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# Generalized Pustular Psoriasis in Portugal: Expert Perspectives on Patient Journey, Diagnosis, Therapeutic Goals, and Healthcare Optimization

# Psoríase Pustulosa Generalizada em Portugal: Perspetivas de Peritos sobre o Percurso do Doente, Diagnóstico, Objetivos Terapêuticos e Otimização dos Cuidados de Saúde

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## ABSTRACT

Generalized pustular psoriasis (GPP) is a rare, severe, and potentially life-threatening inflammatory skin disease associated with high morbidity and significant healthcare burden. Acute flares require rapid and effective treatment to prevent severe complications, including hospitalization and death. This work aimed to gather insights from a Portuguese expert panel on the management of GPP, focusing on the patient journey, diagnostic approaches, treatment goals, and healthcare resource utilization. This qualitative study collected in-depth insights from seven dermatologists geographically distributed across Portugal during a virtual expert panel meeting in June 2025. Several critical challenges in GPP management were identified, including diagnostic delays, lack of disease awareness among non-dermatologists, limited access to novel therapies, and inconsistent referral pathways. The expert panel emphasized the need for urgent treatment of flares, improved diagnostic protocols, and systematic referral of GPP patients to existing specialized centers, better coordination between healthcare levels, and faster access to treatments with proven efficacy. Spesolimab was highlighted for its potential to reduce long-term healthcare expenditure by shortening hospital stays, lowering the need for intensive care, and decreasing the risk of complications, factors that collectively support more efficient resource use and overall cost reduction. This expert insight highlights actionable strategies to optimize GPP care in Portugal, emphasizing early diagnosis, timely initiation of effective treatment, improved multidisciplinary collaboration, and healthcare system reforms as key priorities to improve clinical outcomes, enhance resource efficiency, and reduce the overall burden of GPP.
**Keywords:** Antibodies, Monoclonal, Humanized; Cost of Illness; Disease Management; Portugal; Psoriasis/diagnosis; Psoriasis/drug therapy; Psoriasis/epidemiology

## RESUMO

A psoríase pustulosa generalizada (PPG) é uma doença cutânea inflamatória rara, grave e potencialmente fatal, associada a elevada morbilidade e a um significativo impacto nos cuidados de saúde. Os surtos agudos requerem tratamento rápido e eficaz para prevenir complicações graves, incluindo hospitalização e morte. Este trabalho pretendeu recolher contributos de um painel português de peritos sobre a gestão da PPG, com enfoque no percurso do doente, abordagens diagnósticas, objetivos terapêuticos e utilização de recursos em saúde. Este estudo qualitativo recolheu contributos detalhados de sete dermatologistas, geograficamente distribuídos por Portugal, durante uma reunião virtual realizada em junho de 2025. Foram identificados vários desafios críticos na gestão da PPG, incluindo atrasos no diagnóstico, falta de conhecimento da doença por parte de não dermatologistas, acesso limitado a terapêuticas inovadoras e percursos de referenciação inconsistentes. O painel de peritos destacou a necessidade de tratamento urgente dos surtos, melhoria dos protocolos diagnósticos, referenciação sistemática dos doentes com PPG para centros especializados, melhor coordenação entre níveis de cuidados e acesso mais célere a terapêuticas com eficácia comprovada. O spesolimab foi destacado pelo seu potencial para reduzir os custos a longo prazo com cuidados de saúde, ao diminuir o tempo de hospitalização, a necessidade de cuidados intensivos e reduzir o risco de complicações - fatores que, em conjunto, contribuem para uma utilização mais eficiente dos recursos e para a redução global dos custos. Esta análise de peritos destaca estratégias acionáveis para otimizar os cuidados à PPG em Portugal, enfatizando o diagnóstico precoce, o início atempado de tratamento eficaz, a melhoria da colaboração multidisciplinar e a implementação de reformas no sistema de saúde como prioridades-chave para melhorar os resultados clínicos, aumentar a eficiência na utilização de recursos e reduzir o impacto global da PPG.
**Palavras-chave:** Anticorpos Monoclonais Humanizados/uso terapêutico; Custo da Doença; Gestão da Doença; Portugal; Psoríase/diagnóstico; Psoríase/epidemiologia; Psoríase/tratamento farmacológico

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## INTRODUCTION

Generalized pustular psoriasis (GPP) is a rare, immune-mediated, and potentially life-threatening skin disease characterized by widespread sterile pustules on an erythematous base, often requiring urgent care due to risks of sepsis and multisystem organ failure.[1–6] It is now recognized as a distinct clinical and immunopathological entity, separate from plaque psoriasis (estimated to coexist in approximately half of cases), with differences in genetic, phenotypic, and immunobiological characteristics.[5,7–9]

