PHARMACIST & TECHNICIAN CE:

# Getting Under the Skin: New Medications for Dermatologic Conditions

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CE FOR **PHARMACISTS & TECHNICIANS**

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### Learning Objectives

- Describe the pathophysiology and symptoms of plaque psoriasis, generalized pustular psoriasis flares, and atopic dermatitis.
- Describe the mechanism of action for newly approved dermatologic agents.
- Describe the anticipated place in therapy for newly approved dermatological agents.
- List adverse effects for newly approved dermatological agents.

Plaque psoriasis is a chronic and complex inflammatory disease that predominantly affects the skin. It often presents as inflamed, red, scaly plaques.[1] This condition is caused by uncontrolled keratinocyte proliferation, or adaptive and innate immune system dysregulation or alterations, and primarily involves cytokines tumor necrosis factor alpha (TNF-α), interleukin-17 (IL-17), and IL-23.[2] Generalized pustular psoriasis (GPP) is a rarer variation of the disease that is influenced by a different cytokine pathway and involves a mutation in the interleukin 36 receptor antagonist (IL-36RN).[2,3] Atopic dermatitis (AD) is another chronic inflammatory condition of the skin characterized by episodic flares and periods of remission. Mechanisms involved include epidermal barrier dysfunction, genetics, and dysregulation of the immune system.[4]

Treating these conditions' physical symptoms is crucial because they have the strong potential to affect a person's quality of life.[5] Physical symptoms can also impact the patient's relationships and family. Psychosocial symptoms can arise leading to social avoidance, missing work or school, and economic burdens. These symptoms can lead to mental health disorders such as anxiety and depression.[5,6] Alleviating the physical symptoms can combat some of these possible consequences.

The mainstays of treatment for both psoriasis and AD, particularly for mild disease, are topical medications.[6,7] However, for patients with more severe disease and larger areas of affected body surface area, treatment regimens frequently must incorporate oral systemic therapies or injectable biologics to gain symptom control.[6,8,9] Some patients remain uncontrolled after multiple trials of currently available agents, leading to a demand for the novel treatments discussed in this review. Fortunately, in the past few years, the recent approval of new dermatologic drugs have offered hope. This review will cover six recently approved dermatological medications (Table 1).

## Deucravacitinib

Deucravacitinib is the first selective, tyrosine kinase 2 (TK2) inhibitor to receive Food and Drug Administration (FDA) approval in September of 2022 for the treatment of moderate –to severe plaque psoriasis in adults.[10] There are also currently clinical trials investigating its use in other forms of psoriasis, psoriatic arthritis, alopecia areata, Crohn's disease, ulcerative colitis, and systemic lupus erythematosus. TK2 is a member of the janus kinase (JAK) family that mediates signaling of IL-23 and other cytokines involved in immune-mediated inflammatory diseases.[11-13] TK2 binds with either JAK1 or JAK2 to form dimers, which mediate multiple cytokine pathways and transmit signals, respectively. Deucravacitinib works by locking the regulatory and catalytic domains of TYK2 in an inhibitory confirmation. This leads to downregulation of signal transducers and activators of transcription (STATs)

## Acronyms

**AD -** Atopic dermatitis
**AhR -** Aryl hydrocarbon receptor
**BCRP -** Breast cancer resistance protein
**DRESS -** Drug rash with eosinophilia and systemic symptoms
**FDA -** Food and Drug Administration
**EASI -** Eczema area and severity index
**GPP -** Generalized pustular psoriasis
**GPPGA -** Generalized pustular psoriasis physician global assessment
**IL -** Interleukin
**IL36RN -** Interleukin 36 receptor antagonist
**IGA -** Investigator's global assessment
**JAK -** Janus kinase
**PDE-4 -** Phosphodiesterase 4 inhibitors
**PASI -** Psoriasis Areaand Severity Index
**PGA -** Physician's global assessment
**STATs -** Signal transducers and activators of transcription
**sPGA 0/1 -** Static physician's global assessment
**TNF-α -** Tumor necrosis factor alpha
**TK2 -** Tyrosine kinase 2

**TABLE 1. Review of Recently Approved Medications for Dermatologic Conditions**

| Name | Class | Approved for | Dose | Common Adverse Effects | Significant Adverse Reactions |
|---|---|---|---|---|---|
| Abrocitinib (Cibinqo™) | JAK inhibitor | Atopic dermatitis | 100 mg once daily. May increase dose to 200 mg once daily after 12 weeks | • Infection (35%)<br>• Nasopharyngitis (9-12%)<br>• Nausea (6-15%) | • Cardiovascular/ thrombotic events<br>• Infection<br>• Malignancies |
| Deucravacitinib (Sotyktu®) | TK2 inhibitor | Plaque psoriasis | 6 mg once daily | • Infection (29%)<br>• Upper respiratory tract infection (19%) | Infection |
| Roflumilast 0.3% cream (Zoryve®) | PDE-4 inhibitor | Plaque psoriasis | Apply once daily | • Diarrhea (3%)<br>• Headache 2%) | Not Applicable |
| Spesolimab-sbzo (Spevigo®) | IL-36 antagonist | Generalized pustular psoriasis | 900 mg via IV once; if flare persists, an additional 900 mg may be given one week later | Infection (14%) | Infection |
| Tapinarof 1% cream (Vtama®) | aryl hydrocarbon receptor agonist | Plaque psoriasis | Apply a thin layer to the affected area once daily | • Folliculitis (20%)<br>• Nasopharyngitis (11%) | Not Applicable |
| Tralokinumab-ldrm (Adbry®) | IL-13 antagonist | Atopic dermatitis | 600 mg (four 150 mg injections) once, then 300 mg (two 150 mg injections) every other week | Upper respiratory tract infection (24%) | Ocular effects (conjunctivitis) |

*IL = interleukin; IV = intravenous; JAK = Janus kinase; PDE = phosphodiesterase; TK - tyrosine kinase*

via allosteric inhibition of receptor-mediated activation of TYK2. It is not fully understood how the inhibition of TYK2 works to effectively treat adults with moderate –to severe plaque psoriasis. Deucravacitinib comes as a 6-mg tablet that is taken once daily.

