NICE National Institute for Health and Care Excellence

# Single Technology Appraisal

# Spesolimab for treating generalised pustular psoriasis flares [ID3963]

# Professional organisation submission

Thank you for agreeing to give us your organisation's views on this technology and its possible use in the NHS.

You can provide a unique perspective on the technology in the context of current clinical practice that is not typically available from the published literature.

To help you give your views, please use this questionnaire. You do not have to answer every question – they are prompts to guide you. The text boxes will expand as you type.

**Information on completing this submission**

- Please do not embed documents (such as a PDF) in a submission because this may lead to the information being mislaid or make the submission unreadable
- We are committed to meeting the requirements of copyright legislation. If you intend to include **journal articles** in your submission you must have copyright clearance for these articles. We can accept journal articles in NICE Docs.
- Your response should not be longer than 13 pages.

## About you

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| **1. Your name** | Drs Ser-Ling Chua and Hamish Hunter, on behalf of the on behalf of the BAD Therapy & Guidelines sub-committee, and Prof Catherine Smith on behalf of the BAD Guideline Development Group on biologics for psoriasis. |
| **2. Name of organisation** | British Association of Dermatologists (the BAD) |
| **3. Job title or position** | Consultant Dermatologists |
| **4. Are you (please select Yes or No):** | An employee or representative of a healthcare professional organisation that represents clinicians? **Yes**<br>A specialist in the treatment of people with this condition? **Yes**<br>A specialist in the clinical evidence base for this condition or technology? **Yes**<br>Other (please specify): |
| **5a. Brief description of the organisation (including who funds it).** | The BAD is a not-for-profit organisation whose charitable objectives are the practice, teaching, training, and research of dermatology. It works with the Department of Health and Social Care, patient bodies and commissioners across the UK, advising on best practice and the provision of dermatology services across all service settings. It is funded by the activities of its members. |
| **5b. Has the organisation received any funding from the manufacturer(s) of the technology and/or comparator products in the last 12 months? [Relevant manufacturers are listed in the appraisal matrix.]**<br>**If so, please state the name of manufacturer, amount, and purpose of funding.** | The BAD is a registered charity and owns various companies. The British Association of Dermatologists Biologic Interventions Register (BADBIR) is the national psoriasis biologic and systemic treatment registry (and an NIHR portfolio study) run by the BAD as a non-profitmaking limited company. This company receives funding from most manufacturers of biological drugs for psoriasis on the registry to collect pharmacovigilance data. The BAD does not receive any funding from BADBIR. |

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| **5c. Do you have any direct or indirect links with, or funding from, the tobacco industry?** | No. |

**The aim of treatment for this condition**

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| **6. What is the main aim of treatment? (For example, to stop progression, to improve mobility, to cure the condition, or prevent progression or disability.)** | • To control flare/the acute phase of generalised pustular psoriasis (GPP), i.e. rapid and sustained clearance of pustules, redness, alleviate symptoms of pain and distress, to control systemic aspects (fever, shock, acute respiratory distress syndrome (ARDS), cardiovascular disease (CVD) and renal failure, infection) https://pubmed.ncbi.nlm.nih.gov/36606566/.<br>• To prevent new flares.<br>• To improve the quality of life and reduce disease burden.<br>• To reduce reliance on systemic immunosuppressive strategies that result in long-term, drug-induced morbidity (e.g. ciclosporin, methotrexate, retinoids). |