Epidemiological data on generalized pustular psoriasis remains scarce, reflecting the rarity of the condition. Global prevalence estimates range from 1.8 to 124 cases per million, highlighting substantial ethnic and geographical variability.[5,10–12] Most cases affect adults with a median age at diagnosis of ~50 years.[5,12–14] A recent multi-center Portuguese study found that approximately two-thirds of patients were women, with a mean age of 55 years.[15] Among psoriasis patients, GPP prevalence is estimated at 0.6% to 2.4%.[5,11]

Generalized pustular psoriasis follows a heterogeneous clinical course, ranging from isolated acute flares to chronic or relapsing forms, often overlapping in presentation and severity.[5] Flares may occur spontaneously or be triggered by corticosteroid withdrawal, infections, medications, pregnancy, vaccination, hypocalcemia, and stress.[5,16–19]

Although GPP etiology remains unclear, emerging evidence points to a multifactorial interplay of genetic, environmental, and immune dysregulation factors. Mutations in genes like IL36RN underscore the central role of the interleukin (IL)-36 pathway in GPP pathogenesis.[5,16,20] IL-36, a member of the IL-1 cytokine family, is markedly upregulated in GPP lesions and promotes activation of T cells and neutrophils, leading to their accumulation in the epidermis and the rapid formation of sterile pustules.[20,21] The understanding of the role of this pathway in GPP led to the recent development of targeted therapies, but regardless of these advances, most patients with GPP require inpatient care during flares, and rapid, effective treatment remains a clinical priority.[5,16,18]

Optimal treatment should achieve rapid control of cutaneous and systemic inflammation while ensuring sustained prevention of flare recurrence and maintaining an acceptable safety profile.[5,22] Spesolimab, administered as a single 900 mg intravenous dose over 90 minutes, with an optional second dose within one week if clinically indicated,[23] is currently the only treatment approved in Europe and the United States for the treatment of GPP flares, in adults and adolescents.[23–30] In the pivotal trial, more than half of patients achieved pustule clearance by week one, with many maintaining response beyond the initial dose.[24] Other biologics and systemic agents like tumor necrosis factor (TNF) inhibitors, IL-23 and IL-17 inhibitors, methotrexate, ciclosporin, and retinoids are frequently employed off-label, but their efficacy can vary considerably.[5]

The absence of standardized diagnostic strategies and national treatment guidelines for GPP leads to inconsistencies in clinical practice and restricts the availability of advanced therapies across healthcare facilities. Considering these challenges, a national expert panel (EP) was convened to gather insights from Portuguese dermatologists representing diverse regions and institutional settings. The goal was to document real-world practices, identify persistent gaps in care, and outline opportunities for clinical, organizational, and health policy improvement. This article presents the main insights from the EP, considering recent literature on the subject.

## METHODS

A panel of seven dermatologists with expertise in GPP management in Portugal participated in the virtual GPP Expert Meeting held in June 2025.

The discussion was structured in two working groups, each led by a moderator and comprising dermatologists from different healthcare units ensuring diverse perspectives. Discussed topics included the GPP patient journey, therapeutic goals, and healthcare resource utilization.

Qualitative, descriptive analytical framework was applied to synthesize insights, focusing on thematic analysis of the discussion areas. The aim was to identify common challenges and expert recommendations to inform future clinical practice and research on GPP in Portugal. Specifically, to (1) explore expert perspectives on the patient journey, diagnostic pathways, and therapeutic goals in GPP; (2) identify current barriers and practice variations in GPP care across Portugal; and (3) provide context-specific recommendations to support timely diagnosis, optimized treatment, and better coordination of care, ultimately improving outcomes in this challenging disease.

To contextualize the EP perspectives and statements presented in the following sections, relevant literature shared as initial project background was integrated throughout the results, framing the discussion within the current state of the art and supporting comparison with existing evidence and international recommendations.

## GENERALIZED PUSTULAR PSORIASIS MANAGEMENT, STATE-OF-THE-ART, AND EXPERT INSIGHT

### Patient journey

#### Typical pathways to dermatology care

Generalized pustular psoriasis flares may escalate rapidly, and their severity and unpredictability can lead to life-threatening complications, namely infections, sepsis, cholangitis and hypocalcemis.[14,17] Given these risks, GPP demands prompt and accurate diagnosis, timely initiation of effective treatment and, in most cases, inpatient management.[18,19]

Experts insight: "GPP is a potentially life-threatening condition that requires prompt and effective treatment."

Due to the urgent nature of GPP, most patients are referred to dermatology through emergency departments (ED) rather than routine outpatient services. Even those already under outpatient, routine dermatological care, often present to ED during flares. In hospitals without dermatology care, patients are transferred to tertiary centers, and those seen in private care are often redirected to public ED for proper treatment (Fig. 1). An Italian Delphi consensus similarly identified ED and general practitioners as the most common first points of care for GPP patients, followed by referral to dermatologists for specialist management.[31]

#### Variability in access, diagnostic challenges, and follow-up

While ED are the main entry point for GPP patients requiring urgent dermatological care, the EP noted significant regional disparities in diagnostic accuracy and referral practices. In many cases, GPP is often underrecognized, especially in mild or atypical cases, due to limited awareness among non-dermatologists, and is frequently misdiagnosed as an infectious disease, leading to inappropriate treatment and delays in effective therapy.[31,32]

Although visible symptoms and systemic signs may prompt referral, underdiagnosis and delays persist.[31] To address this, the EP emphasized the need for improving awareness and recognition of GPP among general practitioners, emergency physicians, and internal medicine physicians.