The efficacy and safety of deucravacitinib was investigated in POETYK PSO-1 and POETYK PSO-2, which are companion, phase 3 clinical trials that compared deucravacitinib to placebo and apremilast in moderate to severe plaque psoriasis.[11,12] Both were multicenter, randomized, double-blind, double-dummy, placebo, and active-controlled trials that took place over the course of 52 weeks. Participants were included in the studies if they were age 18 or older, had moderate to severe plaque psoriasis for a duration for 6 months or longer, were eligible for systemic treatment or phototherapy, had not received apremilast or deucravacitinib previously, and underwent a washout period if they were receiving treatment with other medications. Patients (n = 1,684) were randomized 2:1:1 to receive deucravacitinib 6 mg every day, placebo, or apremilast 30 mg twice a day. The coprimary endpoints that were assessed at week 16 in both clinical trials were a ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) and static Physician's Global Assessment score of 0 or 1 (sPGA 0/1) with at least a 2-point improvement from baseline. For both trials, deucravacitinib had statistically significant higher response rates than placebo or apremilastfor PASI 75 (PSO-1: 58.4% vs 12.7% vs 35.1%, respectively, p<0.0001 for both comparisons; PSO-2: 53.0% vs 9.4% and 39.8%, respectively, p<0.0001 vs placebo, p =0.0004 vs apremilast) and sPGA 0/1 (PSO-1: 53.6% vs 7.2% vs 32.1%, respectively, p<0.0001 for both comparisons; PSO-2: 49.5% vs 8.6% vs 33.9%, respectively p<0.0001 for both comparisons). Efficacy improved beyond week 16 and was maintained by trial completion. Deucravacitinib was also able to demonstrate improvements in secondary outcomes such as PASI 90, PASI 100, sPGA 0, measures of clear skin and improvements in scalp psoriasis, psoriasis symptoms, and quality of life at higher rates than the placebo and apremilast groups.

As an immunosuppressant medication, deucravacitinib does come with numerous warnings and precautions. It may increase the risk of infections, which could require patients to temporarily discontinue treatment until the illness resolves.[11-13] Because deucravacitinib suppresses the immune system, patients should be evaluated and, if necessary, treated for tuberculosis prior to initiating treatment. Also, the package labeling indicates patients should avoid live vaccines while taking deucravacitinib.[13] During the PSO-1 and PSO-2 trials, there were 3 participants who developed malignancies.[11,12] Elevations in liver enzymes, creatinine phosphokinase, and triglycerides have been observed in patients treated with deucravacitinib.[11-13] Monitoring patients for liver injury and rhabdomyolysis is also necessary. TYK2 inhibition may carry the same risks related to JAK inhibition, which include higher rates of all-cause mortality (sudden cardiovascular death, major adverse cardiovascular events, thrombosis, and malignancies). Currently, the only contraindication for this medication is known hypersensitivity to the agent or its excipients. In vitro, drug interaction studies revealed that deucravacitinib is a substrate of P-glycoprotein, breast cancer resistance protein (BCRP), and organic cation transporter 1, and it is an inhibitor of BCRP and organic anion transporting polypeptide 1B3.

During the 52 weeks of the PSO-1 and PSO-2 trials, adverse events were reported in 74.4% (395/531) and 72.0% (600/833) of participants receiving deucravacitinib and 42.4% (70/165) and 55.3% (277/501) of participants in the placebo group.[11,12]

The most common adverse events for patients receiving deucravacitinib through week 16 in the PSO-1 and PSO-2 trials were upper respiratory infections (19.2%), elevated blood creatine phosphokinase (2.7%), herpes simplex (2.0%), mouth ulcers (1.9%), folliculitis (1.7%), and acne (1.4%).[13] Participants completing 52 weeks of therapy were eligible to enroll in a single-arm, open-label extension trial to further evaluate safety, tolerability, and efficacy with an estimated completion date in July, 2026.[11,12,14] Limited data exists to provide safe recommendations for use in special populations.[13] However, in animal reproduction studies, no effects on embryo-fetal development were observed in rabbits and rats when given doses at least 91 times the maximum recommended human dose. Deucravacitinib was also present in rat milk, which suggests that it would also be excreted in human milk. Safe and effective use in the pediatric population has not been established. For older adult patients (≥ 65 years old), there were higher rates of overall serious adverse reactions, including serious infections, and discontinuations due to adverse reactions through week 16. It appears that efficacy was consistent among all ages studied.

