National Institute for Health and Care Excellence

Health Technology Evaluation

Spesolimab for treating generalised pustular psoriasis flares ID3963
Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Boehringer Ingelheim	As generalized pustular psoriasis (GPP) is a rare, severe, clinically heterogeneous disease, Boehringer Ingelheim (BI) considers highly specialised technology (HST) to be the most appropriate to assess this topic. Please find below the reasons for this. 1. BI carried out a retrospective study to understand the epidemiology and healthcare resource use of generalised pustular psoriasis (GPP), palmoplantar pustulosis (PPP), and psoriasis vulgaris (PV) patients in the UK (United Kingdom). (1) The reported prevalence of GPP was 2.16 events per 100,000 (95% CI:1.84-2.48) and it was observed that a patient can suffer 0.43 moderate/severe flares per year. (1) A population of 44.6 million over 18 years of age in England was estimated for 2023 and a mortality rate of 2.87% for moderate/severe flares was identified, resulting in 403 patients who could suffer a GPP flare during that year. (2-3) Since GPP is a rare and difficult disease to diagnose, we assumed a diagnosis rate of 80% and 90% of those patients would be eligible to receive spesolimab (excluding contraindicated and specific populations such as pregnant women),	Thank you for your comment. The following points were considered in relation to the HST criteria: • The condition is very rare defined by 1:50,000 in England. • Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500

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		resulting in 290 patients who will be candidates to receive spesolimab during 2023. 2. Although the severity of GPP flares can vary, flares have potential to progress to a life-threatening status requiring hospitalisation and inpatient medical management and monitoring. Studies found that patients with GPP have a greater frequency and duration of hospital visits compared with the general population. (4-5) The CPRD study carried out in the UK demonstrated that GPP patients had a higher overall mean inpatient admissions days (5.8 days, SD:9.7), length of hospitalisation stays (5.8 days, SD:11.1), outpatient visits (39.2 days, SD:34.9) and A&E visits (5 days, SD:11.8) compared to PV between 2015 and 2019. Patients with ≥ 1 comorbidity had a higher mean healthcare resource utilisation in both GPP and PV patients overall and at each year from 2015 to 2019. (1) All-cause mortality was highest among GPP patients compared to PPP and PV patients ($p<0.001$). GPP patients were observed to have a lower mean survival time (1,793.8 days, 95% CI: 1,637.9-1,949.7) compared to PV patients (2,076.5 days, 95% CI: 2,070-2,082.8). (1) Generalised pustular psoriasis can progress over time due to both cutaneous and extracutaneous manifestations contributing to severe morbidity and potential mortality. As a multisystemic disease, GPP can have extracutaneous complications affecting the cardiovascular system, liver, respiratory system, and nervous system. (6-8) Microbial infections can occur within pustular skin, (9) with the potential to develop sepsis that can be fatal. (6,9) During a flare, patients present with systemic inflammation, which can cause a range of symptoms such as malaise, high-grade fever and diarrhoea. (10) Extracutaneous symptoms experienced by patients with GPP can include cholestasis, cholangitis, epigastric pain, arthritis, interstitial pneumonitis, oral	across all its indications. • The very rare condition significantly shortens life or severely impairs its quality • No satisfactory treatment options exist, or, if it does the technology is likely to be of significant additional benefit to those affected Spesolimab was found to not meet all of the HST criteria and will progress as a single technology appraisal.

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		lesions, and acute renal failure. (9) This range of manifestations can lead to serious complications, from acute respiratory distress syndrome (ARDS) to renal failure, or congestive heart failure, which can all result in death. (6, 10-11) During August 2022, Boehringer Ingelheim carried out a structured expert elicitation to better understand the mortality associated with an extended GPP flare in the UK. The experts were asked to predict the number of patients with an extended flare who would die due to any reason and estimated a mortality of 2.87% for patients with moderate/severe flares and 5% for those with severe flares. (3) Over the course of the clinical development program, BI prospectively collected patient experience data in a variety of activities to better understand the experiences and perceptions of GPP from patients globally: Three patient advisory boards were held with between 6 to 9 patient representatives at each meeting, a mixed-methods multi-phase study was conducted (a virtual focus groups, a survey to confirm and expand upon findings in the focus groups, and a post-survey virtual focus group), and a retrospective analysis of the Corrona registry evaluated clinical and patient-reported outcomes in individuals with GPP (n=60) and palmoplantar pustulosis (PPP) (n=64) relative to those with plaque psoriasis (n=4,894). Patients reported substantial physical impacts secondary to both the physical limitations (pain, pustules, fever, etc.) and psychological factors (i.e. avoiding activities due to embarrassment of skin's appearance) across all patient experience activities. Stress and anxiety due to unpredictable flares and the overall burden of living with the disease were reported. In addition, patients also noted that the disease impacted their social lives, for example, being socially rejected and isolated, and feelings of loneliness. Furthermore, a sense of shame associated with GPP was also reported. (12)	

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		"When I am at my worst, every minute of the day is miserable. Small activities like showering can be overwhelming. It can hurt to wear clothes. I plan each activity closely to make sure that I do not overwhelm myself…or my hands and feet. It is extremely mentally exhausting and physically tortuous." (12) *"I feel as though the entire world is looking at me, I feel paranoid and embarrassed. I am in a constant bad mood, tears, practically at the brim of my eye ready to spill out at any given second, for any little reason. I am on edge and irritable. Even if nobody can see my GPP, I still live life as though I am transparent and everyone CAN see it. Therefore, to the outside world that has no idea what is going on, I imagine that I appear a complete basket case or someone with severe mental health issues. I am very tired those times, and I don't want to be touched or bothered. Not only because of the physical pain, but because of the feeling of being gross and unwanted." (12)* 3. In the absence of treatments specifically approved for GPP flares in the UK, treatments approved for PV are used in clinical practice. Multiple approved products are available for the treatment of plaque psoriasis, whereas there are no treatment options for GPP outside of Japan, Taiwan and Thailand as these studies were based on limited evidence from open label studies with very small patient numbers, who were not in active flares. (13-16) Therefore, no specific guidance on usage of these therapies (e.g. dosage or administration) for patients with GPP is provided in these indicated labels and there is limited evidence on the efficacy and safety of these therapies in the treatment of GPP flares. (13)	

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		There is a high unmet need for treatments that rapidly and completely resolve the symptoms associated with moderate/severe GPP flares since no licensed treatments are specifically approved for GPP flares in the UK.	
	UCB Pharma Ltd	UCB considers it appropriate that NICE evaluates this topic under the proposed evaluation route.	Comments noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	It would be entirely appropriate to evaluate spesolimab for treating acute generalised pustular psoriasis. Particularly given the limited treatments available for this rare form of psoriasis. Perhaps given the rarity it should been seen as a rarer condition in its own right, than general psoriasis and viewed in that way.	Comments noted. No action required.
	Psoriasis Association	Yes	Comments noted. No action required.
Wording	Boehringer Ingelheim	The remit of the appraisal should be for the 'treatment of moderate/severe GPP flares'.	Thank you for your comment. After discussion at the scoping workshop, the remit was changed to specify for adults with generalised pustular psoriasis presenting with a flare.
	UCB Pharma Ltd	Yes, wording is appropriate	Comment noted.