Experts insight: "The EP strongly recommended the implementation of targeted medical educational programs for emergency and primary care teams to improve early recognition and accelerate dermatology referrals, alongside specific training for emergency care teams to improve early recognition during acute flares."

Access to dermatology services varies by hospital infrastructure, particularly the availability of on-call or acute care dermatology. Without such support, patients may face delays or require transfer to specialized centers. The absence of dermatologists in some ED creates geographic variability in care. In some regions, local hospitals are integrated into referral networks led by tertiary centers, allowing faster triage and, in some cases, remote diagnosis via clinical photographs.

Experts insight: "The EP strongly advocated simplified referral processes, enabling faster access to dermatology services. They also stressed the importance of promoting direct patient pathways, particularly in urgent cases, to minimize unnecessary delays and optimize coordination between ED, primary care, and dermatology units."

Due to the relapsing nature of GPP, ongoing hospital-based follow-up is essential, with open-access models allowing rapid return during flares. After diagnosis, patients are rarely referred back to primary or private care, as consistent hospital dermatology follow-up is key to disease control and patient trust. Occasionally, discharge may be considered following prolonged remission and systemic therapy discontinuation.

Outpatient care, often delivered in hospital- or community-based clinics, supports long-term monitoring and prevention.[33] Follow-up frequency is tailored to disease severity and history, typically every three months, extending to six months if stable. Teleconsultations may be used in selected cases, but flare-ups trigger more frequent monitoring.

### Diagnosis and clinical evaluation

Generalized pustular psoriasis is a rare, chronic neutrophilic dermatosis with a relapsing-remitting course and considerable clinical heterogeneity. Flare frequency, intensity, and duration vary widely, both between patients, and across episodes in the same individual.[5,14,17]

The most severe presentation involves sudden eruption of numerous sterile pustules (2 - 3 mm), which may coalesce into lakes of pus.[4] Affected skin is erythematous, edematous, and often painful, pruritic, or burning; erythroderma may occur.[6] Systemic signs are common (fever, fatigue, malaise, elevated inflammatory markers), with possible arthralgia, peripheral edema, and mucosal involvement.[2,5,8,17–19]

#### Diagnostic approach: clinical criteria, role of biopsy, differential diagnoses

Classically characterized by widespread pustules on non-acral skin, not restricted to pre-existing psoriatic plaques, GPP diagnosis is primarily clinical, based on patient history, physical examination, laboratory tests, and histopathology to

exclude differential diagnoses.[5,9,18,19] A thorough medical history is essential, focusing on skin involvement pattern, prior or current plaque psoriasis, recent infections, and medications.[5]

Experts insight: "GPP diagnosis relies mostly on clinical features. The EP emphasized the need to integrate patient history, physical examination, and laboratory tests (including complete blood count, renal and liver function tests, serum albumin levels and electrolyte balance and inflammatory markers) to ensure a comprehensive diagnostic approach."

Laboratory evaluation is key to assessing systemic inflammation and identifying potential complications during GPP flares. Common findings include leukocytosis with neutrophilia, anemia, elevated C-reactive protein, increased erythrocyte sedimentation rate, hypoalbuminemia, and hypocalcemia. Blood tests also help detect complications, such as kidney or liver dysfunction. Arterial blood analysis is recommended to identify hypocalcemia, electrolyte imbalances, and potential respiratory compromise. In the presence of significant systemic inflammatory signs, blood cultures should be performed to rule out superimposed infection or sepsis.[5,17–19]

Skin biopsy can complement the differential diagnosis with other pustular dermatoses, but is not required to diagnose GPP, as histologic findings are often nonspecific and may overlap with other pustular dermatoses, particularly acute generalized exanthematous pustulosis (AGEP), drug-induced pustular reactions and other rare pustular disorders.[5,18]

Experts insight: "The EP emphasized that the skin biopsy result should not delay treatment, given the life-threatening nature of GPP. Nonetheless, it may provide supportive evidence for diagnosis and assist in ruling out mimickers."