Most patients with mild to moderate plaque psoriasis are effectively treated with topical medications, so the use of deucravacitinib should be reserved for those with moderate to severe plaque psoriasis who are candidates for systemic or phototherapy.[7,13] Also, because this is a newly approved, branded medication, patients will likely need to fail methotrexate, retinoids, cyclosporine, apremilast, and/or immune-modifying, biologic agents. Deucravacitinib should not be used in combination with other potent immunosuppressant medications.[13] The use of combination treatment with a topical medication and deucravacitinib has not been evaluated for safety and efficacy, but dermatologists may decide to also prescribe topical agents. The Journal of American Academy of Dermatology's most recent guidelines were published in 2020, which predates the approval of deucravacitinib.[8]

## Tapinarof

Tapinarof 1% cream, sold under the brand name Vtama©, is a topical agent approved for the treatment of plaque psoriasis in adult patients.[15] This medication received FDA approval in May of 2022 and is the first topical, novel, chemical entity launched for the indication of psoriasis in approximately 25 years. Tapinarof is an aryl hydrocarbon receptor (AhR) agonist which downregulates interleukin 17 and promotes skin-barrier protein expression along with antioxidant activity. The specific mechanism of tapinarof related to psoriasis treatment is not known. Tapinarof is available as a 60-gram tube of 1% cream that is applied to affected areas once daily. Tapinarof may be used in all affected areas of the skin, including sensitive areas such as the face, neck, intertriginous areas, axillae, genitalia, inframammary areas, and anal crux.

Tapinarof was studied in two identical, phase 3 randomized, controlled, double-blind trials called PSOARING 1 and PSOARING 2.[16] The trials evaluated tapinarof cream compared to vehicle only for the treatment of mild to severe chronic plaque psoriasis in adult patients over a duration of 12 weeks. The trials included 510 and 515 patients, respectively. Patients were randomized 2:1 to receive either once daily treatment with tapinarof 1% cream or vehicle cream to be applied to existing, new, and resolved lesions for the entire duration of the 12-week trial. Patients were prohibited from using concomitant topical, oral, or injectable medications for the treatment of plaque psoriasis throughout the trial, and they could not receive UV light therapy for the duration of the trial. The primary endpoint in the two trials was the proportion of patients achieving a Physician's Global Assessment (PGA) score of 0 or 1, which indicated clear or almost clear skin. Between the two trials, 35.4% and 40.2% of patients receiving tapinarof reached the primary endpoint compared to 6% and 6.3% of patients receiving the control, vehicle cream, with significantly greater achievement of PGA response in the tapinarof groups in both trials ($p<0.001$ for both comparisons). Key secondary endpoints included the proportion of patients achieving 75% or 90%improvement on the PASI. In the tapinarof groups, 36.1% and 47.6% achieved PASI 75 compared to 10.2% and 6.9% in the control groups ($p<0.001$ for both comparisons). For the endpoint of PASI 90, 18.8% and 20.9% of patients in the tapinarof group achieved this endpoint compared to 1.6% and 2.5% of patients receiving the control ($p<0.001$ for both comparisons).

Tapinarof was also studied in a one-year, open-label, extension trial following the PSOARING 1 and PSOARING 2 trials.[17] The extension trial, PSOARING 3, included patients who had completed the two initial trials, and treatment withtapinarof was provided on an intermittent basis determined by the patient's current PGA score. Patients with a PGA score of ≥ 1 at the start of the trial received tapinarof and were treated until they achieved a PGA score of 0, at which time treatment was discontinued and patients were observed. If disease worsened off treatment (defined as a PGA score ≥ 2), tapinarof was restarted and continued until a PGA score of 0 was reached. A total of 763 patients were enrolled in the trial, 508 of whom had been receiving tapinarof in the previous trial, and 255 of whom had been receiving the vehicle. At baseline, approximately two-thirds of patients had a PGA score of 2 or 3, with the remaining patients primarily having a baseline score of 1. The proportion of patients who achieved complete disease clearance (PGA score of 0) at any time during the trial was 40.9%. Tapinarof was also observed to have a remittive, off-therapy effect, which was defined in the trial as duration of efficacy maintenance with a PGA score of 0 or 1 while off therapy. For patients who achieved a PGA score of 0 at any time during the trial, the mean duration of remittive effect was 130.1 days (Standard Deviation: 89.4 days). The median duration of remittive effect for patients entering the trial with a PGA score of 0 was 115 days. These endpoints were not evaluated for statistical significance due to the lack of an active comparator in this trial.

In terms of safety, tapinarof has no contraindications, warnings, or precautions.[15] There are also no known drug interactions with tapinarof based on in vitro studies. In the PSOARING 1 and 2 trials, adverse events were reported in 50.3% and 54.% of patients receiving tapinarof and 22.4% and 26.2% of patients receiving the vehicle.[16] The most common adverse effects seen in clinical trials were folliculitis which occurred in 20% of patients, along with nasopharyngitis and contact dermatitis which occurred in 11% and 7% of participants, respectively. Across the pivotal

trials, roughly 1%-2% of patients withdrew from the trials due to folliculitis or contact dermatitis. There were no new safety signals identified in the extension trial, and the most frequent adverse event continued to be folliculitis, with 22.7% of patients reporting this adverse event.[17] There is limited data on safety of tapinarof in special populations. There were no overall differences seen in efficacy, safety, or tolerability of tapinarof in elderly patients, and 14.5% of trial participants who received tapinarof were aged 65 or older.