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	Psoriasis and Psoriatic Arthritis Alliance	Yes, although is this limiting the scope to 'acute' flaring patients, which may leave those with chronic GPP without access to a therapy that might help them? FDA and EMA authorisation appears to be for the latter.	Thank you for your comment. After discussion at the scoping workshop, the remit was changed to specify for adults with generalised pustular psoriasis presenting with a flare.
	Psoriasis Association	Yes	Comment noted.
Timing Issues	Boehringer Ingelheim	Generalized pustular psoriasis (GPP) is a rare, severe, clinically heterogeneous disease characterised by flares of widespread, non-infectious, macroscopically visible pustules that occur with or without systemic inflammation and are associated with significant morbidity and mortality. (17) The severity of GPP flares can vary, but flares have the potential to progress to a life-threatening status requiring hospitalisation and inpatient medical management and monitoring. Studies have found that patients with GPP have a greater frequency and duration of hospital visits compared with the general population. (4-5) The CPRD study carried out in the UK demonstrated that GPP patients had a higher overall mean inpatient admissions days (5.8 days, SD:9.7), length of hospitalisation stays (5.8 days, SD:11.1), outpatient visits (39.2 days, SD:34.9) and A&E visits (5 days, SD:11.8) compared to PV between 2015 and 2019. Patients with ≥ 1 comorbidity had a higher mean healthcare resource utilisation in both GPP and PV patients overall and at each year from 2015 to 2019. (1) All-cause mortality was highest among GPP patients compared to PPP and PV patients (p<0.001). GPP patients were	Thank you for your comment. In any appraisal NICE aims to publish guidance as close as possible to the granting of a marketing authorisation. No action required.

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		observed to have a lower mean survival time (1,793.8 days, 95% CI: 1,637.9-1,949.7) compared to PV patients (2,076.5 days, 95% CI: 2,070-2,082.8). (1) As stated above and summarising, patients with GPP have a greater number and longer hospitals stays than patients with PV, as well as higher mortality. Patients reported substantial physical impacts secondary to both the physical limitations (pain, pustules, fever, etc.) and psychological factors (i.e. avoiding activities due to embarrassment of skin's appearance) across all patient experience activities. Stress and anxiety due to unpredictable flares and the overall burden of living with the disease were reported. In addition, patients also noted that the disease impacted their social lives, for example, being socially rejected and isolated, and feelings of loneliness. Furthermore, a sense of shame associated with GPP was also reported. (12) Multiple approved products are available for the treatment of plaque psoriasis, whereas there are no licensed treatment options for GPP flares in the UK. (13-16) As such, some of the treatments indicated for plaque psoriasis have been used in patients with GPP in clinical practice. However, no specific guidance on usage of these therapies (e.g. dosage or administration) for patients with GPP is provided in these indicated labels and there is limited evidence on the efficacy and safety of these therapies in the treatment of GPP flares.(13) In the Effisayil™ 1 trial, efficacy and safety of spesolimab were evaluated in 53 patients with a moderate/severe GPP flare. One week after a single intravenous infusion, the proportion of patients with complete pustular clearance was significantly higher in the spesolimab arm (54%) than in the placebo arm (6%; $p < 0.001$), and this was sustained over the 12-week study. (18) Spesolimab is the first-in-class monoclonal antibody against IL-36R that	

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		demonstrates rapid and sustained improvement in clinical symptoms and patient quality of life with a favourable benefit-risk profile for GPP flare. (18-20) Given the high patient burden, the lack of licensed treatment options and the effect shown of Spesolimab the in Effisayil-1 Trial, there is urgency for this review to take place.	
	UCB Pharma Ltd	Timing should reflect NICE timelines for STA evaluation.	Thank you for your comment. No action needed.
	Psoriasis and Psoriatic Arthritis Alliance	Where there are limited effective therapies, the evaluations is urgent, particularly given the potential in-patient stay that a flare could cause.	Thank you for your comment. In any appraisal NICE aims to publish guidance as close as possible to the granting of a marketing authorisation. No action needed.
	Psoriasis Association	Once a marketing authorisation has been obtained the NICE evaluation should be carried out at the earliest convenience so as to give people with GPP access to a dedicated treatment.	Thank you for your comment. In any appraisal NICE aims to publish guidance as close as possible to the granting of a marketing authorisation. No action needed.

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Additional comments on the draft remit	Boehringer Ingelheim	No additional comments.	No action needed.
	UCB Pharma Ltd	No additional comments.	No action needed.
	Psoriasis and Psoriatic Arthritis Alliance	No additional comments.	No action needed.
	Psoriasis Association	No additional comments.	No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Boehringer Ingelheim	Generalised pustular psoriasis (GPP) is a rare, severe, clinically heterogeneous disease characterised by flares of widespread, non-infectious, macroscopically visible pustules that occur with or without systemic inflammation and are associated with significant morbidity and mortality. Historically, GPP has been classified as a variant of psoriasis vulgaris (PV, or plaque psoriasis); however, accumulating evidence indicates that these are distinct conditions, requiring different treatment approaches. (17) More recently, the European Rare and Severe Psoriasis Expert Network (ERASPEN) consensus statement delineated these pustular diseases from PV, noting that 'primary pustules do not form part of the spectrum of PV except when pustules arise within or at the edge of psoriasis plaques' and that 'in these cases, the term to be used is "psoriasis cum pustulatione" (psoriasis with	Thank you for your comment. The background information has been amended to reflect the feedback from the consultation and that heard at the scoping workshop.

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		pustules) [and] this should not be considered pustular psoriasis'. (21) The Japanese Dermatological Association (JDA) diagnostic definition of GPP, which requires the presence of systemic symptoms, extensive flush with multiple sterile pustules, neutrophilic subcorneal pustules, and repeated recurrence, excludes PV with transient pustules. (13) JDA guidelines also indicate that concomitant PV may or may not be present. (13) In recent textbooks, classification of GPP has been refined as a member of a clinically heterogenous group of diseases collectively known as 'pustular psoriasis,' and a 'distinctive acute variant' within the spectrum of psoriatic diseases. (22, 23) Published medical literature reporting cases of GPP also indicate that in a significant proportion of cases, patients with GPP do not have a past history of PV and thus it cannot be considered to be a consequence of PV. (24-27) Furthermore, acute forms can be further divided into GPP with or without concomitant PV. (21, 28) GPP was originally considered a variant or subtype of PV; however, accumulating evidence indicates that although 30–50% of patients with GPP may have a past history of PV, the two diseases are distinct. (6, 25-27, 29-32) As such, it is incorrect to consider GPP part of a continuum of PV severity or an acute form, rather than a condition with its own subtypes and manifestations. This also implies that in individuals with both PV and GPP, the two conditions may be separate and require different treatment considerations. (17) Even prior to the discovery of underlying genetic differences between the two conditions, researchers had proposed independent classifications for GPP or GPP subtypes, such as 'generalized pustular 'dermatosis'. (33) More recently, a better understanding of the genetic markers and molecular pathways involved in the pathology of GPP and PV has led to a wider acceptance that these are likely to be separate entities. (28, 34-37) Considering GPP as a disease in its own right, instead of as a severe form of PV, will enable greater	