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| **7. What do you consider a clinically significant treatment response? (For example, a reduction in tumour size by x cm, or a reduction in disease activity by a certain amount.)** | Rapid resolution of acute flares; prevention of recurrent flares; reduction in use of systemic immunosuppressive strategies (e.g. corticosteroids; ciclosporin particularly); reduction or avoidance of hospital admissions.<br><br>In the acute phase, recommended measures of GPP activity include:<br>• Generalised Pustular Psoriasis Area and Severity Index<br>• Generalised Pustular Psoriasis Physician Global Assessment (GPPGA; https://pubmed.ncbi.nlm.nih.gov/37075220/)<br>• Body surface area (BSA) involvement<br>• Pain scores<br>• DLQI<br>• Alongside measures of systemic features depending on individual characteristics of the patient including fever, levels of C-reactive protein, white cell count and albumin<br><br>A clinically significant response in an acute flare would include:<br>• 0 or 1 in the GPPGA or GPPASI pustular sub-score<br>• Global assessment of at least mild<br>• Resolution of skin pain<br>• Resolution of systemic features<br>• Becoming/remaining afebrile<br><br>A clinically significant indicator of flare prevention includes:<br>• Reduction in number flares (e.g. by at least 50%)<br>• Reduction in severity of flares (e.g. absent systemic symptoms, no hospital admissions)<br>• Reduction in use of systemic immunosuppressants with long-term, associated morbidity (e.g. ciclosporin)<br><br>Given the rarity of GPP, the cited disease severity scores may not be in routine clinical practice in all centres. However, PASI and BSA are widely used in routine clinical care as part of disease severity assessments for |

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| | plaque-type psoriasis so adoption of GPPASI (and BSA) to assess impact of spesolimab can be implemented rapidly. |
| **8. In your view, is there an unmet need for patients and healthcare professionals in this condition?** | Yes. GPP is a severe, potentially life-threatening condition for which there are no licensed therapeutic interventions with proven efficacy. It is episodic, unpredictable, painful and incapacitating, associated with severe systemic features, often requiring hospital admission and organ support in an intensive care setting. It is associated with major morbidity – and in some cases, mortality. The unpredictable nature of the condition further compounds the long-term psychological impact of the disease. |

**What is the expected place of the technology in current practice?**

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| **9. How is the condition currently treated in the NHS?** | Current NICE guidelines state (CG153) that:<br><br>*"People with generalised pustular psoriasis should be referred immediately for same-day specialist assessment and treatment"*<br><br>This means that all patients with GPP are under the care of specialist dermatology services.<br><br>During an acute flare, patients are often/usually admitted for inpatient supportive management (specialist nursing care with topicals, pain management, and for associated systemic upset including fluids, management of infection, liaison with relevant specialists depending on organ involvement; severe cases are managed in HDU/ITU).<br><br>There are no licensed therapeutic interventions for GPP flares. Commonly used strategies include ciclosporin and infliximab/TNF antagonists. In acute cases, methylprednisolone is deployed occasionally and, in less severe cases, methotrexate and retinoids may be used (often in combination). Targeted immunomodulatory therapies developed for plaque-type psoriasis have also been used with variable – and unpredictable – success, including IL17 and IL23 antagonists, the evidence for which is based primarily upon case reports and small case series. |

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| | Ciclosporin and TNF antagonists are probably the most widely used approach to prevent flares, although with variable success, and (in the case of ciclosporin) substantial long-term risk. https://pubmed.ncbi.nlm.nih.gov/34626330/, https://pubmed.ncbi.nlm.nih.gov/38114719/, https://pubmed.ncbi.nlm.nih.gov/36219603/<br><br>Given the rarity of the condition and the lack of clinical trials, coupled with a lack of specific guidelines https://pubmed.ncbi.nlm.nih.gov/38114719/ treatment can be highly individualised, relying on the clinical expertise of healthcare professionals at specialised centres. |
| **9a. Are any clinical guidelines used in the treatment of the condition, and if so, which?** | NICE CG 153 recommends immediate referral to specialist care.<br><br>The BAD guidelines cover GPP in the systematic review scope (currently being updated – last published in 2020) but there was inadequate evidence to produce strong recommendations.<br><br>Weak evidence for TNF antagonists justified consider use of TNF antagonists (and integrated into pathways of care, e.g. Southeast London ICS https://www.selondonics.org/wp-content/uploads/dlm_uploads/2022/11/Psoriasis-Biologic-Pathway-Adults-FINAL-January-2022.pdf).<br><br>In the US and Japan, in light of evidence on spesolimab, spesolimab is strongly recommended https://pubmed.ncbi.nlm.nih.gov/37838256/. |
| **9b. Is the pathway of care well defined? Does it vary or are there differences of opinion between professionals across the NHS? (Please state if your experience is from outside England.)** | In general, the treatment pathway includes a combination of topical and systemic treatments and supportive care, but this may vary depending on the severity of skin and systemic involvement and the extent of affected skin areas. See also section 9 above. |

