

Generalized Pustular Psoriasis (GPP)



RAPID RECAP

Key Takeaways

- GPP is driven by mutation(s) in *IL-36RN*, a gene encoding for a pro-inflammatory protein
 - Some patients do not have mutations in *IL-36RN* and are thought to have overactivation of the IL-36 pathway via other mechanisms
- GPP flares can be driven by withdrawal from corticosteroids or caused by infections, medications, environmental factors, or comorbid conditions
- Pathological confirmation of GPP is dependent on the results of wound cultures, punch biopsies, and blood tests
- It is important to assess severity and changes over time for patients with GPP to prevent future flares and complications
- There are a variety of biologic agents that have demonstrated efficacy in patients with GPP, although only spesolimab has been approved by the FDA
- Motivational interviewing is key to helping patients identify areas of change, impact their disease management, and enhance their quality of life

Pathophysiology of GPP

- The main causes for GPP flares¹:
 - Genetics¹
 - Triggers¹
 - Inflammatory immune responses¹
- Mutations in the *IL-36RN* gene, which codes for IL-36 receptor antagonist (IL-36RA), are thought to be a driver of disease in some patients¹
- Disease may also be caused by overactivation of the IL-36 inflammatory pathway¹

FLARE TRIGGERS	TYPES
Withdrawal	<ul style="list-style-type: none">• Corticosteroids or high potency topical steroids
Infections	<ul style="list-style-type: none">• <i>Streptococcus</i>• <i>Trichophyton rubrum</i>• Cytomegalovirus (CMV)• Epstein-Barr virus (EBV)• Varicella zoster virus (VZV)• SARS-CoV-2

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Pathophysiology of GPP

FLARE TRIGGERS	TYPES
Medications	<ul style="list-style-type: none">• COVID-19 vaccine• Betamethasone ointment• Calcipotriol ointment• Nonsteroidal anti-inflammatory drugs (NSAIDs)• Progesterone• Terbinafine• Penicillin• Lithium• Iodine• Amoxicillin• Cyclosporine• Hydroxychloroquine• Anti-TNF and other biologics
Environmental factors	<ul style="list-style-type: none">• UV light

Diagnosis of GPP

Symptoms

- Abrupt onset of widespread painful erythematous patches that become rapidly covered with tiny, pinhead sized pustules^{1,2}
- Lakes of pus may result²
- Erythroderma may occur²
- May also have lower extremity edema, fever, malaise, arthralgia, jaundice, conjunctivitis, uveitis, or iritis²

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Diagnostic Tests

Diagnosis is dependent on the following procedures³:

PROCEDURE	RESULTS
Wound culture and susceptibility of pustules ³	Sterile
4 mm punch biopsy ³	<ul style="list-style-type: none">• Psoriasiform changes in the epidermis (parakeratosis and elongation of rete ridges)• Numerous epidermal neutrophils and spongiform pustules of Kogoj
Blood test results: ² Complete blood count w/ differential, C-reactive protein test, sedimentation rate, lipid panel, zinc blood test, serum calcium	<ul style="list-style-type: none">• Elevated erythrocyte sedimentation rate• Elevated C-reactive protein levels• An absolute lymphopenia at the onset, quickly followed by polymorphonuclear leukocytosis• Abnormally low plasma albumin, zinc, and calcium• Deranged lipid profile

Comorbidities of GPP

Comorbidities are more common in patients with GPP compared to the general population and can range from mental, metabolic, renal, and hepatic illnesses⁴. Comorbidities that are commonly observed in GPP patients include:

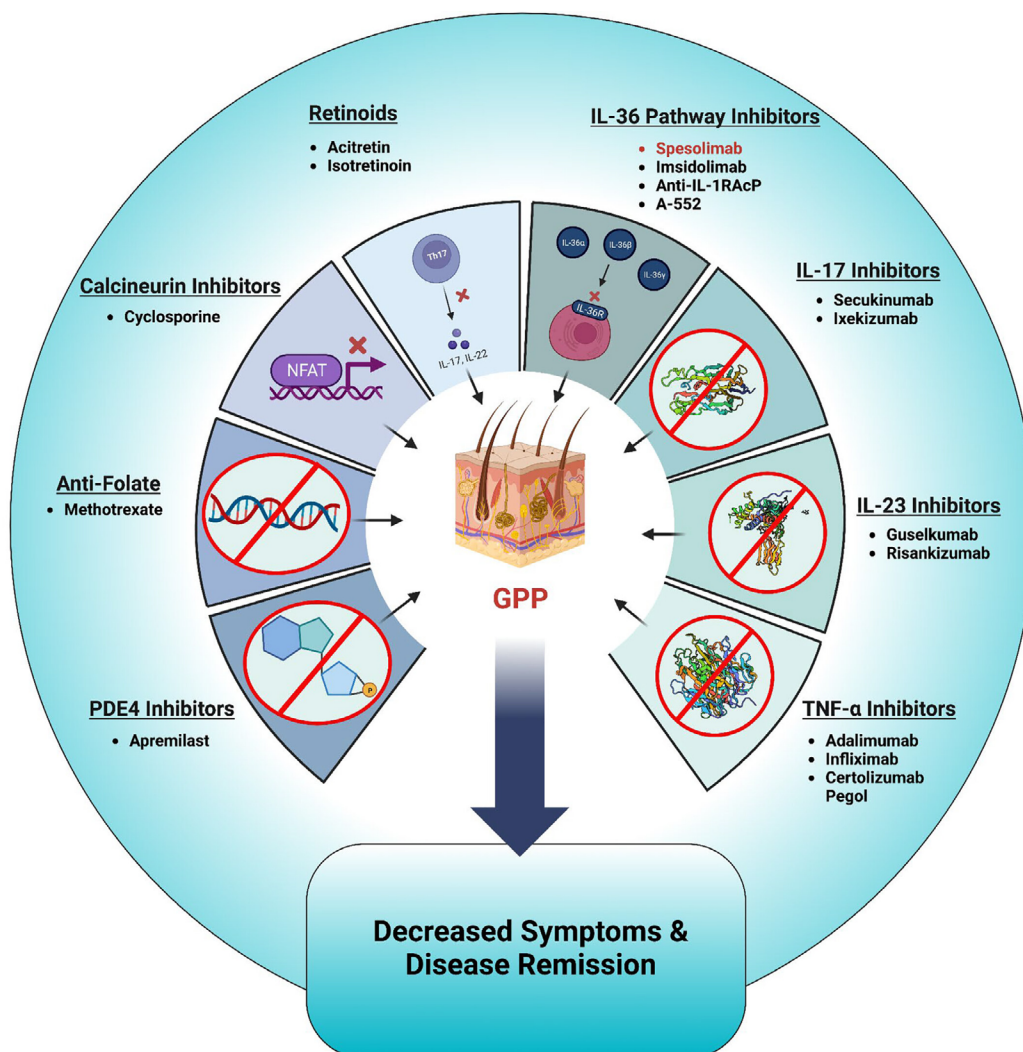
- Type 2 diabetes
- Psoriatic arthritis
- Obesity
- Crohn disease
- Allergies/contact dermatitis
- Hypertension

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Current and Emerging Treatments



Spesolimab is the only FDA-approved therapy for the treatment of GPP flares in adults. Spesolimab is an infusion of monoclonal immunoglobulin G1 antibody that binds specifically to the IL-36 receptor (IL-36R).^{5,6} Adverse reactions to spesolimab include asthenia and fatigue, nausea and vomiting, headache, pruritus and prurigo, infusion site hematoma and bruising, and urinary tract infection.⁷

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Motivational Interviewing

Generalized pustular psoriasis impacts patients physically, emotionally, and mentally. Patients struggle with not only activities of daily living, but also issues of isolation, depression, and hopelessness. It is therefore essential that health care providers address these concerns.

Motivational interviewing is a style of communication that focuses on listening without judgement to discuss **if** the person wants to make a change, **why**, and **what barriers** they perceive. This interviewing style acknowledges that **the person is the expert of their own life**.^{8,9}

1. **Engage:** Create a partnership with the patient. Listen, reflect on what they say and their experiences, support autonomy
2. **Focus:** Decide on an agenda together so that you can move to the topic of change
3. **Evoke:** The “why.” Discuss the person’s goals and reservations. It’s normal for a person to have mixed feelings about change; normalize that and explore
4. **Plan:** Is the person ready to make a change? If so, this step is the “how.” Reaffirm that the person wants to make a change and come to a plan together, incorporating the person’s life and experiences

References:

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