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		focus on its specific pathogenesis and the needs of patients. A therapeutic approach developed specifically for GPP, rather than one based on the PV paradigm, might lead to better patient outcomes. Indeed, many treatments for PV have insufficient efficacy in GPP. (17) Please find below a summary of the main differences between GPP and PV. (17) Table 1. Clinical, histological, and genetic differences between psoriasis vulgaris and generalized pustular psoriasis. **Psoriasis vulgaris** / **Generalized pustular psoriasis** **Dermatologic features** Bright red plaques / Widespread, primary pustules Thick, silvery-white scale / Sterile Well demarcated / Indistinct pustules (often merged) Rarely pruritic / Pruritic Rarely pustules at the edge of plaques / No plaques except when co-occurrence of psoriasis vulgaris **Histology** Thickened epidermis / Subcorneal pustules characterized by Kogoj's spongiform pustules Hyperproliferation/abnormal keratinocyte differentiation / Neutrophil infiltrates predominate Parakeratosis **Clinical features and comorbidities** Chronic presentation / Acute flare Less systemic presentation / Systemic inflammation Outpatient management / Frequent requirement for hospitalization (with flare) Low risk of acute complications and/or death, except when erythrodermic presentation (>90% body surface area involved) / Rarely severe/fatal complications (sepsis, acute respiratory distress syndrome, heart failure) Extra-cutaneous symptoms (cholestasis, cholangitis, interstitial pneumonitis, acute renal failure) Psoriatic arthritis / Obesity Inflammatory bowel disease / Hypertension Diabetes / Hyperlipidemia Cardiovascular disease / Diabetes **Genetics** Multigenic basis / Single gene drivers *HLA-Cw6* involvement / No *HLA-Cw6* involvement Th17 cell activation pathway gene involvement (*IL12B, IL23A, IL23R*, TRAF3IP2, NFKBIZ) / Mutations in *IL36RN, AP1S3, MPO, SERPINA3* (*CARD14**) **Gene expression and immunology** Cytokine expression changes in IL-17A, IL-22, IL-23p19, IFNγ, IL-18 and myxovirus resistance 1 / Cytokine expression changes in IL-1β, IL-36α and IL-36γ Less neutrophilic expression change / Neutrophil/monocyte dominant expression profile changes Little change in expression profiles in non-lesional skin / Considerable change in expression profiles in non-lesional skin Broadly driven by adaptive immune system / Broadly driven by innate immune system *The pathogenicity of *CARD14* mutations for GPP has not been confirmed GPP and PV are distinct in terms of distribution on the body, and histopathologic and clinical appearance: PV is characterised by localized discrete plaques with excess scale resulting from abnormal differentiation of keratinocytes; GPP is characterised by widespread eruption of neutrophilic, non-infectious pustules. (17) GPP is notable for its acute presentation, with disease flares and complications resulting directly from neutrophilic inflammation, often requiring hospitalization; PV is a chronic disease of the skin with multifactorial comorbidities, typically managed in an outpatient setting. Genetic drivers of GPP and PV also differ: many cases of GPP are familial and	

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		seem to follow a monogenic Mendelian model. GPP is frequently associated with mutations in IL36RN, which are not seen in PV. PV follows a complex polygenic model, with the key genetic driver being HLA*C0602, which is not associated with GPP. (17) The IL-36 pathway is predominantly involved in GPP, while the IL-23/IL-17 axis drives plaque psoriasis. (17, 38-41) The separation of GPP from PV in these key guidelines recapitulates the importance of recognizing and treating GPP as an independent disease, linking accurate and specific diagnosis to treatment decisions and patient management recommendations. (17) Generalised pustular psoriasis is therefore a distinct disease from psoriasis vulgaris and should be evaluated as such. The background information has been written describing plaque psoriasis rather than GPP. This could be confusing and is not appropriate, GPP flares must be treated as a distinct disease from PV. Therefore, we ask you to refer only to GPP flares and the background should focus on this disease rather than PV. Furthermore, we strongly suggest that the psoriasis guideline would not be appropriate for treating patients with GPP flares since this condition will require different treatment approaches.	

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		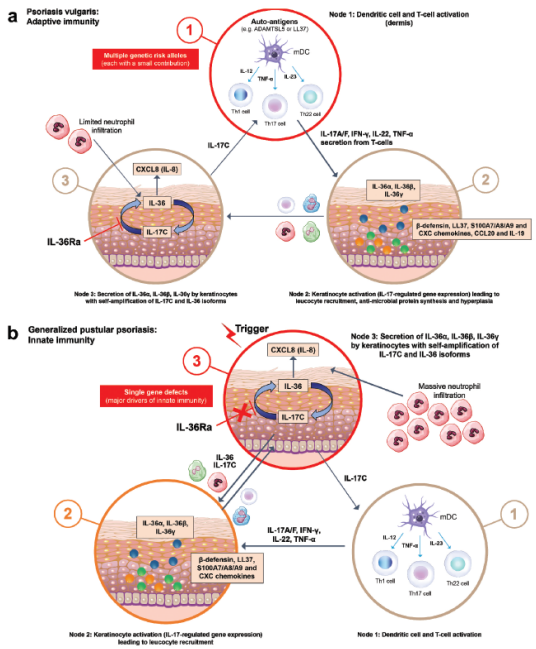 Figure 3. Fundamental variations in the Type 3 immune mechanism differentiate (Aa) PV and (Bb) GPP. Despite the severity of GPP, there are limited therapeutic options, and none have been specifically designed based on the disease pathogenesis. Treatment guidelines typically recommend cyclosporine, retinoids, infliximab, and methotrexate as first-line therapies, based on very weak evidence. (13, 42) These treatments are often unsuitable for long-term use because they are associated with toxicities or are (or become) ineffective. (13, 42) Biologic therapy has been reported to be effective in GPP, and several biologics have been approved for use in Japan, Taiwan, and Thailand. (17) Although this is an important advance in GPP treatment options, current evidence is based on the results of small, single-arm trials using efficacy outcomes and time points	

