Spesolimab for treating generalised pustular psoriasis flares [ID3963]

PART 1 slides: Contains no confidential information

Technology appraisal committee B [02 April 2025]

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Company: Boehringer Ingelheim

Spesolimab for treating generalised pustular psoriasis flares ID3963

- ✓ **Recap to background and key issues**
- ❑ Summary of consultation comments
- ❑ Company's new evidence

NICE National Institute for Health and Care Excellence

Background on generalised pustular psoriasis & flares

RECAP

Diagnosis and classification

- GPP historically considered a variant of psoriasis but is distinct from plaque psoriasis

Epidemiology

- England incidence rates for GPP: 0.25 (95% CI 0.21–0.28) per 100 000 person-years
- GPP has no cure and can be relapsing or persistent

GPP Flares

- Can be life-threatening and require emergency treatment in 2% to 16% of cases
- Develop rapidly, affecting large areas of the body. Pus-filled blisters can merge and are associated with itching, pain and scaling

CI, confidence interval; GPP, generalised pustular psoriasis

RECAP

Spesolimab (Spevigo, Boehringer Ingelheim)

Details of the technology	
Marketing authorisation	• Spesolimab is indicated for the treatment of flares in adult patients with GPP as monotherapy • CMA from MHRA in July 2023 via the EC Decision Reliance Procedure • Data on treatment of subsequent flares was not comprehensive. An additional open-label, single-arm post-authorisation study on the treatment of repeated flares with spesolimab is ongoing
Mechanism of action	• Spesolimab is a humanised monoclonal IgG1 antibody that blocks IL-36R signalling. By binding to IL-36R, spesolimab prevents its activation by ligands (IL-36 α, β, γ) and stops downstream pro-inflammatory pathways.
Administration	• Intravenous infusion • Single dose of 900 mg (two vials of 450 mg) • If flare symptoms persist, an additional 900 mg dose may be administered 1 week after the initial dose
Price	• £15,000 for 900 mg (two vials of 450 mg) • Average cost of a course of treatment (1 GPP flare): £20,265 • Confidential PAS discount in place

Abbreviations: CMA, conditional marketing authorisation; EC, European Commission; GPP, generalised pustular psoriasis; IL, interleukin; IL-36R, interleukin 36 receptor; MHRA, Medicines and Healthcare Products Regulatory Agency

Summary of appraisal to date (clinical effectiveness)

RECAP

Recommendation after ACM 1: Spesolimab is not recommended, within its marketing authorisation, for treating generalised pustular psoriasis (GPP) flares in adults.

Committee considerations from ACM1

Issue	Committee conclusion
Comparators	No licenced treatments for GPP flares: • Spesolimab would be used 1st line (week 1) • Best available care (BAC) with ciclosporin and acitretin relevant comparators at 1st line
Key clinical evidence	Effisayil 1 RCT (n=53) spesolimab vs. placebo with 12 week follow up period • Spesolimab arm: 900 mg IV given on Day 1, Day 8 (in non-responders), Day 9 to 12 weeks (900 mg IV x 1 of rescue therapy) • Placebo arm could crossover to spesolimab at day 8 **Results:** spesolimab more effective than placebo in resolving GPP flares, but uncertainty in size of treatment effect
Generalisability of Effisayil 1 trial	• High % Asian with 0 UK sites • Only moderate to severe GPP flares → would also be offered to mild flares in clinical practice • Did not include people having maintenance therapies → week 1 data not generalisable to UK population with GPP flares

ACM, appraisal committee meeting; BAC, best available care; GPP, Generalised pustular psoriasis, IV, intravenous; UK, United Kingdom; RCT, randomised controlled trial. Link to supplementary appendix: decision problem, treatment pathway, Effisayil 1 details, baseline characteristics, design

Summary of appraisal to date (cost effectiveness)

