: 30938189.

44. Smith MP, Ly K, Thibodeaux Q, Bhutani T, Liao W, Beck KM. Acrodermatitis continua of Hallopeau: clinical perspectives. *Psoriasis (Auckl).* 2019 Aug 9;9:65-72. doi: 10.2147/PTT.S180608. PMID: 31497529; PMCID: PMC6691962.

45. Galluzzo M, D'Adamio S, Teoli M, Bianchi L, Talamonti M. Biologic therapy for acrodermatitis continua of Hallopeau: Successful treatment with secukinumab and review of the literature. *Dermatol Ther.* 2019 May;32(3):e12899. doi: 10.1111/dth.12899. Epub 2019 Apr 29. PMID: 30969010; PMCID: PMC6618131.

46. Potestio L, Camela E, Cacciapuoti S, Fornaro L, Ruggiero A, Martora F, et al. Biologics for the Management of Erythrodermic Psoriasis: An Updated Review. *Clin Cosmet Investig Dermatol*. 2023 Aug 4;16:2045-2059. doi: 10.2147/CCID.S407813. PMID: 37560255; PMCID: PMC10408653.

47. Lo Y, Tsai TF. Updates on the Treatment of Erythrodermic Psoriasis. *Psoriasis (Auckl).* 2021 Jun 9;11:59-73. doi: 10.2147/PTT.S288345. PMID: 34136373; PMCID: PMC8200157.

48. Reynolds KA, Pithadia DJ, Lee EB, Liao W, Wu JJ. A systematic review of treatment strategies for erythrodermic psoriasis. *J Dermatolog Treat.* 2021 Feb;32(1):49-55. doi: 10.1080/09546634.2019.1689228. Epub 2019 Nov 12. PMID: 31682547.