As a new, branded medication, tapinarof's likely place in therapy will be in patients with mild to moderate plaque psoriasis who have failed generic topical therapies such as topical corticosteroids or calcineurin inhibitors. Tapinarof may also be used earlier in treatment for patients with psoriasis in intertriginous areas with psoriasis in intertriginous areas or other sensitive areas where potent, generic topicals are not recommended for use due to potential for skin atrophy. The safety of use in combination with other psoriasis treatment agents has not been evaluated. Providers may choose to use tapinarof in combination with oral systemic agents or injectable biologics in patients with moderate to severe disease. Tapinarof is not currently mentioned in the psoriasis treatment guidelines due to the timing of publication.[8]

## Roflumilast

A topical cream formulation of roflumilast (0.3% concentration) was approved by the FDA in July 2022 for the treatment of plaque psoriasis in patients age 12 and older.[18] Roflumilast belongs in the pharmacological class of phosphodiesterase 4 inhibitors (PDE-4) and leads to anti-inflammatory activity, though the exact mechanism of action that exerts its therapeutic effects is unknown. The topical drug is indicated to be applied once daily to areas affected by plaque psoriasis, including intertriginous areas (i.e. skin folds). Currently, its place in therapy is not well established by experts.[19] First-line treatment for mild disease is topical corticosteroids and emollients; for moderate to severe disease, systemic therapies (such as biologics, methotrexate, apremilast, or cyclosporine) are recommended as first-line.[7,8] Given its topical nature and novel pharmacological class, roflumilast may be useful as an adjuvant to first-line treatments in any disease severity.

Despite its undefined place in therapy, topical roflumilast has proven to be effective in treating plaque psoriasis. In two separate phase 3 randomized controlled trials, DERMIS-1 and DERMIS-2, roflumilast 0.3% cream was compared to vehicle cream (placebo), each applied once daily to affected areas for 8 weeks in both studies.[20] The primary efficacy outcome measured in these studies was whether the investigator's global assessment (IGA) success was achieved. IGA is assessed on a 5-point scale of plaque severity from 0 to 4 (0 indicating clear, 4 indicating severe disease). Treatment was considered an IGA success if the patient reached clear or almost clear plaque status at 8 weeks as well as had at least a 2-point improvement from their baseline IGA score. In both studies, roflumilast 0.3% cream was found to be statistically significantly superior to placebo at inducing successful treatment. DERMIS-1 saw 42.4% of their roflumilast-treated participants achieve IGA success, as opposed to 6.1% of the placebo group, resulting in a 39.6% (95% CI, 32.3-46.9%, p<0.001) increase in success rate . Likewise, DERMIS-2 saw a 28.9% (95% CI, 20.8-36.9%, p<0.001) increase in success rate between roflumilast and placebo, with success in 37.5% and 6.9% of patients, respectively.[20]

As for side effects, topical roflumilast has been found to be a very tolerable medication due to the lack of systemic absorption. The most commonly reported side effects were diarrhea and headache, though the prevalence of these adverse effects are 2% and 3%, respectively.[18] Additionally, prevalence of topical irritation resulting from roflumilast cream is low and very comparable to that of placebo vehicle cream; 98.6% of roflumilast-treated patients and 98.4% of placebo-treated patients reported no signs of skin irritation at 8 weeks of treatment.[20]

At this time, further research is needed to determine topical roflumilast 's place in therapy compared to other active treatments as well as long-term efficacy and side effects. Current data lends support to the idea that topical roflumilast has potential to gain a much larger role in the treatment of plaque psoriasis, especially in intertriginous areas. Skin in these areas tend to be thinner and more sensitive and more prone to adverse effects, making roflumilast cream a desirable option given its confirmed efficacy and favorable safety profile.

## Spesolimab

### *Generalized Pustular Psoriasis*

GPP is an inflammatory condition characterized by recurrent or persistent flares of pustules and erythema.[21] Although GPP is distinct from plaque psoriasis in its underlying pathophysiology, the two can co-occur in a single patient. GPP is a rare form of psoriasis, constituting approximately 1% of all psoriasis diagnoses.[22]

Both genetic and environmental factors are involved in the etiology of GPP.[22] The genes that are implicated in the development of GPP are typically those involved in innate immunity. Although many mutations have been implicated, the most common is a loss-of-function mutation in the IL-36RN gene which affects IL-1 family cytokines and produces a state of heightened inflammation. Both patients with GPP and plaque psoriasis display increased levels of IL-36, with levels being even higher in GPP.

Although the hallmark of GPP is widespread pustules, systemic symptoms can also accompany the cutaneous manifestations and may include fatigue, nausea, or fever.[21,23] Flares can be idiopathic or linked to a trigger, such as infection, stress, or certain medications. One of the most common medication-related causes of flares is withdrawal from systemic corticosteroids.[21] GPP flares can be deadly, with an estimated 3%-7% mortality rate per flare.

Data supporting GPP treatments is sparse. Since GPP is more commonly seen in Asian patients, much of the available information comes from other countries.[22] In particular, Japan has multiple approved therapies for GPP, including adalimumab, infliximab, certolizumab, secukinumab, ixekizumab, brodalumab, risankizumab, and guselkumab, whereas Europe and the United States had no approved therapies before spesolimab.[21]

### *Spesolimab*

Spesolimab-sbzo is the first drug in the United States with a labeled indication for GPP, gaining FDA approval for the treatment of GPP flares in adults in

September 2022.[24] Spesolimab is an IL-36 antagonist that blocks pro-inflammatory signaling downstream of the IL-36 receptor, although it is not known precisely how this translates to its efficacy in GPP flares. This represents a different mechanism of action from GPP agents approved in other countries, which include inhibitors of TNF-α, IL-17, IL-17R, and IL-23.[25] Spesolimab is administered as a single 900 mg dose, infused intravenously over 90 minutes, although the dose may be repeated after a week if symptoms of the GPP flare persist.[24]