RECAP

Table: Committee considerations from ACM1

Issue	Committee conclusion	Further information requested	Company updated?
BAC composition and costs	Structured expert elicitation (SEE) exercise from day 0 due to Effisayil 1 generalisability issues	Market share data of comparator treatments in NHS	Yes – see supplementary appendix
BAC effects	Historical cohort arm of Effisayil 1 from day 0 for BAC treatment effect	Scenario using SEE exercise for BAC treatment response from day 0	Yes – see supplementary appendix 1, 2, 3
Time horizon	12-week horizon sufficiently reflects time for treatment response	N/A	N/A
2nd flares	Include 2nd flare based on rate in Effisayil 1	N/A	Yes – for discussion
Mortality	Uncertain but increased mortality in ICU	Scenarios varying mortality benefit of spesolimab	Yes – for discussion
Admission rates	• Implausible that 0% in ICU with spesolimab • Prefer Wolf et al. (2024) for BAC inpatient rate 50% relative reduction for spesolimab	• UK inpatient & ICU rates + duration of stay for BAC and spesolimab. • Data on spesolimab use in Japan	Yes – for discussion

ACM, appraisal committee meeting; BAC, best available care; GPP, Generalised pustular psoriasis, ICU, intensive care unit; UK, United Kingdom; RCT, randomised controlled trial; SEE, structured expert elicitation. Link to supplementary appendix: sources of evidence, company's model and overview

Equality considerations

- No issues raised at scoping stage, or by patient or professional groups
- Previous technology appraisal (TA986) in skin conditions have noted that some disease measuring scores can underestimate severity in people with darker skin tones as ‘redness’ of skin is used to detect severity, and it was also used as part of the eligibility criteria

No further equality issues identified at consultation

Key issues

Issue
Has the company correctly implemented a 2nd GPP flare in the model? Is it plausible that: • Equal proportion of people have a day 8 dose of spesolimab for non-response? • Equal rates of 2nd flares for spesolimab and BAC? • Identical treatments used to treat GPP flares with no reduction in efficacy for subsequent flares?
• Has the company appropriately modelled the proportion of inpatient and ICU admissions with spesolimab? • Do the company's costs and resource use for hospital visits have face validity?
Should a mortality benefit be included for spesolimab?
Would waning of effect be expected with use of spesolimab as an acute treatment for recurrent flares over a person's lifetime?
Given the 12-week time horizon, are there any other uncaptured benefits for spesolimab?
Should any recommendation: • be limited to the population informing the evidence? • include a definition of GPP flares and response? • consider the rarity of the condition?
Should managed access be considered?

GPP, generalised pustular psoriasis, ICU, intensive care unit

Spesolimab for treating generalised pustular psoriasis flares ID3963

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NICE National Institute for Health and Care Excellence

Consultation comments to draft guidance

Consultation responses from Psoriasis Association and British Association of Dermatologists

Unmet need for new treatments:

- Current treatment substandard → long hospital stays + ineffective non-targeted treatments
- Few dedicated dermatology inpatient beds → specialist nurses not available

Large psychological impact for people with GPP and carers:

- Condition causes stress and anxiety about death from flares
- Hospital stays put pressure on work and family-life

Effisayil 1 trial generalisable to NHS:

- Don't anticipate UK population to differ from trial, given ethnic diversity in NHS
  - ❖ Supported by PLUM study: similar clinical features across ethnicities, use of multiple biologics to treat flares
- GPP flares always severe, never mild or moderate → flares should be classed as medical emergencies

Benefits of spesolimab not full considered:

- Only licenced drug for GPP flares and fast acting → will improve QoL & relieve current pressure on hospital beds
- Cost effectiveness hard to calculate due to poor data. Not captured in model:
  - ❖ Burden of disease on patient, clinicians and health care systems
  - ❖ Course of GPP or cost of BAC drugs not reflected in routine primary healthcare and hospital data
  - ❖ Improved wellbeing from availability of effective treatment

BAC, best available care; GPP, Generalised pustular psoriasis, UK, United Kingdom; QoL, quality of life

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Summary of company's response to consultation