49. Reynolds KA, Pithadia DJ, Lee EB, Wu JJ. Treatments for inverse psoriasis: a systematic

review. *J Dermatolog Treat.* 2020 Dec;31(8):786-793. doi: 10.1080/09546634.2019.1620912. Epub 2019 May 31. PMID: 31100992.
50. Micali G, Verzì AE, Giuffrida G, Panebianco E, Musumeci ML, Lacarrubba F. Inverse Psoriasis: From Diagnosis to Current Treatment Options. *Clin Cosmet Investig Dermatol.* 2019 Dec 31;12:953-959. doi: 10.2147/CCID.S189000. PMID: 32099435; PMCID: PMC6997231.
51. Knabel M, Mudaliar K. Histopathologic features of inverse psoriasis. *J Cutan Pathol.* 2022 Mar;49(3):246-251. doi: 10.1111/cup.14142. Epub 2021 Oct 19. PMID: 34611907.
52. Ocampo D V, Gladman D. Psoriatic arthritis. *F1000Res*. 2019 Sep 20;8:F1000 Faculty Rev-1665. doi: 10.12688/f1000research.19144.1. PMID: 31583079; PMCID: PMC6758836.
53. Perez-Chada LM, Merola JF. Comorbidities associated with psoriatic arthritis: Review and update. *Clin Immunol*. 2020 May;214:108397. doi: 10.1016/j.clim.2020.108397. Epub 2020 Mar 27. PMID: 32229290.
54. Karmacharya P, Chakradhar R, Ogdie A. The epidemiology of psoriatic arthritis: A literature review. *Best Pract Res Clin Rheumatol.* 2021 Jun;35(2):101692. doi: 10.1016/j.berh.2021.101692. Epub 2021 May 18. PMID: 34016528.
55. Smith CH, Barker JN. Psoriasis and its management. *Bmj*. 2006 Aug 17;333(7564):380-4. doi: https://doi.org/10.1136/bmj.333.7564.380
56. Young M, Aldredge L, Parker P. Psoriasis for the primary care practitioner. *J Am Assoc Nurse Pract.* 2017 Mar;29(3):157-178. doi: 10.1002/2327-6924.12443. Epub 2017 Feb 23. PMID: 28233460.
57. Alhammad IM, Aseri AM, Alqahtani SAM, Alshaebi MF, Alqahtani SA, Alzahrani RA, et al. A Review on Updates in Management and Treatment of Psoriasis. *Arch Pharm Pract.* 2021;12(1):74-8. https://doi.org/10.51847/g6sNNo5abA
58. Dutta S, Chawla S, Kumar S. Psoriasis: A review of existing therapies and recent advances in treatment. *J Rational Pharmacother Res.* 2018;4(1):12-23.
59. Rendon A, Schäkel K. Psoriasis Pathogenesis and Treatment. *Int J Mol Sci.* 2019 Mar 23;20(6):1475. doi: 10.3390/ijms20061475. PMID: 30909615; PMCID: PMC6471628.
60. Her M, Kavanaugh A. A review of disease activity measures for psoriatic arthritis: what is the best approach? *Expert Rev Clin Immunol.* 2014 Sep;10(9):1241-54. doi: 10.1586/1744666X.2014.943663. Epub 2014 Aug 4. PMID: 25088300.
61. Pariser DM, Bagel J, Gelfand JM, Korman NJ, Ritchlin CT, Strober BE, et al. National Psoriasis Foundation clinical consensus on disease severity. *Arch Dermatol*. 2007 Feb;143(2):239-42. doi: 10.1001/archderm.143.2.239. PMID: 17310004.
62. Gisondi P, Del Giglio M, Girolomoni G. Treatment Approaches to Moderate to Severe Psoriasis. *Int J Mol Sci.* 2017 Nov 16;18(11):2427. doi: 10.3390/ijms18112427. PMID: 29144382; PMCID: PMC5713395.
63. Maul JT, Anzengruber F, Conrad C, Cozzio A, Häusermann P, Jalili A, et al. Topical Treatment of Psoriasis Vulgaris: The Swiss Treatment Pathway. *Dermatology.* 2021;237(2):166-178. doi: 10.1159/000512930. Epub 2021 Jan 6. PMID: 33406520.
64. Elmets CA, Korman NJ, Prater EF, Wong EB, Rupani RN, Kivelevitch D, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol*. 2021 Feb;84(2):432-470. doi: 10.1016/j.jaad.2020.07.087. Epub 2020 Jul 30. PMID: 32738429.
65. Oranje AP, Marcoux D, Svensson A, Prendiville J, Krafchik B, Toole J, Rosenthal D, de Waard-van der Spek FB, Molin L, Axelsen M. Topical calcipotriol in childhood psoriasis. *J Am Acad Dermatol.* 1997 Feb;36(2 Pt 1):203-8. doi: 10.1016/s0190-9622(97)70281-0. PMID: 9039169.
66. Lee HJ, Kim M. Challenges and Future Trends in the Treatment of Psoriasis. *Int J Mol Sci.* 2023 Aug 28;24(17):13313. doi: 10.3390/ijms241713313. PMID: 37686119; PMCID: PMC10487560.
67. van de Kerkhof PC. An update on topical therapies for mild-moderate psoriasis. *Dermatol Clin.* 2015 Jan;33(1):73-7. doi: 10.1016/j.det.2014.09.006. PMID: 25412784.
68. Nakamura M, Farahnik B, Bhutani T. Recent advances in phototherapy for psoriasis.