Histologically, GPP shares features with plaque psoriasis, including parakeratosis (retention of nuclei in the stratum corneum), acanthosis (epidermal thickening due to keratinocyte hyperproliferation), hyperkeratosis, elongated rete ridges (elongated epidermal projections into the dermis), thinning of the suprapapillary epidermis, and capillary dilation. Subcorneal macropustules and superficial mononuclear infiltrates are common. The histopathological hallmark is the spongiform pustule of Kogoj, resulting from the accumulation of neutrophils within edematous intercellular spaces, leading to keratinocyte apoptosis. Compared to AGEP, GPP pustules are more superficial, show more apoptotic keratinocytes, and lack eosinophils, aiding differential diagnosis.[5,8,14,17,18,34,35]

However, the classification and definitive diagnosis of GPP remains complex, partly reflecting the lack of standardized international criteria. The development of globally accepted guidelines could improve early recognition, ensure more consistent management, and facilitate exclusion of mimicking conditions requiring different treatments.[5] Although genetic testing is not yet routine, approaches such as IL36RN mutation analysis may enhance diagnostic accuracy in the future.[5,19]

Experts insight: "The EP acknowledged that IL36RN mutation testing is rarely requested in clinical practice and does not influence current treatment decisions. While its diagnostic value is acknowledged in specific contexts, clinical decision-making continues to rely primarily on patient history, physical examination, and laboratory findings, which remain the cornerstone of GPP diagnosis."

### Utility and limitations of severity assessment tools

Despite the clinical heterogeneity of GPP, the routine use of standardized severity assessment tools remains limited in practice.[14] Among the validated instruments, the Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) is a visual analogue scale used to rate disease severity,[5,36,37] mainly in clinical trials, with limited relevance in everyday care.

Routinely, clinical assessment tends to prioritize the extent of skin involvement and systemic manifestations. The pustule sub-score within the GPPGA is important for clinical trial endpoints and regulatory purposes but is rarely used in real-world practice, although its value as a standardized measure is recognized.

Experts insight: "The EP agreed that disease severity is primarily driven by systemic involvement and complications (e.g., cholangitis, infections, renal failure, and hypocalcemia) as well as the extent of skin involvement, with clinical evaluation focusing on these aspects rather than formal scoring tools."

The broader adoption of tools, such as the GPPGA in clinical settings, would require targeted training and education initiatives to familiarize dermatologists and other specialists with its use and interpretation. Without such efforts, implementation outside the context of clinical research remains unlikely.

## Management and treatment goals

### Pharmacological strategies overview

The GPP treatment often relies on approaches used for plaque psoriasis, despite significant differences between the two. In the absence of global guidelines, management depends on clinical judgment and local resources, using a multidisciplinary strategy that includes classical systemic drugs, biologics, and supportive care.

In Portugal, conventional systemic therapies, such as acitretin, ciclosporin, and methotrexate have been historically

used off label in GPP. Ciclosporin is preferred for its rapid onset of action, while acitretin has a slower onset (2 - 3 weeks), and methotrexate is reserved for selected cases where other options are contraindicated. Biologics, including anti-TNF drugs, IL-17 and IL-23 inhibitors, have emerged as additional options, although their use is mostly supported by case reports and small case series.[5]

Recognition of the IL-36 pathway as a key driver of GPP has led to targeted therapies. Spesolimab, an IL-36 receptor antagonist, is the only approved treatment for flare management and prevention in adults and adolescents.[5,16,23,28–30,38] It has redefined GPP care as the first mechanism-based, indication-specific option, offering rapid efficacy with a favorable safety profile and marking a shift toward precision medicine.

Experts insight: "Spesolimab has emerged as a first-line treatment due to its rapid efficacy controlling disease activity and favorable safety profile."

Available agents for GPP flares and prevention of flare-ups are presented in Table 1.

**Therapeutic goals and disease control**

Generalized pustular psoriasis therapeutic goals include both short- and long-term objectives. Short-term goals focus on stopping new pustules and rapid pustule clearance, controlling systemic symptoms, and preventing complications. Long-term goals include maintaining remission, preventing flares, managing comorbidities, and restoring quality of life (QoL).[5,9,39]

Experts insight: "Short term treatment goals include stopping pustule formation, resolving skin lesions and systemic symptoms, and normalizing laboratory parameters."

Treatment efficacy is increasingly measured by dynamic markers such as time to complete pustule clearance and resolution of systemic symptoms, practical and meaningful endpoints in trials and real-world care.

Experts insight: "The EP noted that systemic improvement often lags behind cutaneous resolution, with clinically meaningful response generally expected within 1 - 2 weeks with new target therapies, a marked contrast to past standards, when 2 - 3 months of hospitalization were often required."

However, managing both cutaneous and systemic manifestations remains challenging due to potential complications from GPP flares, a major concern especially in patients with comorbidities and outside hospital settings. These include infections and sepsis, electrolyte imbalances, kidney and liver dysfunction, cardiovascular failure, malnutrition, neutrophilic cholangitis, respiratory distress, arthritis, diabetes, and metabolic syndrome.[5,18]

Experts insight: "Addressing potentially life-threatening complications is essential for achieving comprehensive disease control."

The recent availability of targeted therapies, like spesolimab, has transformed treatment expectations. While past approaches involved prolonged disease and gradual improvement, the EP emphasized that current strategies prioritize rapid resolution, early stabilization, and flare prevention. Therefore, treatment strategies should extend beyond flare resolution to include the prevention of systemic complications and the improvement of patients' QoL.

