Psoriasis

Psoriasis is a chronic disease in which the immune system becomes overactive, causing skin cells to multiply too quickly and shed every 3 to 4 days. This results in patches of thick red skin and silvery scales that are typically found on the elbows, knees, scalp, and lower back as well as other parts of the body. Other symptoms can include dry, cracked skin that itches or bleeds and thick, ridged, pitted nails. Symptoms can sometimes go through cycles, flaring for a few weeks or months followed by periods when they subside or go into remission.

According to the National Psoriasis Foundation, more than 8 million people in the United States have psoriasis. It can be diagnosed at any age, but onset often occurs between 20 and 30 years of age or between 50 and 60 years of age. Men and women seem to have equal risk, but it appears to be more common in non-Hispanic whites.

Psoriasis is not just a cosmetic concern. Individuals with psoriasis are at risk for having other serious conditions. An estimated 30 percent of patients with psoriasis develop psoriatic arthritis, a chronic form of arthritis that causes pain, swelling, and stiffness of the joints. Patients also experience higher rate of comorbidities, including cardiovascular disease, heart attack, stroke, anxiety, and depression. Finally, people with psoriasis have an increased risk of certain cancers, Crohn's disease, diabetes, metabolic syndrome, obesity, osteoporosis, liver disease, and kidney disease.

Scientists do not fully understand what causes psoriasis, but they know it is not contagious. Instead, it involves a mix of genetics and environmental factors. Many people with psoriasis have a family history of the disease, and researchers have pinpointed some of the genes that may contribute to its development. Most of the identified genes play a role in immune system function. External factors that may increase the chances of developing psoriasis include cold or dry weather conditions, smoking, heavy alcohol use, obesity, and infections, especially streptococcal and HIV infections. Certain medicines, such as drugs for treating heart disease, malaria, or mental health problems may also enhance the risk of developing psoriasis.

While there is currently no cure for psoriasis, there are treatments that keep symptoms under control to help patients resume daily activities and sleep better. To determine the best treatment, several factors are considered including location on the body, disease severity, how much skin is affected, other comorbidities, the efficacy and safety profile of each therapy option, and patient preference. The severity of plaque psoriasis is generally defined by the total body surface area (BSA) involved. The Joint American Academy of Dermatology–National Psoriasis Foundation (JAAD–NPF) guidelines consider BSAs of <3%, 3% to 10%, and >10% as mild, moderate, and severe disease, respectively. The JAAD/NPF guidelines also note that psoriasis can be considered severe irrespective of BSA when it occurs in select locations like the hands, feet, scalp, face, or genital area, or when it causes significant itching.

The American Academy of Dermatology psoriasis treatment guidelines recommend topical corticosteroids for first line therapy in limited disease that encompasses less than 5% of body surface area. Corticosteroids slow cell growth while exerting anti-inflammatory and immunosuppressive actions. Vitamin D analogs such as calcipotriene, calcipotriol, and calcitriol, are other first line agents and are often used in combination with topical corticosteroids. Like corticosteroids, they are thought to work by slowing down skin cell growth. Most patients with mild disease can be managed with one or more topical agents.

For moderate-to-severe psoriasis, three categories of treatments are usually considered: phototherapy, conventional oral medications, and biologic medications. Phototherapy, or light therapy, uses specific ultraviolet light wavelengths to treat psoriasis. Phototherapy is typically given 2 to 3 times per week in a dermatologist's office.

Both oral and biologic medications are systemic medications, which means that they affect not only the skin but also other parts of the body. Some of the most utilized conventional oral agents include cyclosporine, methotrexate, or acitretin. While cyclosporin and methotrexate work differently, they both suppress the immune system and slow skin growth. Acitretin is a retinoid, or vitamin A derivative, and helps to normalize the speed of skin cell growth. In addition to these conventional oral agents, other newer oral therapies are also available to treat various forms of psoriasis. Otezla® (apremilast), an oral phosphodiesterase-4 (PDE-4) inhibitor, is an option for patients with mild disease who are inadequately controlled with topical therapies. Otezla works by suppressing the immune system and reducing inflammation. Sotyktu® (deucravacitinib), a tyrosine kinase 2 (TYK2) inhibitor, was recently approved to treat adults with moderate to severe plaque psoriasis.

Biologic medications are generally used when one or more traditional agents fail to produce an adequate response. Most biologics work by reducing specific inflammation molecules that are abnormally elevated in psoriasis. There are currently three categories of biologics that block different points in the psoriasis inflammatory process: tumor necrosis factor Inhibitors (TNF), interleukin (IL) antagonists, and tyrosine kinase-2 (TYK2) blockers. All TNF inhibitors have a boxed warning for serious infections and malignancies.