F1000Res. 2016 Jul 13;5:F1000 Faculty Rev-1684. doi: 10.12688/f1000research.8846.1. PMID: 27499849; PMCID: PMC4946393.
69. Lapolla W, Yentzer BA, Bagel J, Halvorson CR, Feldman SR. A review of phototherapy protocols for psoriasis treatment. *J Am Acad Dermatol*. 2011 May;64(5):936-49. doi: 10.1016/j.jaad.2009.12.054. Epub 2011 Mar 22. PMID: 21429620.
70. Richard EG, Hönigsmann H. Phototherapy, psoriasis, and the age of biologics. P*hotodermatol Photoimmunol Photomed*. 2014 Feb;30(1):3-7. doi: 10.1111/phpp.12088. Epub 2013 Dec 3. PMID: 24313462.
71. Racz E, Prens EP. Phototherapy and photochemotherapy for psoriasis. *Dermatol Clin.* 2015 Jan;33(1):79-89. doi: 10.1016/j.det.2014.09.007. PMID: 25412785.
72. Armstrong AW, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. *JAMA.* 2020 May 19;323(19):1945-1960. doi: 10.1001/jama.2020.4006. PMID: 32427307.
73. Jiang Y, Chen Y, Yu Q, Shi Y. Biologic and Small-Molecule Therapies for Moderate-to-Severe Psoriasis: Focus on Psoriasis Comorbidities. *BioDrugs.* 2023 Jan;37(1):35-55. doi: 10.1007/s40259-022-00569-z. Epub 2023 Jan 2. PMID: 36592323; PMCID: PMC9837020.
74. Campanati A, Paolinelli M, Diotallevi F, Martina E, Molinelli E, Offidani A. Pharmacodynamics OF TNF α inhibitors for the treatment of psoriasis. *Expert Opin Drug Metab Toxicol.* 2019 Nov;15(11):913-925. doi: 10.1080/17425255.2019.1681969. Epub 2019 Oct 29. PMID: 31623470.
75. Reid C, Griffiths CEM. Psoriasis and Treatment: Past, Present and Future Aspects. *Acta Derm Venereol*. 2020 Jan 30;100(3):adv00032. doi: 10.2340/00015555-3386. PMID: 31971601; PMCID: PMC9128930.
76. Wcisło-Dziadecka D, Kaźmierczak A, Grabarek B, Zbiciak-Nylec M, Brzezińska-Wcisło L. Are new variants of psoriasis therapy (IL-17 inhibitors) safe? *Int J Dermatol.* 2019 Dec;58(12):1360-1365. doi: 10.1111/ijd.14509. Epub 2019 Jun 13. PMID: 31192456.
77. Ghoreschi K, Balato A, Enerbäck C, Sabat R. Therapeutics targeting the IL-23 and IL-17 pathway in psoriasis. *Lancet.* 2021 Feb 20;397(10275):754-766. doi: 10.1016/S0140-6736(21)00184-7. Epub 2021 Jan 27. PMID: 33515492.
78. Ten Bergen LL, Petrovic A, Krogh Aarebrot A, Appel S. The TNF/IL-23/IL-17 axis-Head-to-head trials comparing different biologics in psoriasis treatment. *Scand J Immunol.* 2020 Oct;92(4):e12946. doi: 10.1111/sji.12946. PMID: 32697374.
79. Jeon C, Sekhon S, Yan D, Afifi L, Nakamura M, Bhutani T. Monoclonal antibodies inhibiting IL-12, -23, and -17 for the treatment of psoriasis. *Hum Vaccin Immunother.* 2017 Oct 3;13(10):2247-2259. doi: 10.1080/21645515.2017.1356498. PMID: 28825875; PMCID: PMC5647990.
80. Hoffman MB, Hill D, Feldman SR. Current challenges and emerging drug delivery strategies for the treatment of psoriasis. *Expert Opin Drug Deliv.* 2016 Oct;13(10):1461-73. doi: 10.1080/17425247.2016.1188801. Epub 2016 May 25. PMID: 27164301.
81. Sun X, Cui Z, Wang Q, Liu L, Ding X, Wang J, Cai X, Li B, Li X. Formation and clinical effects of anti-drug antibodies against biologics in psoriasis treatment: An analysis of current evidence. *Autoimmun Rev*. 2024 Apr;23(4):103530. doi: 10.1016/j.autrev.2024.103530. Epub 2024 Mar 17. PMID: 38499168.
82. Kvist-Hansen A, Hansen PR, Skov L. Systemic Treatment of Psoriasis with JAK Inhibitors: A Review. *Dermatol Ther (Heidelb).* 2020 Feb;10(1):29-42. doi: 10.1007/s13555-019-00347-w. Epub 2019 Dec 31. PMID: 31893355; PMCID: PMC6994544.
83. Balogh EA, Bashyam AM, Ghamrawi RI, Feldman SR. Emerging systemic drugs in the treatment of plaque psoriasis. *Expert Opin Emerg Drugs.* 2020 Jun;25(2):89-100. doi: 10.1080/14728214.2020.1745773. Epub 2020 Mar 31. PMID: 32192366.