Spesolimab was approved based on data from the phase 2 Effisayil-1 trial.[25] Since spesolimab was designated as an orphan drug by the FDA, no phase 3 trial was performed prior to approval.[26,27] Effisayil-1 was a randomized, double-blind, placebo-controlled trial, enrolling 52 patients aged between 18 and 75 who were experiencing a moderate to severe GPP flare.[25] Patients were excluded if they had a flare requiring intensive care or if they were on concomitant therapy with methotrexate, cyclosporine, or retinoids. Once enrolled, patients were assigned in a 2:1 ratio to receive either a single 900 mg infusion of spesolimab or placebo, with patients stratified based on Japanese ethnicity. To assess outcomes, the Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) scoring tool was used. The GPPGA scale assigns a score of 0 to 4 in the categories of erythema, pustulation, and scaling, with 0 being the least severe and 4 being the most severe. For example, a score of 0 in the pustulation subcategory indicates that the patient has no visible pustules, whereas a score of 4 indicates a high density of coalescing pustules. The scores from the three subcategories are then averaged to calculate a final score. The primary endpoint of this trial was achieving a score of 0 in the GPPGA pustulation subcategory, and a key secondary outcome was achieving a total GPPGA score of 0 to 1. Both of these outcomes were assessed at the end of week 1, as patients from both the spesolimab and placebo groups were eligible to receive an open-label dose of spesolimab on day 8 if they were still experiencing symptoms; therefore, any outcomes measured beyond that point were considered exploratory. At the end of week 1, 54% of patients receiving spesolimab achieved a GPPGA pustulation subscore of 0, compared to 6% of patients in the placebo group (difference = 48%, 95% CI: 21 to 67%, p<0.0001). Furthermore, 43% of patients receiving spesolimab achieved a total GPPGA score of 0 to 1, compared to 11% of patients in the placebo group (difference = 32%, 95% CI: 2 to 53%, p=0.02). Based on this data, the investigators concluded that spesolimab led to significant improvements in pustulation at one week. However, this trial is limited by its small sample size and its inability to track efficacy outcomes beyond one week.

Effisayil-1 was also the main trial used to assess the safety of spesolimab.[25] By the end of week 1, 66% of patients in the spesolimab group experienced an adverse event, with 6% having a serious adverse event, whereas 56% of patients in the placebo group had an adverse event, with none having a serious adverse event. Most notably, the rate of infection at the end of week 1 was higher in the spesolimab group than the placebo group at 17% and 6% respectively. Adverse events were also assessed at 12 weeks, although at this point in the trial patients were no longer blinded and the majority (49/52 patients) had received at least one dose of spesolimab. At week 12, 82% of patients who had received any doses of spesolimab, including those originally assigned to the placebo group, had an adverse event, with 12% having a serious adverse event and 47% having an infection. In patients with infection, there was no predominance in causative pathogens or areas of the body affected. By week 12, one patient reported possible drug rash with eosinophilia and systemic symptoms (DRESS), although this diagnosis could not be confirmed. Given the increased risk of infection in patients who receive spesolimab, the package insert warns against using spesolimab in patients with active infection.[23]

Since spesolimab is the only FDA-approved treatment for GPP in the United States, it may emerge as a first-line therapy for this rare disease.

## Abrocitinib

Abrocitinib is an oral medication that was approved by the FDA in February 2023 for moderate –to severe AD treatment in patients who are 12 years or older.[28] Abrocitinib is a JAK inhibitor, which is a small-molecule ligand that reversibly inhibits adenosine triphosphate. The inhibition prevents the signaling of multiple cytokines, including, but not limited to, IL-4, IL-13, and thymus- and activation-regulated chemokine, which are involved in the development and progression of AD.[28,29] Abrocitinib is mainly metabolized by liver enzymes, with both the parent drug and its metabolites having JAK inhibition activities. The recommended starting dose for abrocitinib is 100 mg orally once daily, which can be increased to a maximum dose of 200 mg orally once daily if there is an inadequate response at 12 weeks.[28] However, it is recommended to discontinue abrocitinib if therapy is not effective at its maximum dose.

Abrocitinib is recommended for use in patients who have uncontrolled, moderate –to severe AD who have failed or have contraindications to other systemic therapies including biologics.[28] The efficacy of abrocitinib was evaluated in the JADE-MONO-1 trial, a randomized, double-blind, multi-center phase 3 trial conducted in patients 12 years or older with moderate to severe plaque psoriasis, where abrocitinib 100 mg and 200 mg were compared to a placebo.[30] The primary efficacy endpoints in this trial included the proportion of patients who achieved a 5-point IGA response with a 2 or more point improvement from baseline at 12 weeks, and the proportion of patients who achieved a 75% or more improvement in Eczema Area and Severity Index (EASI) score from baseline at 12 weeks. In regard to the IGA response, there were statistically significantly higher proportions of patients who achieved a 2 or more point A 2 or more point improvement from baseline at 12 weeks in the abrocitinib 100 mg and 200 mg groups when compared to the placebo group, with a 15.8% (95% CI of 6.8%-24.8%, p=0.0037) and 36.0% (95% CI of 26.2%-45.7%, p<0.0001) increase respectively. In regard to the EASI-75 response, there were statistically significantly higher proportions of patients who achieved at least 75% improvement in EASI score at 12 weeks in the abrocitinib 100 mg and 200 mg groups when compared to the placebo, with a 27.9% (95% CI of 17.4%-38.3%, p<0.0001) and 51.0% (95% CI of 40.5%-61.5%, p<0.0001) increase respectively. The investigators concluded that abrocitinib dosed at 100 mg and 200 mg once a day is effective in treating moderate –to severe AD

as monotherapy. However, due to the short study period of only 12 weeks, the long-term efficacy of abrocitinib in controlling AD is uncertain.