Over the last 18 months, additional treatment options for psoriasis have become available. The following products have not yet been included in the most recent treatment guidelines that were last updated in 2021.

On September 9, 2022, the FDA approved Sotyktu® (deucravacitinib), to treat adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy. The oral drug is the first tyrosine kinase 2 (TYK2) inhibitor to gain FDA approval for any condition. TYK2 is an enzyme responsible for causing inflammation in the body and part of a pathway in the body's immune response system. TYK2 inhibitors block the function of these enzymes, with the goal of reducing or preventing inflammation. The approval of Sotyktu was based on results from the Phase 3 POETYK PSO-1 and POETYK PSO-2 clinical trials, both of which compared Sotyktu head-to-head with Otezla as well as with placebo in a total of 1,684 study participants. The co-primary endpoints of both POETYK PSO-1 and POETYK PSO-2 were the percentage of patients who achieved Psoriasis Area and Severity Index (PASI) 75 and the percentage of patients who achieved static Physician's Global Assessment (sPGA) score of 0 or 1 at week 16 versus placebo. Psoriasis Area and Severity Index (PASI) and static Physician's Global Assessment (sPGA) are two commonly used measures for assessing skin clearing. At week 16, in POETYK PSO-1, 53% of Sotyktu-treated patients, 9.4% of placebo patients, and 39.8% of Otezla-treated patients achieved ≥75% reduction from baseline in PASI and a physician's global assessment score of 0/1 in 54%, 7%, and 32% respectively. In POETYK PSO-2, PASI 75 was achieved at week 16 in 53% of Sotyktu-treated patients versus 9% and 40% of placebo and Otezla-treated patients respectively. A physician's global assessment score of 0 or 1 was achieved in 50% of Sotyktu-treated patients vs 9% and 34% of placebo and Otezla patients. In both studies efficacy was maintained until week 52 with continuous Sotyktu. To date, there have been no head-to-head studies comparing Sotyktu to TNF inhibitors or IL antagonists. As oral tablets, Otezla and Sotyktu could be more appealing to patients who do not want to treat their condition with an injectable drug.

During 2022, the FDA approved two new topical treatments for plaque psoriasis: Zoryve® (roflumilast) and Vtama® (tapinarof). Zorvyve cream is the first topical phosphodiesterase-4 (PDE-

4) inhibitor approved for treatment of mild, moderate, and severe plaque psoriasis in patients 12 years of age or older. The approval was based on results from the pivotal DERMIS-1 and DERMIS-2 Phase 3 studies. Zoryve improved the severity and impact of itch, as early as Week 2. In both studies, Zoryve improved overall signs and symptoms of psoriasis at Weeks 4 and 8 compared to placebo. Of the individuals who continued treatment with Zoryve for at least 52 weeks in an open-label long-term safety trial, 45% evaluated as "Clear" or "Almost Clear" at Week 52. Unlike topical steroids, Zoryve does not have limitations on the duration of treatment or where on the body it may be applied. Topical corticosteroids should not be used on the face for more than two weeks and other parts of the body for more than a few months depending on potency.

Vtama cream was approved in May 2022 for the treatment of adults with mild, moderate or severe plaque psoriasis. It has a novel mechanism of action as an aryl hydrocarbon receptor (AhR) agonist. Vtama is thought to act by downregulating inflammatory proteins, as well as promoting skin barrier. The approval was based on findings from identical phase 3 trials, PSOARING 1 and PSOARING 2, that had over 1,000 study participants. In the PSOARING-1 study, after 12 weeks, 36% of patients treated with Vtama cream achieved clear or almost clear skin, compared with just 6% of patients treated with placebo. In the PSOARING-2 study, 40% of the patients who were treated with Vtama cream achieved clear or almost clear skin versus 6% with placebo. Like Zoryve, Vtama does not have limitations on the duration of treatment and is safe to apply anywhere on the body.

Most recently, during 2023, nine biosimilars for Humira (adalimumab) launched in the market and are FDA approved to treat psoriasis. Like Humira, its biosimilars are administered via a subcutaneous injection. Some of the biosimilar manufacturers have made their products available at a significant discount to Humira creating more competition and treatment options for patients with psoriasis. Additional adalimumab biosimilars are expected to become available in 2024.