Requested by committee at ACM1	Company response
Committee preferred assumptions	
Current 1st line BAC = ciclosporin & acitretin • SEE exercise for composition and costs in BAC arm from Day 0	Included in updated base case
Effisayil 1 historical cohort for treatment response in the BAC arm from Day 0	
Include 2nd flare within 12 weeks	
Proportion inpatients: Wolf et al. (2024) for BAC (77.6%) and spesolimab (38.8%)	
Proportion in ICU: >1% having spesolimab in ICU with 50% relative reduction vs BAC if no data to inform	
Additional scenarios requested by committee	
Clinical data on inpatient and ICU admission rates for BAC and spesolimab, ideally UK registry data or UK real-world evidence	Partially
Scenario analyses of SEE exercise to inform BAC efficacy	Yes
Additional insights from data on spesolimab use in Japan	None available
Market share data for BAC treatments to verify SEE exercise estimates	None available
Scenario analyses on the reduction in mortality benefit of spesolimab	Yes

Company also provided an updated PAS for ACM2

ACM, appraisal committee meeting; BAC, best available care; ICU, intensive care unit; PAS, patient access scheme; UK, United Kingdom; SEE, structured expert elicitation

RECAP: Defining flares

Effisayil 1 trial and model define subsequent flares differently

Link to supplementary appendix: Scoring for GPPGA, Effisayil 1 historical cohort

	Initial flare	Resolved flare	2nd flare
Effisayil 1	• GPPGA score of at least 3 (moderate) • Presence of fresh pustules (new or worsening) • GPPGA pustulation sub score of ≥ 2 (mild) • At least 5% of body surface area covered with erythema and presence of pustules	• Primary outcome: GPPGA pustulation subscore of 0 at week 1 • Secondary outcome: GPPGA total score of 0 or 1 at week 1	≥2 point increase in GPPGA total & pustulation subscore after initial GPPGA total score 0 or 1
Company model	Effisayil 1 cohort	• Spesolimab: GPPGA pustulation subscore of 0 or 1 • BAC: time-to-pustular-clearance as proxy for GPPGA pustular subscore	GPPGA pustulation subscore ≥2 (with no BAC during week 1)

- How are the following defined in clinical practice:
  - ❖ Subsequent flares?
  - ❖ Response to treatment for first and subsequent flares?
- Would rescue therapy with spesolimab only be given for new flares (i.e. if the previous flare has resolved)? If not:
  - ❖ Is there a specific timepoint where a partially resolved flare is classed as a subsequent flare?
  - ❖ How often do unresolved flares become subsequent flares?
- Would 2nd flares be more severe than initial flares?
- Are the definitions of GPP flares and response in the company's model appropriate?
- Should any recommendation be in line with the trial evidence or wider GPP population?

BAC, best available care; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment

Key issue: Modelling flares (1)

Company include 2nd flares for both arms based on re-treatment rate in Effisayil 1

Background: At ACM1, company modelled 1 flare only as clinical experts agreed flares resolve in 12 weeks

- But, in Effisayil 1 N=4 (11.3%) had rescue treatment with spesolimab for 2nd flares (after day 8)

Committee conclusion: people whose flare only partially controlled may have 2nd flare within 12 weeks → should be modelled based on rate in Effisayil 1

Company: Includes 2nd flares at ACM2 based on rate in Effisayil 1:

- Only 2/4 having rescue therapy in Effisayil 1 met model definition of response (7.14% of the 28 responders)
- 2nd flares occur at constant rate after week 4 (observed pattern in Effisayil 1)
- Equal flare rates for BAC and spesolimab (no specific data for placebo due to crossover at 8 days)
- Only 1 rescue dose allowed in Effisayil 1, but model assumes same % have day 8 dose for 1st and 2nd flare
- No extra visits for administering treatment for 2nd flares

Explored alternative data sources:

- English Hospital Episode Statistics (HES): re-admission rate around 73% for GPP flare within 12 weeks
  - ❖ Limitations: a) only people admitted for both initial and 2nd flare, b) assumes 2nd admission for new flare