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		derived from psoriasis vulgaris (PV) trials and not specifically designed for GPP. (17) Up to date, no treatments have been approved specifically for the treatment of GPP flares and there is very weak evidence, if any, for the effectiveness of existing options for flare prevention. (3) The lack of approvals in the UK/Europe for biologics that are approved for use in PV supports this distinction between PV and GPP. (17) As a relatively common disease, evidence, and recommendations for the treatment of PV are well developed and provide multiple, approved therapeutic options for all disease grades. (43-46) The same is not true for GPP; in part because its rarity makes the conduct of clinical trials more challenging, but also because treatment is needed for both flare control and flare prevention. (13) Indeed, many treatments for PV have insufficient efficacy in GPP. (13) As understanding of the causes and unique nature of GPP has improved, the opportunity for appropriately targeted therapy to improve patient outcomes has increased. (17) Since these are two different diseases, with two different pathogenesis, we request that the psoriasis guideline is not considered for this evaluation. Boehringer Ingelheim will carrying out a structured expert elicitation exercise to understand and quantify the efficacy of the most commonly used treatments in GPP flares in the UK. These results will be shared in Dec 2022.	
	UCB Pharma Ltd	UCB wants to flag that the description of NICE clinical guideline 153 on the management of general psoriasis is incomplete. The background provides information about topical treatments, phototherapy, and systemic non-biological therapies, but there is no mention of systemic biological therapies. UCB believes it will be more appropriate to present the full range of therapies, including biological treatments, as outlined in the guideline to allow readers to put things into perspective, especially since systemic non-biological therapies are included in the comparator list.	Thank you for your comment. The text has changed to align with the therapies used in clinical practice in the NHS according to the feedback from the consultation and that

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			heard at the scoping workshop.
	Psoriasis and Psoriatic Arthritis Alliance	There is some published evidence that some forms of pustular psoriasis are associated with smoking, although we would not want to stigmatise those with the condition, as being the sole cause, it is perhaps worth exploring the wider influence or triggers that perhaps are not captured in the trial data.	Thank you for your comment. The background section is meant to be a brief summary of the condition. The influence of smoking or other factors can be explored in the evidence submissions. No action needed.
	Psoriasis Association	The background information does lean somewhat on the NICE Guideline 153 for plaque psoriasis and this is not always appropriate. As stated within the scope, GPP is a medical emergency and cycling through topical / UV / systemics may not be appropriate when time is of the essence. Topical treatments would be used in addition to other therapies such as systemics / biologics.	Thank you for your comment. The text has changed to align with the therapies used in clinical practice in the NHS according to the feedback from consultation and that heard at the scoping workshop.
Population	Boehringer Ingelheim	We would like to suggest the population be amended to “adult patients with GPP presenting with a moderate/severe flare”, since this was the population defined in the Effisayil-1 Trial and where the greatest unmet need for treatment is from a patient perspective: • 18 to 75 years of age	Thank you for your comment. After discussion at the scoping workshop, the population was

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		• A history of GPP consistent with the diagnostic criteria of the European Rare and Severe Psoriasis Expert Network. • A GPP flare of moderate-to-severe intensity (Defined as a Generalized Pustular Psoriasis Physician Global Assessment - GPPGA- total score of ≥3, new or worsening pustules, a GPPGA pustulation subscore of ≥2, and ≥5% of body-surface area with erythema and the presence of pustules). (18)	changed to specify for adults with generalised pustular psoriasis presenting with flares.
	UCB Pharma Ltd	No comments	No action needed.
	Psoriasis and Psoriatic Arthritis Alliance	There is a paucity of epidemiology data, with a wide-ranging prevalence, it is also noted in some studies, that it peaks between 40 and 59 years of age. Women appear to outnumber men 2 to 1, although not in all cohorts. There are also associated comorbidities such as metabolic syndrome. Generalized Pustular Psoriasis: Mirza HA, Badri T, Kwan E. Generalized Pustular Psoriasis. [Updated 2021 Sep 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493189/	Thank you for your comment. The population in the scope is in line with the population in the relevant clinical trials.
	Psoriasis Association	No comments.	No action needed.
Subgroups	Boehringer Ingelheim	As described above, GPP is a distinct disease from psoriasis vulgaris and therefore it is not appropriate to use this as a subgroup in the evaluation of a therapy for GPP. Please note that patients with plaque psoriasis without pustules or with pustules restricted to psoriatic plaques were excluded from the Efiisayil-1 Trial. (38) In sub-analysis studies, spesolimab has been shown to be a viable treatment option for patients with GPP, regardless of their plaque psoriasis status. (47)	Thank you for your comment. After discussion at the scoping workshop, the subgroups were removed from the scope.

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		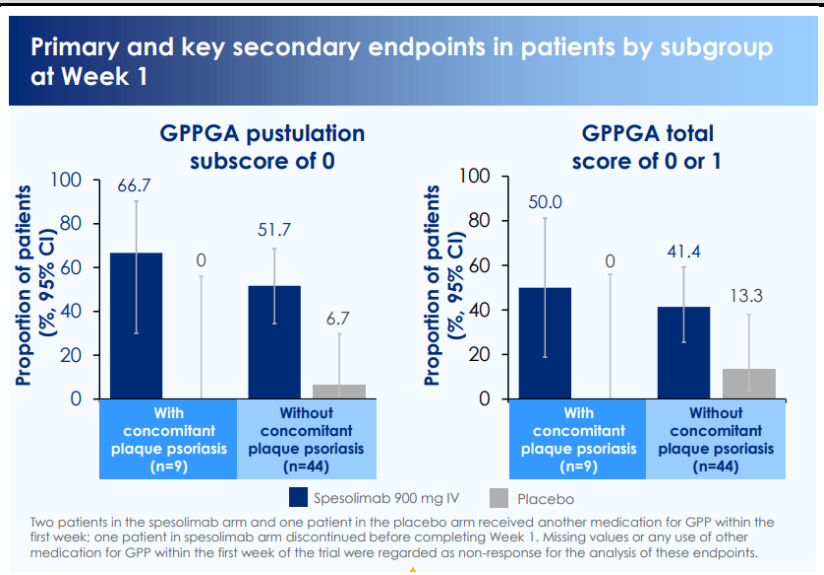 It is for all these reasons that we request to remove 'severity of psoriasis' as well as 'severity of psoriasis flare' (directly considered in the scope of the population) from the subgroups.	
	UCB Pharma Ltd	No comments	No action needed.
	Psoriasis and Psoriatic Arthritis Alliance	Perhaps it might be worth exploring those that also have generalised plaque psoriasis, and or psoriatic arthritis and GPP versus those that just present with GPP, with perhaps seeing if the pure GPP cohort benefit more. Or indeed chronic versus acute.	Thank you for your comment. After discussion at the scoping workshop, the subgroups were

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			removed from the scope.
	Psoriasis Association	No comments.	No action needed.
Comparators	Boehringer Ingelheim	Since the psoriasis guidelines focus on the chronic treatment of psoriasis rather than treating GPP flares and since GPP is a different disease than PV, we do not believe it is appropriate to use the treatment guidelines from PV. Instead it is more appropriate to understand the (off-label) treatments that are being used in UK clinical practice to treat GPP flares. Boehringer Ingelheim carried out a robust structured expert elicitation exercise to identify the treatments used for GPP flares in the UK. As part of this exercise, experts told us that ciclosporin, acitretin, infliximab and methotrexate are used as therapies for the treatment of GPP flares in the UK. (3) This study will be completed by December 2022. The list of comparators in the draft scope has been presented to a panel of experts and they agreed vitamin D analogues, dithranol and phototherapy, are not currently used in the UK not only because of the distinct nature of PV and GPP, but also because of the severity of the disease to which we are referring in this scoping process. They acknowledged that ciclosporin (70%) or infliximab (15%) or methotrexate (5%) or acitretin (10%) on top of topical corticosteroids are currently used as first line treatment for GPP flares. (3,48)	Thank you for your comment. The comparators listed in the scope aimed to be inclusive. The scope has been updated to reflect treatments in use in clinical practice in the NHS according to the feedback heard in the scoping workshop and from consultation.
	UCB Pharma Ltd	No comments	No action needed.