Experts insight: "The EP emphasized that no new pustule formation within the first week, with complete pustular resolution within one month, represents a realistic target in the current therapeutic landscape. Systemic symptoms should improve within this timeframe as well."

Due to chronicity or frequent recurrence of GPP, many patients require ongoing management to prevent recurrent flares and control residual disease. Although spesolimab is approved in Portugal as monotherapy for treating and preventing GPP flares in adults and adolescents, access to preventive dosing remains limited in practice. Still, the panel considered continued therapy clinically relevant for selected patients, especially those with frequent (> 1/year) or severe flares, prolonged exacerbations, or residual inflammation between flares (e.g., erythema or desquamation). In such cases, subcutaneous spesolimab may be needed chronically to maintain control and prevent recurrence. The EP also noted that over 50% of patients on maintenance therapy may still show active disease, though mild to moderate, reinforcing the need for individualized long-term strategies.

Experts insight: "Preventing flares, improving QoL, and reducing systemic complications are key long-term goals. In patients with recurrent flares or persistent low grade systemic inflammation (e.g., elevated inflammatory markers in the absence of visible skin symptoms), the decision to continue therapy between flares, particularly with biologics, may be clinically justified."

Long-term disease control strategies vary by individual presentation. In patients with concomitant plaque psoriasis, topical treatments may suffice for mild disease, whereas systemic agents are used in more severe forms. In the absence of plaque psoriasis, therapy for flare prevention may include retinoids, methotrexate, or biologics, depending on clinical

severity and patient profile. Preventing recurrence additionally involves patient education and trigger identification, although formal prevention strategies remain non-standardized.

**Treatment decision-making and risk considerations**

Therapeutic decisions in GPP must consider disease severity, comorbidities and patient's age and sex (due to teratogenic risks of certain systemic treatments). Additional considerations include urgency of disease control, treatment access, cost, and the overall impact on QoL. Treatment selection is thus highly individualized and often guided by urgency, tolerability, and care setting.

The setting (outpatient *versus* inpatient) can influence therapeutic choices. While mild cases may be managed as outpatients, admission can expedite diagnosis and access to biologics.

Efficacy and safety also impact treatment selection. The EP noted that older off-label systemic agents, though still used, may pose substantial risks in fragile patients, particularly due to the risk of immunosuppression-related complications, like sepsis. These concerns, combined with the need for rapid action, support the growing preference for the approved, on label targeted therapies in both acute and preventive settings.

One specific consideration involves latent tuberculosis screening prior to spesolimab initiation. While typically recommended before biologics, testing delays may conflict with the urgency of treating acute flares. Evidence supports that in patients without clinical signs of active tuberculosis or known risk factors (e.g., exposure, residence in endemic areas), spesolimab initiation should not be delayed. Testing can occur concurrently or soon after starting treatment, as early intervention is critical to reduce GPP-related morbidity and mortality.[38]

Experts insight: "In cases without significant tuberculosis risk factors, the EP agreed that treatment with spesolimab should not be delayed by tuberculosis screening. Testing can proceed concurrently or after treatment initiation, as prompt intervention takes precedence in acute GPP flares."

**Access challenges and future perspectives**

IL-36 inhibitors, including spesolimab, represent a paradigm shift in GPP management, given its targeted mechanism, rapid onset of action, and favorable safety profile, with the added potential to shorten hospitalizations. However, limited access to these novel therapies remains a major barrier, restricting their use in preventive or maintenance settings, even when clinically justified.[18] The EP stressed the need for clear clinical indications and improved reimbursement pathways to ensure timely access to effective treatments, a critical factor to reducing morbidity and mortality in GPP.[18,40] Open questions also remain regarding optimal long-term use, including re-dosing criteria and indications for patients with infrequent flares.

Experts insight: "The EP strongly urged timely access to spesolimab, given the increased mortality risk associated with this rapidly progressive and life-threatening disease."

**Healthcare resource utilization**

Generalized pustular psoriasis' burden on healthcare systems reflects its rarity, clinical severity, and need for specialized, multidisciplinary care. Moreover, the economic and personal impact of psoriasis, including GPP, justifies appropriate healthcare expenditure to ensure effective treatments and disease control.[41]

**Patterns of resource use: emergency care, hospitalizations, diagnostic testing and outpatient management**

Generalized pustular psoriasis flares carry significant morbidity and mortality, and can rapidly progress to life-threatening complications, with over half of patients requiring prolonged hospitalization and many needing intensive care units (ICU) admission. Average hospital stays last ~10 days, with a maximum of 44 days, with flares typically lasting 16 days.[38,40] The reported mortality rate reaches up to three deaths per 100 patient-years, with sepsis and multiorgan failure as the leading causes.[18,38,42]

Experts insight: "The EP unanimously confirmed that hospital admission is the standard practice during GPP flares, as systemic severity is often underestimated in outpatient settings and generally becomes fully recognized only after admission."