Base case: Includes 2nd flare for 7.14% people, same treatment for initial and recurrent flares

Scenario: Different treatment for 2nd flares that don't respond within 1 week of treatment:

a) Spesolimab arm: ciclosporin at day 8

b) BAC arm: biologics at day 8 based on clinical advice (40% guselkumab, 30% secukinumab, 30% ustekinumab)

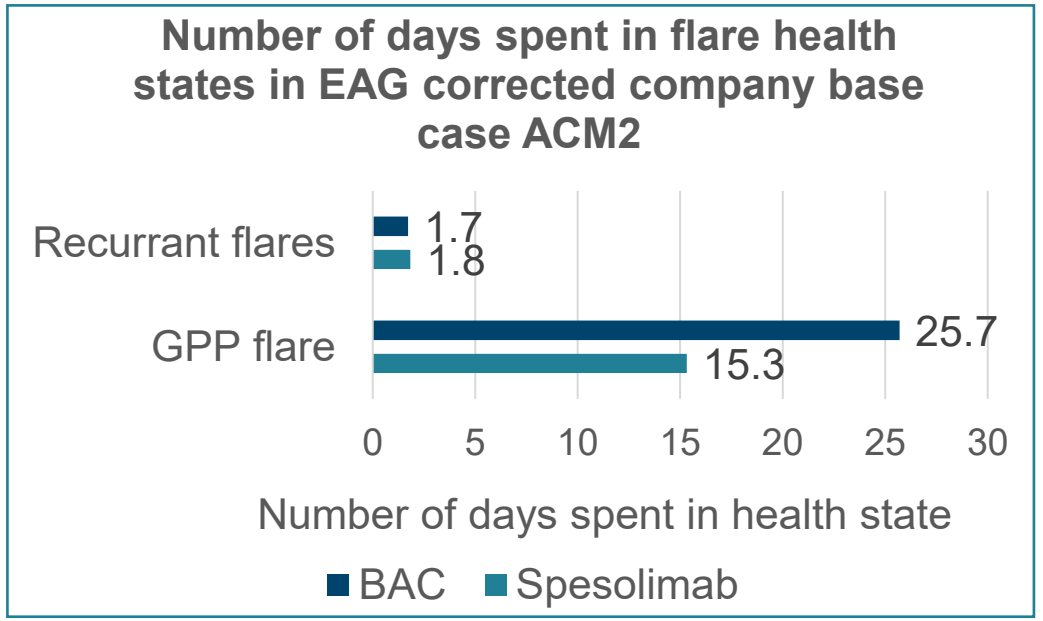
ACM, appraisal committee meeting; BAC, best available care; GPP, generalised pustular psoriasis; N, number

Key issue: Modelling flares (2)

EAG corrected company's implementation of 2nd flares in model

EAG comments: EAG corrected company's modelling :

- Incorrect to present results with and without 2nd flares simultaneously as % admitted varies by flare number
- Total QALYs including 2nd flares higher than when excluded → lacks face validity
  - Company approach: QALYs excluding flares x total incidence of recurrence
  - EAG's corrected approach applies daily QALY loss for people in recurrent flare health state using the difference in daily QALYs between resolved and flare health state



NICE Technical team: Unclear if proportion needing a Day 8 dose for non-response would be the same for 1st and subsequent flares

- Company assumes with spesolimab: quicker resolution of flares vs BAC (see supplementary appendix: efficacy inputs in model) but higher proportion of recurrent flares as more responders than to BAC

For 1st and subsequent flares, is it plausible to assume:

- Equal risk of 2nd flares for spesolimab and BAC?
- Equal proportion of people have a day 8 dose of spesolimab for non-response?
- Identical treatments for all GPP flares with no reduction in efficacy for subsequent flares?

Is the EAG's corrected modelling suitable for decision making?

ACM, appraisal committee meeting; BAC, best available care; GPP, generalised pustular psoriasis; QALY, quality adjusted life year.