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| **9c. What impact would the technology have on the current pathway of care?** | Spesolimab is the first, targeted intervention for GPP, developed as a result of understanding the disease biology, with evidence for benefit from trials that have been well designed, especially in the context of it being a rare disease, with heterogenous clinical manifestations, and its episodic and unpredictable disease course. Following approval in the US and Europe, it is recognised as the "first-in-class" medication, setting the standard of care for treating GPP flares in adults.<br><br>Given the benefit in acute flares in very rapidly resolving symptoms, signs and systemic upset (within days), this technology would have a very major impact on the current pathway https://pubmed.ncbi.nlm.nih.gov/34936739/. CG153 already states that patients with GPP should be referred immediately to secondary care. At the point of referral, if spesolimab is approved for use first line, then access to facilities for IV administration will be required. Use of spesolimab would be expected to reduce the need for hospital admission, reduce the length of stay, reduce escalation of care to HDU/ITU and reduce or prevent systemic complications (from GPP as well as drug-related toxicity) and the significant psychological impact of the disease.<br><br>If approved for *prevention* of flares, this would be expected to reduce the need for repeated follow-up appointments, and the use of interventions of unproven/variable benefit. |
| **10. Will the technology be used (or is it already used) in the same way as current care in NHS clinical practice?** | This technology can be used within the current NHS care pathway. Within specialist care, administration of IV drugs is well established for dermatological conditions and the SmPC (posology, administration, adverse effects) do not pose any specific or unique challenges. |
| **10a. How does healthcare resource use differ between the technology and current care?** | See above. This is the first technology specifically available for the management of acute GPP.<br><br>Within specialist care, administration of IV drugs is well established for dermatological conditions.<br><br>Use of spesolimab would be expected to reduce the need for hospital admission, reduce the length of stay, reduce escalation of care to HDU/ITU and reduce or prevent systemic complications (from GPP as well as drug-related toxicity) and the significant psychological impact of the disease. |

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| | If approved for *prevention* of flares, this would be expected to reduce the need for repeated follow-up appointments, and the use of interventions of unproven/variable benefit. |
| **10b. In what clinical setting should the technology be used? (For example, primary or secondary care, specialist clinics.)** | Secondary care with specialist dermatology (and multi-disciplinary) expertise. |
| **10c. What investment is needed to introduce the technology? (For example, for facilities, equipment, or training.)** | Nothing specific other than development of guidelines for safe and effective use (as with any new intervention). |
| **11. Do you expect the technology to provide clinically meaningful benefits compared with current care?** | Yes. |
| **11a. Do you expect the technology to increase length of life more than current care?** | Yes. |
| **11b. Do you expect the technology to increase health-related quality of life more than current care?** | Yes. |

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| **12. Are there any groups of people for whom the technology would be more or less effective (or appropriate) than the general population?** | The technology appears to be effective in patients with a clinical diagnosis of GPP.<br><br>Individuals carrying the IL36RN mutation *may* have specific additional benefit, although more research is required. See results presented at the EADV 2022 in poster format (not yet published in full) https://www.avancesenppg.com/arxius/imatgesbutlleti/Burden-D-EADV-2022-Poster-1224.pdf. |

## The use of the technology

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| **13. Will the technology be easier or more difficult to use for patients or healthcare professionals than current care? Are there any practical implications for its use (for example, any concomitant treatments needed, additional clinical requirements, factors affecting patient acceptability or ease of use or additional tests or monitoring needed.)** | It would be easier for patients and healthcare professionals than current care. The treatment acts rapidly, is easy to administer, should negate the need for concomitant therapies, and requires no additional tests or monitoring. Current strategies are unpredictably effective, burdensome, and may be associated with significant drug-related toxicity. |
| **14. Will any rules (informal or formal) be used to start or stop treatment with the technology? Do these include any additional testing?** | The BAD will be integrating the evidence for spesolimab in the upcoming update of our guideline on the use of targeted immunomodulatory therapies for psoriasis. Spesolimab is likely to be recommended for patients with an acute, severe flare of GPP in the absence of any other licensed or effective treatment.<br><br>This is a rare disease with a very substantial health burden. |