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	Psoriasis and Psoriatic Arthritis Alliance	Yes, those are what are generally offered.	Thank you for your comment. The scope has been updated to reflect treatments in use in UK clinical practice according to the feedback heard in the scoping workshop and from consultation.
	Psoriasis Association	No – dithranol is not used for pustular psoriasis.	Thank you for your comment. The scope has been updated to reflect treatments in use in UK clinical practice according to the feedback heard in the scoping workshop and from consultation.
Outcomes	Boehringer Ingelheim	Severity of psoriasis: We strongly suggest replacing the 'severity of psoriasis' outcome with Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) pustulation subscore, as this measures the primary component of GPP flares (pustules). Psoriasis symptoms: As previously explained, GPP is a distinct disease from psoriasis vulgaris, in consequence 'psoriasis symptoms' should be removed from the list. Mortality, and relapse rate were not included as outcomes in the EFFISAYIL-1 trial. Relapse rate will be one of the main outcomes of the EFFISAYIL-2 trial.	Thank you for your comment. The scope outcomes have been updated to reflect the feedback heard at the scoping workshop and from consultation. '*Severity of psoriasis'* has been removed and replaced with '*severity of flares'*. Also

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		Then, we do not expect to include evidence on these outcomes in our submission and request that it is removed from the scope. However, we will present evidence on the remaining outcomes. We believe that the relevant outcomes for this evaluation are: GPPGA pustulation subscore, GPPGA total score, response rate, duration of the response, adverse effects of treatment, and health-related quality of life.	'*symptoms specific to GPP including pain'* has also been added as an outcome.
	UCB Pharma Ltd	No comments	No action needed.
	Psoriasis and Psoriatic Arthritis Alliance	Yes	Thank you for your comment. No action needed.
	Psoriasis Association	Yes	Thank you for your comment. No action needed.
Equality	Boehringer Ingelheim	No comments	No action needed.
	UCB Pharma Ltd	No comments	No action needed.
	Psoriasis and Psoriatic Arthritis Alliance	None that apply under wording of the act.	Thank you for your comment. No action needed.
	Psoriasis Association	No comments	No action needed.

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Other considerations	Boehringer Ingelheim	Since GPP is distinct from plaque psoriasis, these are not relevant appraisals. The same is true for the related guidelines, interventional procedures and quality standards mentioned.	Thank you for your comment.
	UCB Pharma Ltd	No comments	No action needed.
	Psoriasis and Psoriatic Arthritis Alliance	No comments	No action needed.
	Psoriasis Association	Would / could / should the dose be adjusted for obese patients?	Thank you for your comment. The committee will consider the clinical evidence presented to it and make recommendations based on that.
Questions for consultation	Boehringer Ingelheim	1. Are there any statistics for the prevalence of GPP in England or the UK? Boehringer Ingelheim carried out a retrospective study using the Clinical Practice Research Datalink (CPRD) AURUM. Diagnosis codes in CPRD AURUM were coded using SNOMED (Systematized Nomenclature of Medicine) which were used to identify and extract patient cohorts. The CPRD database chosen for this study used the December 2020 data build which included a coverage of approximately 40 million patients and 1,373 practices. Patients in contributing CPRD practices that were eligible to be linked to hospital records within the Hospital Episodes Statistics (HES) database were identified and extracted using ICD-10 coding. Patients were linked to the Office of National Statistics (ONS) to describe mortality data and Index of Multiple	Thank you for your comments. The responses to these questions were presented at the scoping workshop. Details of any changes to the scope have been mentioned in the responses above. No further action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Deprivation (IMD) quartiles as proxy for socioeconomic status of area of the GP (general practitioner, general practice) practice. (1) *Study design and sample selection:* Patients with a diagnosis code indicative of GPP, PPP, or plaque psoriasis were identified in the study period from 01 January 2008 to 31st December 2019. Eligible patients included those that are alive, with a minimum of 1-year prior registration before entering the study cohort. Prior registration ensures the data to be analysed in the study is of research quality standard. The index date was defined as the date the patients enter the study cohort at the latter of 1st January 2008, 1 year from first registration in CPRD, or 1 year from the date the practice became research quality standard (the latter two ensures at least year look back period is available from study entry). Incident cases were identified as eligible patients that have a first diagnosis code earliest date of CPRD SNOMED or HES ICD-10 coding system where no previous code was recorded in the year of diagnosis. Although clinical coding was not available for GPP patients with flares, a proxy definition of GPP flares was used which includes GPP incident patients with at least 3 consecutive inpatient hospitalisation stays associated with an ICD-10 code of L40.1 indicative of GPP diagnosis. Patients with a prior code or a history of code were removed from the numerator and denominator of the incidence population. Patients who were diagnosed with GPP along with PPP where categorised into the GPP patient cohort and GPP was the primary diagnosis. Likewise, patients with a PPP diagnosis along with PV were categorised into the PPP patient cohort as PPP was the primary diagnosis. Prevalent cases were those with a minimum of 1 diagnostic code (SNOMED or ICD-10) at any time before the study end. Patients are considered prevalent at baseline if a medical code indicative of GPP, PPP, or plaque psoriasis was recorded at any time during the minimum of 1-year look back period. All-cause mortality was analysed using Kaplan-Meier and log-rank tests for each patient cohort. Survival in patients in the GPP flare group and PV group were stratified by age of disease onset, gender, and	

