Plaque Psoriasis

Psoriasis is a chronic disease in which the immune system becomes overactive, causing skin cells to multiply too quickly and shed every three to four 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.

It is estimated that 60 million people worldwide have psoriasis, with the prevalence varying by geographic region. In Western Europe, the prevalence rate is estimated to be 2.5 percent, while in some countries in Northern Europe, the prevalence rate is as high as 10 percent. Psoriasis can be diagnosed at any age, but it is more common in adults than children. 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.

Several distinctive clinical variants of psoriasis are recognised, with plaque psoriasis (also referred to as psoriasis vulgaris) being the most common. Other variants include guttae psoriasis, nail psoriasis, pustular psoriasis and psoriatic arthritis (PsA). About 80 to 90 percent of people with psoriasis have plaque psoriasis, either alone or in combination with another type of the disease.

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 PsA, a chronic form of arthritis that causes pain, swelling, and stiffness of the joints. They also experience higher rate of comorbidities, including cardiovascular disease, heart attack, stroke, anxiety, and depression. In addition, they 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 do 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. When choosing the most appropriate treatment, several factors are taken into consideration including disease severity, location on the body, 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. Psoriasis Area and Severity Index (PASI) is the most established parameter to measure the severity of skin symptoms in psoriasis.

The 2011 European Consensus Programme defined moderate-to-severe disease as (PASI > 10 or BSA > 10) AND Dermatology Life Quality Index [DLQI] > 10. Mild disease was defined as PASI ≤ 10 AND BSA ≤ 10 AND DLQI ≤ 10. It also noted that the disease can be moderate-to-severe if there is major involvement of visible areas, major involvement of the scalp, involvement of genitals, onycholysis or onychodystrophy of at least two fingernails, presence of itch leading to scratching or the presence of recalcitrant plaques.

Following the European consensus, discussions regarding the definition of disease severity continue to evolve. For example, the International Psoriasis Council (IPC) preferred definition is that psoriasis patients should be classified as either candidates for topical therapy or candidates for systemic

therapy. The latter are patients who meet at least one of the following criteria: (1) BSA >10%, (2) disease involving special areas, and (3) failure of topical therapy.

Often, topical corticosteroids are recommended for first line therapy in limited disease that encompasses less than 5% of BSA. Corticosteroids slow cell growth while exerting anti-inflammatory and immunosuppressive actions. Vitamin D analogues are frequently used in combination with corticosteroids and 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 treatment categories are usually considered: phototherapy, conventional oral medications, and biologic medications.

According to the EuroGuiDerm Guideline for the systemic treatment of Psoriasis Vulgaris, safety, efficacy, time to onset of treatment response, comorbidities and individual patient factors should be taken into account when choosing a systemic treatment. National regulations and reimbursement status also need to be considered.

Conventional systemic agents are recommended as first line treatment in the majority of patients. Some of the most utilised conventional oral agents include cyclosporine, methotrexate and acitretin. While cyclosporine and methotrexate have different mechanisms of action, they both suppress the immune system and slow skin growth. Acitretin is a retinoid, or vitamin A derivative, and helps to normalise the speed of skin cell growth.

In addition to these conventional agents, other newer oral therapies are available to treat psoriasis, namely Otezla® (apremilast) and Sotyktu® (deucravacitinib). Otezla® is a phosphodiesterase-4 (PDE-4) inhibitor, approved for use adults with moderate-to-severe chronic plaque psoriasis who are inadequately controlled or have a contraindication to systemic therapies including cyclosporine, methotrexate or psoralen and ultraviolet-A light (PUVA). The EuroGuiDerm Guideline recommends Otezla® is used if oral treatment is desired and conventional agents have failed or are contraindicated. Sotyktu®(deucravacitinib) is a tyrosine kinase 2 (TYK2) inhibitor, approved for use in adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy. The marketing authorization approval for Sotyktu® was granted subsequent to the EuroGuiDerm Guideline being written.

The EuroGuiDerm Guideline recommends use of a biologic agent when conventional agents are inadequate in eliciting a response. They also suggest that in the case of severe disease, where a sufficient treatment response cannot be expected with the use of conventional agents, that a biologic with a first line label is considered first line. Most biologics function by reducing specific inflammatory molecules that are abnormally elevated in psoriasis. Currently, there are three categories of biologics that target various stages in the psoriasis inflammatory process: tumour necrosis factor (TNF) inhibitors, interleukin (IL) antagonists, and tyrosine kinase-2 (TYK2) blockers.

Overview of Biologic and Newer EMA Approved Medications to Treat Plaque Psoriasis

Drug	Manufacturer	Therapeutic Category		Route of Administration	
TNF Inhibitors					
Humira®[a] (adalimumab)	AbbVie	TNF-α inhibitor		Subcutaneous injection	
Enbrel® (etanercept)	Amgen	TNF-α inhibitor		Subcutaneous injection	
Remicade®[b] (infliximab)	MSD	TNF-α inhibitor		Intravenous infusion	
Cimzia® (certolizumab)	UCB Pharma	TNF-α inhibitor		Subcutaneous injection	
IL Antagonists					
Stelara® (ustekinumab)	Janssen	IL-12, IL-23 antagonist		Subcutaneous injection	
Tremfya® (guselkumab)	Janssen	IL-23 antagonist		Subcutaneous injection	
Ilumetri® (tildrakizumab)	Almirall	IL-23 antagonist		Subcutaneous injection	
Skyrizi® (risankizumab	AbbVie	IL-23 antagonist		Subcutaneous injection	
Cosentyx® (secukinumab)	Novartis	IL-17 antagonist		Subcutaneous injection	
Taltz® (ixekizumab)	Lilly	IL-17 antagonist		Subcutaneous injection	
Kyntheum® (brodalumab)	Leo Pharma	IL-17 antagonist		Subcutaneous injection	
Bimzelx® (bimekizumab)	UCB Pharma	IL-17 antagonist		Subcutaneous injection	
Orals					
Sotyktu® (deucravacitinib)	BMS	TYK2 inhibitor		Oral	
Otezla® (apremilast)	Amgen	PDE-4 Inhibitor		Oral	

a Biosimilars to Humira have been approved and launched into the market.

Drug	Manufacturer	Therapeutic Category		Route of Administration	
b Biosimilars to Remicade are approved and launched into the market.					

Psoriasis is a complex skin disorder that significantly impacts the physical and emotional well-being of those affected. Moreover, it increases the risk of other comorbidities. Despite the progress in understanding the underlying mechanisms of psoriasis and the development of various treatment options, challenges persist in achieving optimal outcomes. While topical treatments can effectively control symptoms in many cases of mild psoriasis, there is a need for more targeted and effective systemic therapies for patients who do not respond adequately. Although biologic agents have shown high response rates, there is still 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 and better disease control. They also improve 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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