Overview of Newer FDA Approved Medications to Treat Psoriasis

Drug	Manufacturer	Therapeutic Category		Route of Administration	Maintenance Dosing Schedule
TNF Inhibitors					
Humira®[a] (adalimumab)	AbbVie	TNF Inhibitor		Subcutaneous injection	Q 2 weeks
Enbrel®[b] (etanercept)	Amgen	TNF Inhibitor		Subcutaneous injection	Once weekly
Remicade®[c] (infliximab)	J&J	TNF Inhibitor		Intravenous infusion	Q 8 weeks
Cimzia® (certolizumab)	UCB	TNF Inhibitor		Subcutaneous injection	Q 2 weeks
IL Antagonists					
Stelara®[d] (ustekinumab)	J&J	IL-23, IL-12 Antagonist		Subcutaneous injection	Q 12 weeks

Drug	Manufacturer	Therapeutic Category		Route of Administration	Maintenance Dosing Schedule
Tremfya® (guselkumab)	J&J	IL-23 Antagonist		Subcutaneous injection	Q 8 weeks
Ilumya® (tildrakizumab)	Sun	IL-23 Antagonist		Subcutaneous injection	Q 12 weeks
Skyrizi® (Risankizumab	AbbVie	IL-23 Antagonist		Subcutaneous injection	Q 12 weeks
Cosentyx® (secukinumab)	Novartis	IL-17 Antagonist		Subcutaneous injection	Q 4 weeks
Taltz® (ixekizumab)	Lilly	IL-17 Antagonist		Subcutaneous injection	Q 4 weeks
Siliq® (brodalumab)	AZ	IL-17R Antagonist		Subcutaneous injection	Q 2 weeks
Orals					
Sotyktu® (deucravacitinib)	BMS	TYK2 inhibitor		Oral	Once daily
Otezla® (apremilast)	Amgen	PDE4 Inhibitor		Oral	Twice daily
Topicals					
Zoryve® (roflumilast)	Arcutis Biotherapeutics	PDE4 Inhibitor		Topical	Once daily
Vtama® (tapinarof)	Dermavant Sciences	AhR) agonist		Topical	Once daily

a Numerous biosimilars to Humira have been approved and launched into the market.
b Biosimilars approved but not launched.
c Biosimilars to Remicade are approved and launched into the market.
d Biosimilar competition to Stelara is anticipated to begin in 2025.

While there are several investigational medications in advanced clinical trials for plaque psoriasis. Bimzelx (bimekizumab) appears closest to FDA approval. This a subcutaneous treatment may be approved in early 2024. Bimekizumab is an interleukin (IL) antagonist and utilizes a combination approach against two different interleukins to decrease the inflammatory process in psoriasis. During three separate head-to-head clinical studies, bimekizumab was more successful at treating psoriasis than three of its biggest competitors including Stelara, Humira, and Cosentyx. In one study comparing bimekizumab to Stelara, 85% of patients in the bimekizumab group had PASI-90 versus 50% in the Stelara group at week 16. PASI or the Psoriasis Area and Severity Index is the most widely used tool for the measurement of severity of psoriasis. PASI-90 indicates a 90% or greater reduction in PASI scores from baseline and is indicative of excellent disease improvement. Likewise, in a separate study versus Humira, 86% of patients who received bimekizumab and 47% who

received Humira had a PASI 90 response at week 16. Finally, in another study, when compared to Cosentyx at week 16, almost 62% in the bimekizumab group and 49% in the Cosentyx group had a 100% reduction from baseline in the PASI score (PASI 100). Results from a two-year extension study demonstrated its efficacy to be long-lasting in a large majority of patients who responded at week 16. Despite its demonstrated effectiveness, uptake may be a challenge with its late entry into the market against several competing, very effective products. Additionally, as previously stated, multiple biosimilars to Humira are now available and Stelara biosimilars are expected to start entering the market starting in January 2025.

Psoriasis is a complex skin disorder with significant physical and emotional impacts on affected individuals. The disease also puts patients at risk for other comorbidities. Despite the progress in understanding the underlying mechanisms of psoriasis and the development of various treatment options, challenges remain in achieving optimal outcomes. The available topical treatments for mild psoriasis can effectively control symptoms in many cases, however, there is a need for more targeted and effective systemic therapies for patients who do not respond adequately to topical treatments. While biologic agents have shown high response rates, there is a subset of patients who may not respond to these treatments. Fortunately, the future of psoriasis treatment looks promising with the emergence of additional novel biologic agents targeting new specific inflammatory pathways as well as more biologic agents available in oral formulations. These agents offer the potential for enhanced efficacy, better disease control and improved compliance with the goal of improved outcomes and a better quality of life for individuals living with this chronic skin condition.

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