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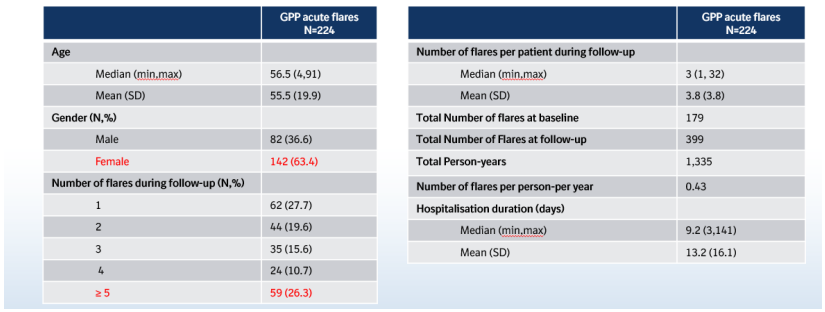
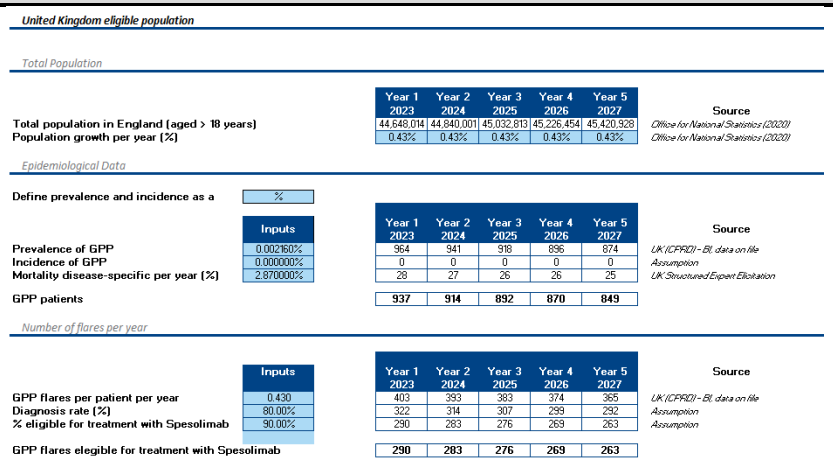
		comorbidity status for all incident cases and visualised using the log-rank test. (1) *Findings* According to the data collected, the GPP prevalence in England was 0.31 per 100,000 in 2008 to 2.16 per 100,000 (95% CI:1.84-2.48) in 2019. 2. Are there any statistics for the prevalence of acute flares of GPP in the England or the UK? In the CPRD study previously mentioned, a prevalence of 0.26 events per 100,000 in 2008 to 1.63 per 100,000 in 2019 was reported.(1) It is important to note that although no clinical coding was available for GPP patients with flares, a proxy definition of GPP flares was used that included GPP incident patients with at least 3 consecutive inpatient hospitalisation stays associated with an ICD-10 code of L40.1 indicative of GPP diagnosis.(1) Characteristics of GPP acute flares (Sub-group Analysis)  It was also calculated that a patient can suffer from 0.43 flares per year, resulting from the ratio between number of flares and total person-year. (1)	

	GPP acute flares N=224
Age	
Median (min,max)	56.5 (4,91)
Mean (SD)	55.5 (19.9)
Gender (N,%)	
Male	82 (36.6)
Female	142 (63.4)
Number of flares during follow-up (N,%)	
1	62 (27.7)
2	44 (19.6)
3	35 (15.6)
4	24 (10.7)
≥ 5	59 (26.3)

	GPP acute flares N=224
Number of flares per patient during follow-up	
Median (min,max)	3 (1, 32)
Mean (SD)	3.8 (3.8)
Total Number of flares at baseline	179
Total Number of Flares at follow-up	399
Total Person-years	1,335
Number of flares per person-per year	0.43
Hospitalisation duration (days)	
Median (min,max)	9.2 (3,141)
Mean (SD)	13.2 (16.1)

Section	Consultee/ Commentator	Comments [sic]	Action
		In France they have also calculated the frequency of flares from the SNDS database and concluded that a patient with GPP experiences 0.4 flares per year. (49) 3. How many people would be expected to be eligible for spesolimab in England? BI carried out a retrospective study to understand the epidemiology and healthcare resource use of generalised pustular psoriasis (GPP), palmoplantar pustulosis (PPP), and psoriasis vulgaris (PV) patients in the UK (United Kingdom). (1) The reported prevalence of GPP was 2.16 events per 100,000 (95% CI:1.84-2.48) and it was observed that a patient can suffer 0.43 moderate/severe flares per year. (1) A population of 44.6 million over 18 years of age in England was estimated for 2023 and a mortality rate of 2.87% for moderate/severe flares was identified, resulting in 403 patients who could suffer a GPP flare during that year. (2-3) Since GPP is a rare and difficult disease to diagnose, we assumed a diagnosis rate of 80% and 90% of those patients would be eligible to receive spesolimab (excluding contraindicated and specific populations such as pregnant women), resulting in 290 patients who will be candidates to receive spesolimab during 2023.	

Section	Consultee/ Commentator	Comments [sic]	Action
			

United Kingdom eligible population

Total Population

	Year 1 2023	Year 2 2024	Year 3 2025	Year 4 2026	Year 5 2027	Source
Total population in England (aged > 18 years)	44,648,014	44,840,001	45,032,813	45,226,454	45,420,928	Office for National Statistics (2020)
Population growth per year (%)	0.43%	0.43%	0.43%	0.43%	0.43%	Office for National Statistics (2020)

Epidemiological Data

Define prevalence and incidence as a %

	Inputs	Year 1 2023	Year 2 2024	Year 3 2025	Year 4 2026	Year 5 2027	Source
Prevalence of GPP	0.002160%	964	941	918	896	874	UK (CPRD) - BI data on file
Incidence of GPP	0.000000%	0	0	0	0	0	Assumption
Mortality disease-specific per year (%)	2.870000%	28	27	26	26	25	UK Structured Expert Elicitation
GPP patients		937	914	892	870	849	

Number of flares per year

	Inputs	Year 1 2023	Year 2 2024	Year 3 2025	Year 4 2026	Year 5 2027	Source
GPP flares per patient per year	0.430	403	393	383	374	365	UK (CPRD) - BI data on file
Diagnosis rate (%)	80.00%	322	314	307	299	292	Assumption
% eligible for treatment with Spesolimab	90.00%	290	283	276	269	263	Assumption
GPP flares elegible for treatment with Spesolimab		290	283	276	269	263	

4. How often do people experience a generalised pustular psoriasis flare up?

In the CPRD study previously mentioned, it was reported that a patient can suffer from 0.43 flares per year, resulting from the ratio between number of flares and total person-year. (1)

It is important to note that although no clinical coding was available for GPP patients with flares, a proxy definition of GPP flares was used that included GPP incident patients with at least 3 consecutive inpatient hospitalisation stays associated with an ICD-10 code of L40.1 indicative of GPP diagnosis. (1)

Section	Consultee/ Commentator	Comments [sic]	Action

Characteristics of GPP acute flares (Sub-group Analysis)

	GPP acute flares N=224
Age	
Median (min,max)	56.5 (4,91)
Mean (SD)	55.5 (19.9)
Gender (N,%)	
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Number of flares per patient during follow-up	
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Number of flares per person-per year	0.43
Hospitalisation duration (days)	
Median (min,max)	9.2 (3,141)
Mean (SD)	13.2 (16.1)

In France they have also calculated the frequency of flares from the SNDS database and concluded that a patient with GPP experiences 0.4 flares per year. (49)

5. Where do you consider spesolimab will fit into the existing treatment pathway for acute generalised pustular psoriasis?