Abrocitinib can be used together with topical corticosteroids if needed, but it is not recommended to use in combination with other JAK inhibitors, biologic immunomodulators, or other immunosuppressants.[28] The JADE MONO-1 phase 3 trial also examined the safety of abrocitinib at once-a-day doses of 100 mg and 200 mg.[30] The most frequently reported side effects were nausea (placebo = 3%, abrocitinib 100 mg = 9%, abrocitinib 200 mg = 20%), nasopharyngitis (placebo = 10%, abrocitinib 100 mg = 15%, abrocitinib 200 mg = 12%), and headache (placebo = 3%, abrocitinib 100 mg = 8%, abrocitinib 200 mg = 10%). Serious adverse events including chronic inflammatory bowel disease and acute pancreatitis were observed with an incidence of less than or equal to 4% among both the intervention groups and placebo group. However, the patients recovered after permanently discontinuing the medication. Death was not observed in any of the study groups during the study period; however, abrocitinib still carries a warning regarding increased mortality including sudden cardiovascular death based on research from other JAK inhibitors.[28,30] The JADE MONO-1 investigators concluded that abrocitinib dosed at 100 mg and 200 mg once a day is tolerable and safe for patients to use.[30] However, as with the efficacy data, it is unclear whether abrocitinib is safe for long-term use due to the short study period of 12 weeks.

## Tralokinumab

Tralokinumab is a newly approved drug used for the treatment of moderate –to severe atopic dermatitis (AD). Tralokinumab is a monoclonal antibody that works as an IL-13 antagonist. IL-13 is thought to be an important factor in the pathophysiology of AD, as increased expression of the cytokine is found in AD lesions on human skin.[31] Binding of IL-13 to its receptor in the body results in a signal transduction pathway. This pathway decreases the amount of stratum-corneum strengthening molecules such as ceramides and filaggrin, and it increases the amount of proinflammatory proteins.[32] Overall, greater activation of the IL-13 receptor leads to the weakening of the stratum-corneum, which allows for more allergens and bacteria to enter the skin, resulting in a more severe disease state. Tralokinumab works to treat AD by tightly binding to IL-13, so the cytokine cannot bind to its receptor and initiate its signaling cascade.

The drug is currently formulated as a subcutaneous injection available for patients in a prefilled syringe containing 150 mg of the drug. Tralokinumab is first given as a 600 mg loading dose, and then 300 mg doses are administered every other week for maintenance. If a patient weighs less than 100 kg and is able to achieve clear or almost clear skin after 16 weeks of using the therapy, 300 mg can then be administered every 4 weeks.[31]

Clinical trials for tralokinumab tested the efficacy of the drug by using the primary endpoints of proportion of patients who achieved an IGA score of 0 (clear skin) or 1 (almost clear skin) and the proportion of participants who achieved EASI 75.[33] In the randomized, double-blinded, phase 3 trials ECZTRA 1 and ECZTRA 2, subjects with moderate –to severe AD were assigned to receive either 300 mg of subcutaneous tralokinumab every 2 weeks or placebo. There was a statistically significant increase in the proportion of participants with an IGA score of 0 or 1 in those receiving the drug versus placebo in both trials. In ECZTRA 1, 15.8% of patients receiving tralokinumab achieved an IGA score of 0 or 1 after 16 weeks of therapy and only 7.1% of patients receiving placebo achieved this endpoint (MD: 8.6%, 95% CI 4.1-13.1%, p=0.002). In ECZTRA 2, 22.2% of tralokinumab patients and only 10.9% of placebo patients achieved this endpoint after the 16 week trial (MD: 11.1%, 95% CI 5.8-16.4%, p<0.001).[33] The tralokinumab group also had a statistically significant increase in the proportion of patients achieving EASI 75 after 16 weeks of therapy. In ECZTRA 1, 25.0% of tralokinumab patients and 12.7% of placebo patients achieved this endpoint (MD: 12.1%, 95% CI 6.5-17.7%, p<0.001), and in ECZTRA 2, 33.2% of tralokinumab patients and 11.4% of placebo patients achieved this endpoint (MD: 21.6%, 95% CI 15.8-27.3%, p<0.001) at the end of the trial.[33] The ECZTRA 3 trial was another randomized, double-blinded trial comparing 300 mg tralokinumab every 2 weeks along with topical corticosteroids versus placebo and topical corticosteroids.[34] In ECZTRA 3, 38.9% of tralokinumab patients and 16.2% of placebo patients achieved an IGA score of 1 or 0 (MD: 12.4%, 95% CI 2.9-21.9, p=0.015). Additionally, 56.0% of tralokinumab patients and 35.7% of placebo patients achieved an EASI 15 at the end of the ECZTRA 3 trial(MD: 20.2%, 95%CI 9.8-30.6, p<0.001).[34] The most frequent adverse events occurring in ECZTRA 1, 2, and 3 were similar. Patients taking tralokinumab reported experiencing viral upper respiratory tract infection (23.1%, 8.3%, 19.4%), conjunctivitis (7.1%, 3%, 11.1%),and headache (4.7%, 2.7%, 8.7%).[33,34]