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| | No additional testing required. |
| **15. Do you consider that the use of the technology will result in any substantial health-related benefits that are unlikely to be included in the quality-adjusted life year (QALY) calculation?** | Time lost at work. Social impact and burden. |
| **16. Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how might it improve the way that current need is met?** | Yes. |
| **16a. Is the technology a 'step-change' in the management of the condition?** | Yes, for reasons stated above.<br><br>This is the first technology specifically available for the management of acute GPP. In the US and Europe where its use has been approved, it is recognised as the "first-in-class" medication, setting the standard of care for treating GPP flares in adults. |
| **16b. Does the use of the technology address any particular unmet need of the patient population?** | Yes https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8801408/. GPP is a severe, potentially life-threatening condition. This group of patients' acute healthcare needs have not been adequately met due to the lack of licensed therapeutic interventions with proven efficacy. |
| **17. How do any side effects or adverse effects of the** | The overall number of patients treated with spesolimab is limited, as this is rare disease. As with any new intervention, vigilance will be required to ensure drug-related problems are identified early and managed. To date, |

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| **technology affect the management of the condition and the patient's quality of life?** | the side effect profile of spesolimab is favourable; infection has been cited as a potential complication (also a problem with GPP itself) and will be managed in line with current practice when using targeted immunomodulatory therapy for other indications. |

## Sources of evidence

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| **18. Do the clinical trials on the technology reflect current UK clinical practice?** | Largely yes; however, there is no established pathway of care for GPP in the UK. Consideration should be made for the use of the technology at a much earlier stage in the pathway.<br><br>https://pubmed.ncbi.nlm.nih.gov/34936739/<br>https://pubmed.ncbi.nlm.nih.gov/37738999/<br>https://pubmed.ncbi.nlm.nih.gov/36282833/<br>https://pubmed.ncbi.nlm.nih.gov/36527385/<br>https://pubmed.ncbi.nlm.nih.gov/37140190/<br>https://pubmed.ncbi.nlm.nih.gov/36870370/ |
| **18a. If not, how could the results be extrapolated to the UK setting?** | N/A |
| **18b. What, in your view, are the most important outcomes, and were they measured in the trials?** | Resolution of flares, and prevention of flares. Both these key outcomes are captured using accepted standards in the trials. The trials were designed and supported by acknowledged experts in the field of GPP. |
| **18c. If surrogate outcome measures were used, do they adequately predict long-term clinical outcomes?** | N/A |
| **18d. Are there any adverse effects that were not apparent in clinical** | None that we are aware of. |

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| **trials but have come to light subsequently?** | |
| **19. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence?** | This is a rare disease. There seems to be variation in the epidemiology of GPP with it being more common in Asia so inclusion of all languages in the search strategy will be important. |
| **20. How do data on real-world experience compare with the trial data?** | Not available yet. |

## Equality

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| **21. Are there any potential equality issues that should be taken into account when considering this treatment?** | As with all skin disease, commonly used tools may underestimate redness in people with darker skin tones.<br><br>There are major challenges in the delivery of dermatology services post-Covid pandemic and in light of escalating skin cancer burden, expertise in management of complex rare conditions such as GPP may not be widely available. Equality of access may be difficult in certain areas.<br><br>It is also worth noting that epidemiological evidence suggests that GPP may be more prevalent in non-white populations particularly East Asians (trials do include these populations). |
| **22. Consider whether these issues are different from issues with current care and why.** | These issues are similar for the current standard of care for patients with GPP. |

## Key messages

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| **23. In up to 5 bullet points, please summarise the key messages of your submission.** | • GPP is a severe, rare and life-threatening condition for which there are currently no licensed treatments or established standard of care.<br>• This is a first-in-class, effective intervention targeting known pathological drivers of GPP.<br>• We strongly support adoption of this technology into NHS care as it is likely to reduce length of hospital stay, reduce or prevent systemic complications (from GPP as well as drug-related toxicity), prevent flares of GPP after the acute phase hence reducing the need for follow-up appointments, use of interventions with unproven or variable benefit, thereby reducing mortality and morbidity due to GPP, including its psychological impact. |

Thank you for your time.

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