Early discussions with experts reflected that spesolimab would be used as a first-line treatment for moderate/severe GPP flares. (48)

6. Are the following treatments for severe or very severe plaque psoriasis used off license for acute flares of GPP?
7. TNF-alpha inhibitors (adalimumab, etanercept, infliximab and certolizumab pegol)
8. IL-17 family inhibitors or receptor inhibitors (brodalumab, ixekizumab, secukinumab and bimekizumab)
9. IL-23 inhibitors (guselkumab, tildrakizumab and risankizumab)

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		10. IL-12/IL-23 inhibitors (ustekinumab) 11. JAK inhibitors (upadacitinib) 12. Apremilast 13. Dimethyl fumarate Boehringer Ingelheim carried out a robust structured expert elicitation exercise to identify the treatments used for GPP flares in the UK. As part of this exercise, experts told us that ciclosporin, acitretin, infliximab and methotrexate are used as therapies for the treatment of GPP flares in the UK. (3) The list of comparators in the draft scope has been presented to a panel of experts and they agreed vitamin D analogues, dithranol and phototherapy, are not currently used in the UK not only because of the distinct nature of PV and GPP, but also because of the severity of the disease to which we are referring in this scoping process. They acknowledged that cyclosporine (70%) or infliximab (15%) or methotrexate (5%) or acitretin (10%) on top pf topical corticosteroids are currently used as first line treatment for GPP flares. (3,48) This study will be completed by December 2022. The National Psoriasis Foundation Medical Board guideline for the treatment of pustular psoriasis and the Japanese guideline for the management and treatment of generalized pustular psoriasis recommend ciclosporin retinoids, infliximab, and methotrexate as first-line therapies, based on very weak evidence. (13, 42) 14. How should best supportive care be defined? We believe best supportive care consists of bed rest, symptom and pain relief, management of co-morbidities, psychological support. Experts agreed that	

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		best supportive care would not be a suitable comparator as it could be used in any line of treatment. (48) 15. Is spesolimab expected to be of significant additional benefit compared to current treatment? Despite the severity of GPP, there are limited therapeutic options, and none have been specifically designed based on the disease pathogenesis. The National Psoriasis Foundation Medical Board guidelines for the treatment of pustular psoriasis and the Japanese guidelines for the management and treatment of generalized pustular psoriasis recommend cyclosporine, retinoids, infliximab, and methotrexate as first-line therapies, based on very weak evidence. (13, 42) These treatments are often unsuitable for long-term use because they are associated with toxicities or are (or become) ineffective. (13, 42) Several biologics have been approved for use in Japan, Taiwan, and Thailand based on the results of small, single-arm trials using efficacy outcomes and time points derived from psoriasis vulgaris (PV) trials and not specifically designed for GPP. (17) None of these studies assessed biologics for the treatment of flares of GPP and up to date, no treatments have been approved specifically for the treatment of GPP flares in the UK/Europe. Spesolimab has been studied in Effisayil-1, the only and largest ever clinical trial of patients with GPP flares. At the end of week 1, a total of 19 of 35 patients (54%) in the spesolimab group had a pustulation subscore of 0, as compared with 1 of 18 patients (6%) in the placebo group (difference, 49 percentage points; 95% confidence interval [CI], 21 to 67; P<0.001). A total of 15 of 35 patients (43%) had a GPPGA total score of 0 or 1, as compared with 2 of 18 patients (11%) in the placebo group (difference, 32 percentage points; 95% CI, 2 to 53; P=0.02). Patients showed sustained full pustular clearance or improvement of skin for study duration and an overall manageable safety and	

Section	Consultee/ Commentator	Comments [sic]	Action
		tolerability profile. No differences based on pre-specified subgroups were observed. Furthermore, significant improvements at week 1 in patient-reported outcomes as pain (43%), psoriasis symptoms (39%), fatigue (71%) and DLQI (24%) were reported. (18) 16. Does generalised pustular psoriasis significantly shorten life or severely impair its quality? GPP can progress over time due to both cutaneous and extracutaneous manifestations contributing to severe morbidity and potential mortality. As a multisystemic disease, GPP can have extracutaneous complications affecting the cardiovascular system, liver, respiratory system, and nervous system. (6-8) Microbial infections can occur within pustular skin, (9) with the potential to develop sepsis that can be fatal. (6,9) During a flare, patients present with systemic inflammation, which can cause a range of symptoms such as malaise, high-grade fever and diarrhoea. (10) Extracutaneous symptoms experienced by patients with GPP can include cholestasis, cholangitis, epigastric pain, arthritis, interstitial pneumonitis, oral lesions, and acute renal failure. (9) This range of manifestations can lead to serious complications, from acute respiratory distress syndrome (ARDS) to renal failure, or congestive heart failure, which can all result in death. (6, 10-11) Although the severity of GPP flares can vary, flares have potential to progress to a life-threatening status requiring hospitalisation and inpatient medical management and monitoring. Studies found that patients with GPP have a greater frequency and duration of hospital visits compared with the general population. (4-5) The CPRD study carried out in the UK demonstrated that GPP patients had a higher overall mean numbers of inpatient admissions days (5.8 days, SD:9.7),	

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		length of hospitalisation stays (5.8 days, SD:11.1), outpatient visits (39.2 days, SD:34.9) and A&E visits (5 days, SD:11.8) compared to PV between 2015 and 2019. Patients with ≥ 1 comorbidity had a higher mean healthcare resource utilisation in both GPP and PV patients overall and at each year from 2015 to 2019. (1) All-cause mortality was highest among GPP patients compared to PPP and PV patients ($p<0.001$). GPP patients were observed to have a lower mean survival time (1,793.8 days, 95% CI: 1,637.9-1,949.7) compared to PV patients (2,076.5 days, 95% CI: 2,070-2,082.8). (1) During August 2022, Boehringer Ingelheim carried out a structured expert elicitation to better understand the mortality associated with an extended GPP flare in the UK. The experts were asked to predict the number of patients with an extended flare who would die due to any reason and estimated a mortality of 2.87% for patients with moderate/severe flares and 5% for those with severe flares. (3) Over the course of the clinical development program, BI prospectively collected patient experience data in a variety of activities to better understand the experiences and perceptions of GPP from patients globally: Three patient advisory boards were held with between 6 to 9 patient representatives at each meeting, a mixed-methods multi-phase study was conducted (a virtual focus groups, a survey to confirm and expand upon findings in the focus groups, and a post-survey virtual focus group), and a retrospective analysis of the Corrona registry evaluated clinical and patient-reported outcomes in individuals with GPP (n=60) and palmoplantar pustulosis (PPP) (n=64) relative to those with plaque psoriasis (n=4,894). Patients reported substantial physical impacts secondary to both the physical limitations (pain, pustules, fever, etc.) and psychological factors (i.e. avoiding activities due to embarrassment of skin's appearance) across all patient experience activities. Stress and anxiety due to unpredictable flares and the overall burden of living with the disease were	

Section	Consultee/ Commentator	Comments [sic]	Action
		reported. In addition, patients also noted that the disease impacted their social lives, for example, being socially rejected and isolated, and feelings of loneliness. Furthermore, a sense of shame associated with GPP was also reported. (12) *"When I am at my worst, every minute of the day is miserable. Small activities like showering can be overwhelming. It can hurt to wear clothes. I plan each activity closely to make sure that I do not overwhelm myself…or my hands and feet. It is extremely mentally exhausting and physically tortuous." (12)* *"I feel as though the entire world is looking at me, I feel paranoid and embarrassed. I am in a constant bad mood, tears, practically at the brim of my eye ready to spill out at any given second, for any little reason. I am on edge and irritable. Even if nobody can see my GPP, I still live life as though I am transparent and everyone CAN see it. Therefore, to the outside world that has no idea what is going on, I imagine that I appear a complete basket case or someone with severe mental health issues. I am very tired those times, and I don't want to be touched or bothered. Not only because of the physical pain, but because of the feeling of being gross and unwanted."(12)* An online survey consisting of 43 questions answered by individuals recruited from an opt-in market research database was carried out by Boehringer Ingelheim. A substantial proportion of respondents had symptoms for years, had consulted multiple healthcare professionals, and experienced misdiagnoses before receiving a diagnosis of GPP. Emotional stress was the most common cause of flares and many respondents reported a fear of flares. Respondents defined flares by the presence of itching, an increase in the size of the affected area, more crusts or pustules, and fatigue. A change in mood was the most burdensome symptom. GPP had an impact on activities of daily living even in the absence of flares and many respondents felt that their	