Managing systemic complications often requires collaboration with internal medicine and intensive care teams to address organ dysfunction, infections, and other acute issues. Despite advances in care, ICU admission remains common. French national claims databases show ~25% of hospitalized GPP patients required ICU care during flares, with a mean stay of 18 days.[24,43] Italian data similarly reflect high burden, with about half of patients hospitalized during flares, mainly in internal medicine or dermatology wards. Although ICU use was lower in this cohort, flares still led to substantial healthcare

resource use.[31]

Beyond hospitalization, GPP management involves extensive diagnostic tests, such as laboratory and microbiological analyses, to exclude infections, electrolyte imbalance and other conditions, increasing healthcare demands.

**Economic and logistical implications of inpatient care**

Hospital admissions, particularly ICU stays, are major drivers of GPP-related healthcare costs. It imposes a markedly higher burden than plaque psoriasis, with greater morbidity, systemic complications, and resource demands. Generalized pustular psoriasis is linked to substantially higher direct and indirect medical and pharmacy costs than in plaque psoriasis or the general population.[44–46] A significant portion stems from medications, especially biologics and targeted therapies. However, upfront expenses may be offset by reduced hospital stays, ICU admissions, and broad immunosuppression. Spesolimab is expected to accelerate flare resolution, potentially shortening hospitalizations, reducing intensive care needs, long-term immunosuppressive use, and complication risks.[24,47–53] These effects contribute to more efficient resource use and overall cost reduction.

Despite high costs, the EP noted that improving access to effective therapies could significantly reduce the economic burden by enhancing disease control and preventing complications.

Experts insight: “The EP expressed concern regarding the high costs associated with hospitalization, particularly in intensive care settings. Earlier and broader access to novel targeted therapies, such as spesolimab, may improve cost-effectiveness by reducing hospital length of stay and overall healthcare resource use during acute flares, and, ultimately, by lowering hospitalization rates.”

**Access barriers to dermatologists and specialized centers**

Access to dermatologic care remains uneven.

Limited availability of dermatologists, particularly during weekends or off-hours, can delay diagnosis and treatment initiation, increasing the risk of severe complications.[54] Geographic disparities worsen these issues, as patients in rural or remote areas often face delays and reduced access to specialized care, leading to suboptimal disease control.

Experts insight: “The EP emphasized that shortages of specialized dermatology support in some public hospitals hinder timely and effective management of GPP.”

Despite the complexity of care required, the EP noted that dermatology beds and inpatient dermatology infrastructure are increasingly limited, with insufficient on-call dermatologist availability. In many hospitals, management depends on interhospital collaboration and centralized urgent care networks. Similar shortages are reported in other European settings, namely Italy, where experts cited this as a barrier to timely admission and efficient resource use.[31] To address these gaps, the EP emphasized strengthening referral pathways to existing reference centers, ensuring systematic referral of all GPP patients to specialized units with appropriate expertise and resources.

Experts insight: “The EP advocated systematic referral of GPP patients to specialized centers to ensure timelier and more coordinated care.”

Teledermatology emerged as a valuable tool to expand access to specialist consultations, particularly for patients in medically underserved or remote areas, helping to overcome geographic and logistic barriers to dermatologic care.[54,55]

Experts insight: “The EP supported the expansion of teledermatology networks to reduce geographical inequities and ensure broader access to specialized dermatologic care.”

Optimizing treatment regimens, particularly through timely use of targeted therapies, is essential to enhance the cost-effectiveness of care and improve both outcomes and QoL.[31,41,56]

Experts insight: “Accelerating access to approved therapies was identified as a critical priority to improve clinical outcomes and reduce long-term healthcare costs, including hospitalization and ICU burden.”

**Expert recommendations**

Table 2 summarizes the recommendations formulated to guide clinicians, healthcare institutions, decision-makers, payors and patients in GPP management.

## CONCLUSION

This expert perspective offers key insights into current challenges and opportunities in GPP management in Portugal. Despite advances in disease understanding and targeted therapies, major gaps persist in diagnosis, treatment access, and healthcare organization.

The EP strongly recommended structural measures to improve GPP care. Priorities included enhancing early recognition by non-dermatologists, streamlining referrals, and expanding access to effective therapies, especially spesolimab, a perceived key for rapid control. The EP also stressed multidisciplinary care, timely treatment during flares, and long-term strategies to prevent recurrences and systemic complications. Optimizing resource use through earlier diagnosis, faster access and better care coordination was highlighted as essential to improve outcomes and reduce costs.

This article calls on clinicians, healthcare institutions, and decision-makers to act on these recommendations without delay, aiming at ensuring equitable access to effective care and improving quality of care and clinical outcomes for patients with GPP.

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**AUTHOR CONTRIBUTIONS**

TT, MG: Conceptualization, methodology, investigation, supervision, project administration, validation, and writing - review & editing.

AR, CM, JF, MJC, MJG: Investigation, resources, validation, and writing - review & editing.