Link to supplementary appendix: Health state occupancy with recurrent flares, ACM2

Key issue: Proportion of inpatients and ICU patients

Company identified no additional data sources to inform hospitalisation and ICU rates

Background: ACM1 company assumed spesolimab decreases hospitalisation rates by reducing active flares:

- Inpatient rate based on Wolf et al. for BAC arm (77.6%), with reduction for spesolimab to 38.8% inpatient rate (similar to observed in Effisayil 1 trial)
- 0% having spesolimab require ICU admission due to spesolimab's rapid onset of action

Committee preference: further data to inform ICU and inpatient rates, including data from Japan. If unavailable base inpatient and ICU rates on Wolf et al for BAC arm with:

- 50% reduction in inpatient rates for spesolimab; implausible that no patients having spesolimab in ICU

Company: Considered alternative data sources for ICU and inpatient rates, including from countries where spesolimab already in use (see supplementary appendix)

- No data to inform inpatient or ICU rates for GPP flares
- Effisayil REP trial data suggests modelled inpatient rate for spesolimab conservative, but HES data supports inpatient rate from Wolf et al for BAC
- Consensus statements by clinicians in UK, China and US support 50% reduction in hospital admissions with reduced stay duration and need for high dependency care (ICU) for spesolimab vs BAC

Base case: 50% reduction in hospital and ICU admissions with spesolimab with BAC rates from Wolf et al:

- Inpatient rate: 77.6% for BAC, 38.8% for spesolimab
- ICU admission rate: 11.5% for BAC (as per DG), 5.75% for spesolimab

Scenario: 30% reduction in inpatient and ICU rates for spesolimab

ACM, appraisal committee meeting; BAC, best available care; DG, draft guidance; GPP, generalised pustular psoriasis; HES, hospital episode statistics; ICU, intensive care unit; UK, United Kingdom; US, United States

Key issue: Proportion of inpatients and ICU patients (2)

Data from Effisayil REP, HES and consensus statements to support company assumptions

Source	Description	Indicative hospitalisation rate
Effisayil REP	Open-label, single-arm study for recurrent GPP flares with spesolimab	[redacted]% with spesolimab
HES	Company analysis of inpatient admissions with primary diagnosis of L40.1 (assumed to represent admission for GPP flare) admitted between April 2019 and July 2024	73% with BAC

Consensus statement on hospital admissions

Country	Supported by	Consensus statement:		
		80% UK patients need inpatient care with BAC	At least 50% reduction in admissions with spesolimab vs. BAC	Reduced inpatient stay and need for high dependency care vs BAC
UK	29 UK clinicians	✓	✓	✓
Japan*	5 Japan clinicians	N/R	N/R	✓ (4 of 5 agreed reduced high dependency care)
US and China	9 US and 5 China dermatologists	N/R	✓	✓

*Spesolimab must be administered as an inpatient in Japan

BAC, best available care; GPP, generalised pustular psoriasis; HES, hospital episode statistics; ICU, intensive care unit; UK, United Kingdom; US, United States

Key issue: Proportion of inpatients and ICU patients (3)

EAG corrected error in company's modelling of mechanical ventilation

EAG comments: base case inputs aligned with committee preference given lack of data

- Acknowledge company base case may be conservative but no specific data to inform rates
- Note consensus statements do not estimate length of stay or % needing high dependency care
- Corrected error in company's modelling of mechanical ventilation for people in ICU to apply equal rates to spesolimab and BAC

Scenarios:

- Inpatients in spesolimab: a) 77.6% (0% reduction vs BAC), b) 73.7% (5% reduction), c) 69.84% (10% reduction), d) 62.08% (20% reduction), e) 54.32% (30% reduction)
- In ICU in spesolimab arm: a) 0%, b) 5%, c) 10%, d) 15%, e) [redacted]

British Association of Dermatologists

- Routinely collected primary healthcare data, and hospital episodes statistics (HES) data likely to under-represent GPP admissions (poor coding of hospital admissions).
- Less severe but still significant flares with major patient impact managed through day centres and repeated outpatient visits for systemic treatment monitoring and topicals/supportive care.