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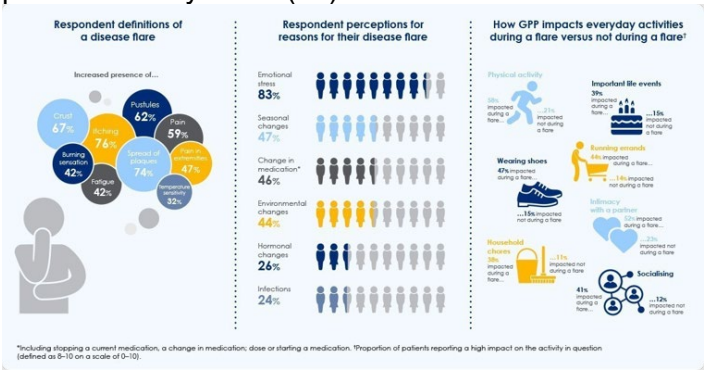
		physician did not understand the level of emotional, psychological, or physical pain caused by GPP. (59)  In the absence of treatments specifically approved for GPP flares in the UK, treatments approved for PV are used in clinical practice. Multiple approved products are available for the treatment of plaque psoriasis, whereas there are no treatment options for GPP outside of Japan, Taiwan and Thailand as these studies were based on limited evidence from open label studies with very small patient numbers, who were not in active flares. (13-16) Therefore, no specific guidance on usage of these therapies (e.g. dosage or administration) for patients with GPP is provided in these indicated labels and there is limited evidence on the efficacy and safety of these therapies in the treatment of GPP flares. (13) There is a high unmet need for treatments that rapidly and completely resolve the symptoms associated with moderate/severe GPP flares since no licensed treatments are approved for GPP flares in the UK. 17. Would spesolimab be a candidate for managed access? Yes, at this stage we could consider it.	

Section	Consultee/ Commentator	Comments [sic]	Action
		18. Do you consider that the use of spesolimab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Skin diseases can have a major impact on patients' lives in terms of psychological well-being, social functioning, and everyday activities. Over the past two decades the effect of different skin diseases on the quality of life (QoL) of patients has been extensively documented and various dermatology-specific instruments have been described to measure this impact. QoL assessment has become an important endpoint in clinical trials in addition to the traditional clinical outcomes. It is also increasingly being used in routine clinical practice and by policy makers and health administrators. Because patient-reported outcomes such as QoL measures reflect patients' perspectives, they have the potential to encourage patients' active involvement in clinical management decision-making. In dermatology, QoL and its measurement hold a special meaning as many skin diseases are chronic and their burden is associated with living with the disease. Moreover, the visible nature of many skin diseases is associated with significant psychosocial impact, something not directly measurable with traditional clinical outcome measures and which makes evaluation of QoL even more crucial in dermatology. It was for this reason that various dermatology-specific and disease-specific measures have been developed to quantify the impact of skin diseases on patients' QoL. (51) The Dermatology Life Quality Index (DLQI) was the first dermatology-specific QoL instrument and to date is the most commonly used. The literature related to its technical properties as well as to its use in clinical research is expanding rapidly. (51) As none of the instruments can capture 100% of the information, we considered that DLQI is most widely used measure to assess HRQOL related to skin diseases and the most sensitive measure for capturing improvements in health-	

Section	Consultee/ Commentator	Comments [sic]	Action
		related quality of life (HRQOL) during dermatological treatments. Furthermore, the reliability, construct validity, and responsiveness of the DLQI have all been demonstrated in patients with psoriasis. (51-55) 19. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. As mentioned above, we believe that the DLQI could be a reliable, accepted and more widely used instrument to adequately measure the quality of life associated with skin diseases. (51-55) We therefore request that this information must be taken into account. 20. In people with darker skin is the appearance of pustular psoriasis less obvious, and may severity may be underestimated? Early discussions with experts suggested that in people with darker skin the appearance of GPP could be less obvious, and the severity may be underestimated. Expert opinion: *'Erythema, in particular, may be underestimated in darker skins, although I don't think that pustules would be harder to see. So scores such as GPPGA may underestimate severity, whereas pustulation subscore not.'* (56) 21. Would it be appropriate to use the cost-comparison methodology for this topic? No 22. Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators? No	

Section	Consultee/ Commentator	Comments [sic]	Action
		23. Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant? Yes 24. Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year? Effisayil-2 trial will be completed during February 2023. This multi-center, randomized, parallel group, double blind, placebo controlled, phase IIb dose-finding study is evaluating the efficacy and safety of BI 655130 (spesolimab) compared to placebo in preventing GPP flares in patients with history of GPP. (57)	
	UCB Pharma Ltd	Are the following treatments for severe or very severe plaque psoriasis used off license for acute flares of generalised pustular psoriasis? • TNF-alpha inhibitors (adalimumab, etanercept, infliximab and certolizumab pegol) • IL-17 family inhibitors or receptor inhibitors (brodalumab, ixekizumab, secukinumab and bimekizumab) • IL-23 inhibitors (guselkumab, tildrakizumab and risankizumab) • IL-12/IL-23 inhibitors (ustekinumab) • JAK inhibitors (upadacitinib) • Apremilast • Dimethyl fumarate UCB notes the JAK inhibitor, upadacitinib, is not licensed for the management of severe or very severe psoriasis, hence it should not be part of this list.	Thank you for your comment. As noted above, the scope comparators have been amended to reflect UK clinical practice in the treatment for this condition. No further action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
	Psoriasis and Psoriatic Arthritis Alliance	Where do you consider spesolimab will fit into the existing treatment pathway for acute generalised pustular psoriasis? Third-line, although in a life-threatening flare scenario perhaps when hospital admission is likely to be urgent, more immediate.	Thank you for your comment. No action needed.
	Psoriasis Association	Would patients have access to this therapy for future flares?	Thank you for your comment. Information on the use of spesolimab is contained in the summary of product characteristics. No action needed.
Additional comments on the draft scope	Boehringer Ingelheim	Boehringer Ingelheim is carrying out a structure expert elicitation to understand and quantify the efficacy of the most commonly treatments used in GPP flares in the UK. These results will be shared in Dec 2022.	Thank you for your comment. The information provided has been noted.
	UCB Pharma Ltd	No additional comments	No action needed.
	Psoriasis and Psoriatic Arthritis Alliance	No additional comments	No action needed.
	Psoriasis Association	No additional comments	No action needed.

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

AbbieVie

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