All authors participated in the expert panel meeting, critically reviewed the manuscript, and approved the final version.

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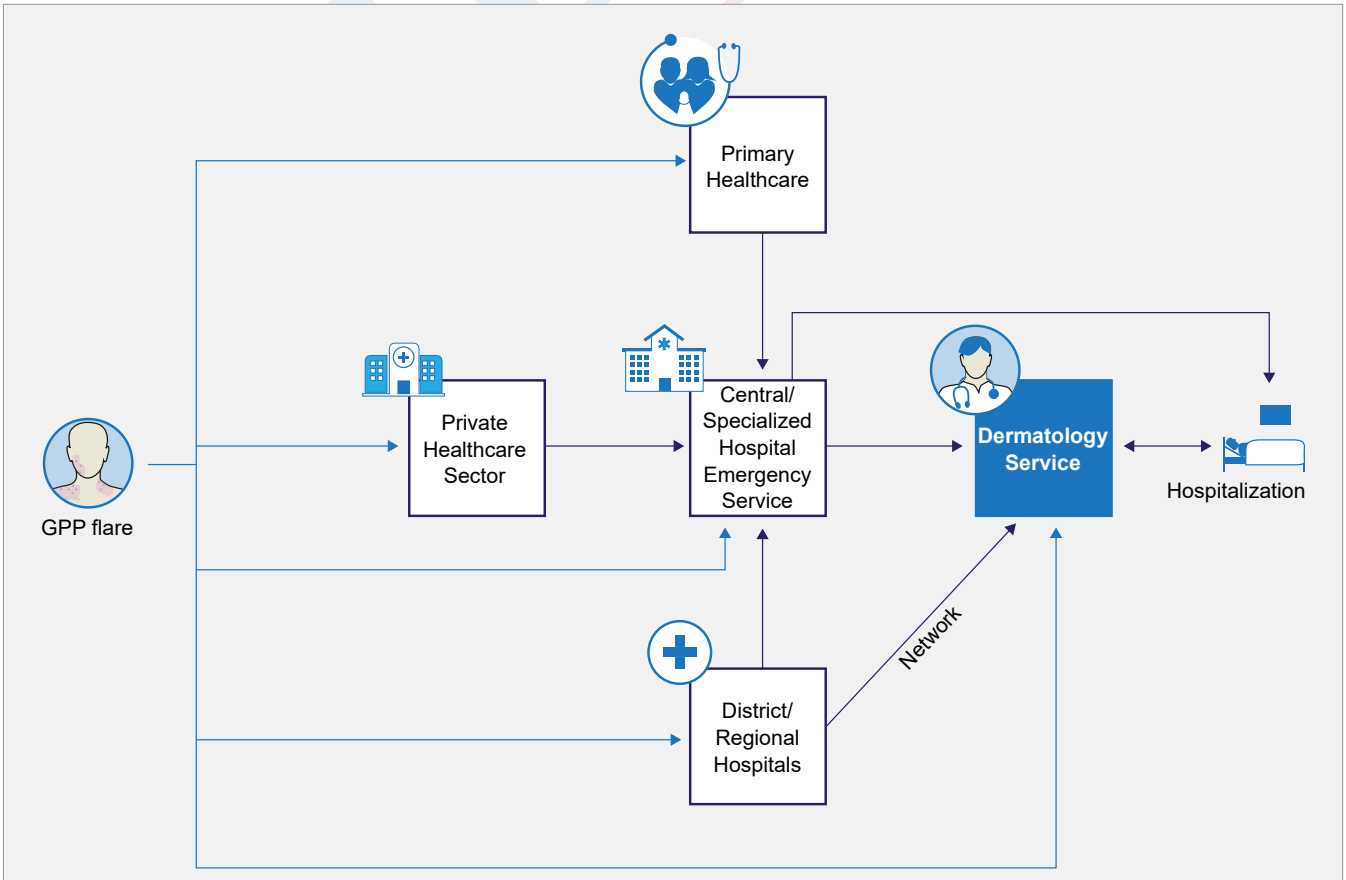


Figure 1 – Schematic of the typical severe GPP patient journey in Portugal
GPP: generalized pustular psoriasis