Tralokinumab should be used in adults with moderate –to severe atopic dermatitis after failure of topical corticosteroids with appropriate adherence and avoidance of triggers.[35] Dupilumab is currently the biologic drug of choice for AD due to its promising safety and efficacy data, and the comfortability of clinicians prescribing it. Tralokinumab is new to the market, and its exact place in therapy compared to similar biologics, such as dupilumab, is currently unknown but will become clearer as it is prescribed to a larger number of patients. As seen from the phase 3 clinical trials, tralokinumab could be used as monotherapy or in combination with topical corticosteroids.[33,34]

## Conclusion

In conclusion, the treatment of psoriasis and atopic dermatitis has and will continue to advance. These newly approved treatments and their novel mechanisms of action introduce potentially promising treatment options for patients dealing with these inflammatory dermatological conditions. Having more treatment options may allow refractory patients to find a treatment that helps them gain disease control and improve their quality of life. However, as is the case with any new-to-market medications, post-market surveillance will be crucial to assessing their long-term effects and use in special populations. In the future, there is potential for these drugs to be approved for other indications, as these treatments are being studied for other disease states. For example, Tapinarof has reached phase three trials for

use in atopic dermatitis.[36] The treatment of dermatologic diseases is ever evolving, and clinicians will need to continue to closely monitor for new drug approval and expanding indications to best serve patients.

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## References

1. Kim WB, Jerome D, Yeung J. Diagnosis and management of psoriasis. *Can Fam Physician*. 2017;63(4):278-285.
2. Singh R, Koppu S, Perche PO, Feldman SR. The cytokine mediated molecular pathophysiology of psoriasis and its clinical implications. *Int J Mol Sci.* 2021;22(23):12793. doi: 10.3390/ijms222312793
3. Marrakchi S, Puig L. Pathophysiology of Generalized pustular psoriasis. *Am J Clin Dermatol*. 2022;23(suppl 1):13-19. doi: 10.1007/s40257-021-00655-y
4. Kim J, Kim BE, Leung DYM. Pathophysiology of atopic dermatitis: clinical implications. *Allergy Asthma Proc.* 2019;40(2):84-92. doi: 10.2500/aap.2019.40.4202
5. Langley RGB, Krueger GG, Griffiths CEM. Psoriasis: epidemiology, clinical features, and quality of life. *Ann Rheum Dis.* 2005;64(suppl 2):ii18-23; discussion ii24-25. doi: 10.1136/ard.2004.033217
6. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: a review. *JAMA*. 2020;323(19):1945-1960. doi: 10.1001/jama.2020.4006
7. Elmets CA, Korman NJ, Farley Prater E, 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;84(2):432-470. doi: 10.1016/j.jaad.2020.07.087
8. Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol*. 2020;82(6):1445-1486. doi: 10.1016/j.jaad.2020.02.044
9. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072. doi: 10.1016/j.jaad.2018.11.057
10. Hoy SM. Deucravacitinib: first approval. *Drugs*. 2022;82(17):1671-1679. doi:10.1007/s40265-022-01796-y
11. Armstrong AW, Gooderham M, Warren RB, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. *J Am Acad Dermatol.* 2023;88(1):29-39. doi: 10.1016/j.jaad.2022.07.002
12. Strober B, Thaçi D, Sofen H, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, phase 3 Program fOr Evaluation of TYK2 inhibitor psoriasis second trial. *J Am Acad Dermatol.* 2023;88(1):40-51. doi: 10.1016/j.jaad.2022.08.061
13. SOTYKTU [package insert]. Princeton, NJ: Bristol-Myers Squibb Company. Published September, 2022. Accessed May 24, 2023. https://www.bmsmedinfo.com/prescribing-information/prescribing-pdf-view.00P0000000002301.html
14. Long-term study that measures the safety and efficacy of deucravacitinib (BMS-986165) in participants with psoriasis (POETYK PSO-LTE). ClinicalTrials.gov identifier: NCT04036435. Updated April 26, 2023. Accessed May 24, 2023. https://www.clinicaltrials.gov/ct2/show/NCT04036435
15. VTAMA [prescribing information]. Long Beach, CA: Dermavant Sciences Inc.; May 2022.
16. Lebwohl MG, Stein Gold L, Strober B, et al. Phase 3 trials of tapinarof cream for plaque psoriasis. *N Engl J Med.* 2021;385(24):2219-2229. doi: 10.1056/NEJMoa2103629
17. Strober B, Stein Gold L, Bissonnette R, et al. One-year safety and efficacy of tapinarof cream for the treatment of plaque psoriasis: Results from the PSOARING 3 trial. *J Am Acad Dermatol.* 2022;87(4):800-806. doi: 10.1016/j.jaad.2022.06.1171
18. Roflumilast (topical). Lexicomp. May 19, 2019. Accessed May 23, 2023. https://online.lexi.com/lco/action/home
19. Feldman SR. Treatment of psoriasis in adults. UpToDate. February 21, 2023. Accessed May 23, 2023. https://www.uptodate.com/contents/treatment-of-psoriasis-in-adults
20. Lebwohl MG, Kircik LH, Moore AY, et al. Effect of roflumilast cream vs vehicle cream on chronic plaque psoriasis: the DERMIS-1 and DERMIS-2 randomized clinical trials. *JAMA.* 2022;328(11):1073-1084. doi:10.1001/jama.2022.15632
21. Gooderham MJ, Van Voorhees AS, Lebwohl MG. An update on generalized pustular psoriasis. Expert *Rev Clin Immunol.* 2019;15(9):907-919. doi: 10.1080/1744666X.2019.1648209.
22. Romiti R, Hirayama ALDS, Arnone M, Magalhães RF. Generalized pustular psoriasis (von Zumbusch). *An Bras Dermatol.* 2022;97(1):63-74. doi: 10.1016/j.abd.2021.05.011
23. Robinson A, Van Voorhees AS, Hsu S, et al. Treatment of pustular psoriasis: from the medical board of the national psoriasis foundation. *JAAD.* 2012;67(2):279-288. doi: 10.1016/j.jaad.2011.01.032
24. Spevigo [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; September 2022.
25. Bachelez H, Choon S, Marrakchi S. Trial of spesolimab for generalized pustular psoriasis. *N Engl J Med*. 2021;385(26):2431-2440. doi: 10.1056/NEJMoa2111563
26. U.S. Food and Drug Administration. Search Orphan Drug Designations and Approvals. Accessed September 1, 2023. https://www.accessdata.fda.gov/scripts/opdlisting/oopd/listResult.cfm
27. Institute of Medicine (US) Committee on Accelerating Rare Diseases Research and Orphan Product Development; Field MJ, Boat TF, editors. Rare diseases and orphan products: accelerating research and development. Washington (DC): National Academies Press (US); 2010. 3, Regulatory Framework for Drugs for Rare Diseases. https://www.ncbi.nlm.nih.gov/sites/books/NBK56185/
28. Cibinqo. Prescribing information. Pfizer Inc. 2022. Accessed March 26, 2023. https://labeling.pfizer.com/ShowLabeling.aspx?id=16652
29. Bieber T, Simpson EL, Silverberg JI, et al; JADE COMPARE Investigators. Abrocitinib versus placebo or dupilumab for atopic dermatitis. *N Engl J Med.* 2021;384(12):1101-1112. doi: 10.1056/NEJMoa2019380
30. Simpson EL, Sinclair R, Forman S, et al. Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet.* 2020;396(10246):255-266. doi: 10.1016/S0140-6736(20)30732-7
31. Silverberg JI, Kantor R. The role of interleukins 4 and/or 13 in the pathophysiology and treatment of atopic dermatitis. *Dermatol Clin*. 2017;35(3):327-334. doi: 10.1016/j.det.2017.02.005
32. Adbry. Package Insert. LEO Pharma Inc. Accessed February 10, 2023. https://mc-df05ef79-e68e-4c65-8ea2-953494-cdn-endpoint.azureedge.net/-/media/corporatecommunications/us/therapeutic-expertise/our-product/adbrypi.pdf?rev=64ed2d0493af4881bede5853dde9f5bf
33. Wollenberg A, Blauvelt A, Guttman-Yassky E, et al. Tralokinumab for moderate-to-severe atopic dermatitis: results from two 52-week, randomized, double-blind, multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2). *Br J Dermatol.* 2021;184(3):437-449. doi:10.1111/bjd.19574
34. Silverberg JI, Toth D, Bieber T, et al. Tralokinumab plus topical corticosteroids for the treatment of moderate-to-severe atopic dermatitis: results from the double-blind, randomized, multicentre, placebo-controlled phase III ECZTRA 3 trial. *Br J Dermatol.* 2021;184(3):450-463. doi:10.1111/bjd.19573
35. Howe W, Paller AS, Butala S. Treatment of atopic dermatitis (eczema). UpToDate. Accessed February