- Have hospital and ICU admissions been correctly modelled for BAC and spesolimab in the company's updated model?
- Have there been any recent updates in treatment for chronic GPP that might impact admission rates?

BAC, best available care; GPP, generalised pustular psoriasis; ICU, intensive care unit

Hospitalisation costs in EAG corrected company base case

Key model inputs for hospitalisation

Parameter	GPP flare				Resolved flare	
	% treated as outpatients	% treated as inpatients	% inpatients in ICU	Total % time in flare (including recurrent)	% treated as outpatients	Total % time in resolved flare
Spesolimab	61%	39%	6%	17%	100%	68%
BAC	22%	78%	12%	27%	0%	57%

Assumed equal between arms:

- % in ICU having MV
- number outpatient visits
- max days in ICU and in hospital

Modelled outputs for hospitalisation

Multiplicative difference between BAC and spesolimab	General ward	ICU (no MV)	ICU (MV)	Day care	Outpatient	Terminal care
Hospitalisation costs	x 3.4	x 7.0	x 6.7	x 3.2	x -1.5	x 1.7

Green: BAC costs higher than spesolimab. **Orange**: spesolimab costs higher than BAC
Difference in costs driven by varying time spent in each location for BAC and spesolimab

Are the EAG's costs and resource use inputs for hospitalisation plausible?

BAC, best available care; GPP, generalised pustular psoriasis; ICU, intensive care unit; MV, mechanical ventilation. Lnk to supplementary appendix: full hospitalisation costs in the EAG corrected company model

Key issue: Mortality

Company provided scenarios with additional mortality benefit for recurrent flares

Background: ACM1: company modelled daily death rate of 0.096% for people in ICU only

- Derived from French data in which 2.6% died within 4 weeks of last flare
- Spesolimab has mortality benefit because reduced ICU rates vs. BAC

Committee conclusion: plausible that spesolimab reduces longer-term mortality not directly linked to ICU stay → scenarios should be provided with additional mortality benefit

Company: calculated lifetime mortality benefit for spesolimab vs BAC of [redacted] QALYs accrued due to the reduced risk of death due to recurrent flare, assuming:

- people with GPP have:
  - 1 flare per year
  - an average life expectancy of 16 years after entering the model based on:
    - the average age of patients in POLARIS trial
    - an elevated mortality risk for people with GPP vs general public (HR 1.81)
- spesolimab avoids 1% of deaths vs. BAC.

Presented scenarios including recurrent flare long-term mortality benefit.

ACM, appraisal committee meeting; BAC, best available care; GPP, generalised pustular psoriasis; HR, hazard ratio; ICU, intensive care unit; QALY, quality adjusted life year

Key issue: Mortality

Company's scenarios assume no treatment waning when spesolimab used for recurrent flares

EAG: several problems with company's calculations:

1. Adjusted life expectancy of 16 years from model start age, uses average age and % female from POLARIS but QALYs taken from model which uses Effisayil 1 trial baseline characteristics
2. HR of 1.81 from by Ericson et al. (2023) → not included in original company submission so EAG not critiqued
3. Company's calculation crude & doesn't account for differences in mortality HR by age (reported by Ericson et al.)
4. 16-year life expectancy not discounted
   - Acceptable not to discount over a 12 weeks time horizon but should include over longer time period
5. No age-adjustment of utilities over life expectancy period for decline in QoL due to comorbidities
6. EAG unable to replicate company's scenario and company not provided a model including long-term mortality benefit calculations → application of estimated gain of [redacted] QALYs unclear

NICE Technical team: company assumes 1 flare per year with no treatment waning – clinically plausible?

- Note that QALY difference between spesolimab and BAC is minimal in company base case

- Is there an expected mortality benefit with spesolimab vs. BAC beyond reducing ICU admissions for flares?
- If yes, has this been captured in the company's scenario and should this be included in the model?
- Would treatment waning be expected with spesolimab as an acute treatment for recurrent flares over a person's lifetime?