Table 1 – Therapeutic approaches for GPP flares and prevention of flare-ups

| | Treatment | Action mechanism | Regulatory status |
|---|---|---|---|
| Conventional systemic therapies | Cyclosporine | Calcineurin inhibitor | Off label |
| | Methotrexate | Antimetabolite that inhibits folate-dependent enzymes | Off label |
| | Acitretin | Retinoid (oral) | Off label |
| | Corticosteroids | Broad immunosuppressive effects | Off label |
| Biologic therapies | Adalimumab | TNF inhibitor | On label for GPP flares in Japan<br>Off label in Europe and US |
| | Infliximab | TNF inhibitor | On label for GPP flares in Japan<br>Off label in Europe and US |
| | Secukinumab | IL-17A inhibitor | On label for GPP flares in Japan<br>Off label in Europe and US |
| | Ixekizumab | IL-17A inhibitor | On label for GPP flares in Japan<br>Off label in Europe and US |
| | Brodalumab | IL-17 receptor antagonist | On label for GPP flares in Japan<br>Off label in Europe and US |
| | Ustekinumab | IL-12/IL-23 inhibitor | Off label |
| | Risankizumab | IL-23 inhibitor (p19 subunit) | On label for GPP flares in Japan<br>Off label in Europe and US |
| | Guselkumab | IL-23 inhibitor (p19 subunit) | On label for GPP flares in Japan<br>Off label in Europe and US |
| | Spesolimab | IL-36 receptor antagonist | On label for GPP flares and prevention.<br>Approved by FDA and EMA |

EMA: European Medicines Agency; FDA: Food and Drug Administration; GPP: generalized pustular psoriasis; IL: interleukin; TNF: tumor necrosis factor; US: United States

Table 2 – Expert recommendations to optimize patient care and healthcare resource use in GPP

| | | |
|---|---|---|
| 1. | Treatment urgency and efficacy | GPP is a potentially life-threatening condition that requires prompt and effective treatment. |
| 2. | Raise disease awareness | Enhance GPP awareness among non-dermatology healthcare professionals, particularly family physicians, emergency physicians, and internal medicine physicians, to reduce misdiagnosis, underdiagnosis and diagnostic delays. |
| 3. | Targeted education | Implement targeted medical educational programs for emergency and primary care teams to improve early recognition and accelerate dermatology referrals. |
| 4. | Streamline referral pathways | Simplify and expedite referral processes to ensure rapid access to dermatology services, particularly in acute settings. |
| 5. | Diagnostic precision | GPP diagnosis is based on a thorough clinical assessment, including medical history, physical examination, and laboratory tests (including complete blood count, renal and liver function, inflammatory markers). |
| 6. | Rational use of skin biopsy | Skin biopsy is not required for the diagnosis. Histopathologic findings may support the diagnosis in selected cases but should not delay GPP management. |
| 7. | Limited genetic testing | Restrict IL36RN genetic testing to specific cases, as it has no current impact on treatment decisions or routine practice. |
| 8. | Prioritize clinical evaluation | Prioritize clinical evaluation to assess disease severity, focusing on systemic involvement and skin extent, reserving GPPGA scale for clinical trials and regulatory purposes, as it has limited utility in clinical practice. |
| 9. | Define clear treatment goals in acute flares | Short-term treatment goals include stopping new pustule formation, pustule clearance, resolution of systemic symptoms, and normalization of laboratory parameters. |
| 10. | Long-term disease control goals | Focus on preventing flares, improving QoL, and reducing systemic complications as key long-term goals. |
| 11. | Flare prevention and education | Educate patients on trigger avoidance and self-monitoring to support early identification of flares and reduce preventable exacerbations. |
| 12. | First line treatment | Use spesolimab as a first-line treatment for flare management, given its rapid efficacy controlling disease activity and favorable safety profile. |
| 13. | Timely therapeutic response | A clinically meaningful response is generally expected within 1-2 weeks, particularly with spesolimab |
| 14. | Therapeutic expectations | Define early treatment success as the absence of new pustules within the first week and complete pustular resolution within one month. |
| 15. | Long-term management strategy | In patients with frequent or recurrent flares, or persistent low-grade systemic inflammation (e.g., elevated inflammatory markers in the absence of visible skin symptoms), chronic maintenance treatment may be clinically justified to prevent recurrence. |
| 16. | Patient monitoring | Establish individualized follow-up plans, typically every 3 months, with flexibility to intensify during active phases and space out during stable remission. |
| 17. | Expedite therapy in flares | Treatment with spesolimab should not be delayed by tuberculosis screening. Testing can proceed concurrently or after treatment initiation. |
| 18. | Ensure timely access to effective therapies | Timely access to spesolimab is strongly urged, given the increased mortality risk associated with this rapidly progressive and life-threatening disease. |
| 19. | Cost-effectiveness | Although associated with high upfront costs, spesolimab may reduce long-term expenditure by decreasing the need for prolonged hospitalization and for intensive care. |
| 20. | Recognize healthcare burden | GPP imposes substantial healthcare utilization, including frequent hospitalizations and emergency care needs. |
| 21. | Optimize referral pathways | Ensure systematic referral of GPP patients to specialized centers to guarantee timely and coordinated care. |
| 22. | Leverage teledermatology | Expand teledermatology use to support remote diagnosis, follow-up, and expedite specialist input, especially in underserved areas. |
| 23. | Accelerate access to approved therapies | Prioritize rapid and equitable access to approved therapies to improve clinical outcomes and reduce long-term healthcare costs. |

GPP: generalized pustular psoriasis; GPPGA: Generalized Pustular Psoriasis Physician Global Assessment; IL36RN: interleukin-36 receptor antagonist; QoL: quality of life