10, 2023. UpToDate Inc. http://www.uptodate.com
36. National Library of Medicine. ClinicalTrials.gov. Accessed September 2, 2023. https://clinicaltrials.gov/search?intr=Tapinarof&page=2

## Assessment Questions

1. Which of the following is a common comorbidity among patients with dermatologic conditions, such as psoriasis?
   a. Asthma
   b. Benign prostatic hyperplasia
   c. Depression
   d. Epilepsy

2. Which of the following statements are correct about GPP?
   a. Withdrawal of corticosteroids is a common cause of flares
   b. Spesolimab is the first FDA-approved treatment for GPP
   c. GPP constitutes approximately 15% of all psoriasis diagnoses
   d. During GPP flares, patients may experience systemic symptoms like fever, fatigue, and nausea

3. What is the mechanism of action for abrocitinib?
   a. IL-36 antagonist
   b. JAK inhibitor
   c. Phosphodiesterase 4 inhibitor
   d. tyrosine kinase 2 inhibitor

4. Which of the following medications may be especially useful for patients with plaque psoriasis in intertriginous areas?
   a. Abrocitinib
   b. Decuravacutunib
   c. Topical roflumilast
   d. Tralokinumab

5. When is abrocitinib recommended for use?
   a. Uncontrolled moderate-to-severe atopic dermatitis who have failed or have contraindications to other systemic therapies including biologics
   b. As it is the only agent approved by the FDA for generalized pustular psoriasis and therefore is expect to emerge as a first line agent
   c. It is expected to be used as a first-line treatment for mild-to-moderate atopic dermatitis
   d. Second-line treatment of plaque psoriasis, especially in intertriginous areas

6. Which of the following adverse effects is of concern for spesolimab?
   a. Acute pancreatitis
   b. Diarrhea
   c. Headache
   d. Infection

7. Which of the following is a warning that all JAK inhibitors carry?
   a. Acute pancreatitis
   b. Cardiovascular death
   c. Hyperlipidemia
   d. Pruritus

8. For patients taking decravacitinib, what should they do in the case of an infection?
   a. Discontinue decravacitinib and trial a new medication, it is too dangerous to continue
   b. Discontinue decravacitinib until the illness resolves at which time decravacitinib can be restarted
   c. Continue decravacitinib without concern for the infection, it should have no impact
   d. Increase the dose of decravacitinib, it will help treat the infection

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