BAC, best available care; HR, hazard ratio; ICU, intensive care unit; QALY, quality adjusted life year; QoL, quality of life

Managed access and innovation

ACM1: Company did not submit an MAA proposal

NICE MAA team: feasibility assessment showed:

- current UK data sources do not allow use of routinely collected data to reduce uncertainties
- no appropriate processes in place to establish new data collection based on existing procedures

Update at consultation: company consulted clinical experts to assess potential for MAA data collection

Potential sources unlikely to address uncertainty about relative hospitalisation and ICU rates:

- **BADBIR registry:** collects baseline and follow up data limited group of GPP patients
  - ❖ Not representative of BAC → biological cohort confined to treatments provided by the companies that fund registry.
  - ❖ Limited patients: significant confounding factors in any matched cohort for BAC and spesolimab
- **HES:** Uses ICD-10 code, L40.1, to identify patients admitted to hospital with primary diagnosis of GPP
  - ❖ Doesn't identify GPP flares, severity, treatments used or the resulting outcomes or provides information of whether ICU admissions result of GPP flare-ups

Professional organization: Managed access scheme could generate UK real world evidence

ACM, appraisal committee meeting; BAC, best available care; BADBIR, British Association of Dermatologists Biologic and Immunomodulators Register; GPP, generalised pustular psoriasis; HES, hospital episode statistics; HR, hazard ratio; ICD, International Classification of Diseases; ICU, intensive care unit; QALY, quality adjusted life year; UK, United Kingdom

Other considerations: rarity of the condition

NICE health technology evaluations: the manual states

"…the committee will be mindful that there are certain technologies or populations for which evidence generation is particularly difficult because they are:

- ***rare diseases***
- *for use in a population that is predominantly children (under 18 years old)*
- *innovative and complex technologies.*

In these specific circumstances, the committee may be able to make recommendations accepting a higher degree of uncertainty. The committee will consider how the nature of the condition or technology(s) affects the ability to generate high-quality evidence before applying greater flexibility."

Epidemiology of GPP: Incidence rates in England for GPP is 0.25 (95% CI 0.21–0.28) per 100 000 person-years

Psoriasis Association: concerned that seriousness of GPP has been overlooked due to rareness of condition, and that some references to more common plaque psoriasis may have been drawn unintentionally.

Should rarity of the condition be considered in any recommendation?

CI, confidence interval; GPP, generalised pustular psoriasis

Recommendation wording considerations

Include definitions of GPP flare, resolved flare and optimise population by severity?

Should any positive recommendation:

1. **Optimise by severity of flares?**
   - Effisayil 1 cohort and model included people with moderate and severe flares only → clinical expert advice suggests spesolimab would be used in people with flares of all severities

2. **Define criteria for resolved flares?**
   - using modelled definition of GPPGA pustulation subscore of 0 or 1?

3. **Define criteria for starting spesolimab for subsequent flares?**
   - If yes, using trial definition (≥2 point increase in GPPGA total & pustulation subscore after initial GPPGA total score 0 or 1) or model definition (GPPGA pustulation subscore ≥2 (with no BAC during week 1)?

BAC, best available care; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment

Company and EAG base case

Company and EAG align base case at ACM2

Requested by committee at ACM1	Company base case ACM1	Company and EAG base case ACM2
Current 1st line BAC = ciclosporin & acitretin • SEE exercise for composition and costs in BAC arm from Day 0	Effisayil 1 (week 1), SEE exercise (after week 1)	BAC composition and costs from SEE exercise from Day 0
Effisayil 1 historical cohort for treatment response in the BAC arm from Day 0	Effisayil 1 (week 1), Effisayil 1 historical cohort GPPGA pustulation subscore 0-1 (after week 1)	Effisayil 1 historical cohort GPPGA pustulation subscore 0-1 from Day 0
Include 2nd flare within 12 weeks	Not included	2nd flares for 7.14% BAC and spesolimab arm (EAG corrected error)
Wolf et al. (2024) for spesolimab inpatient rate at 38.8%	77.6% for BAC, 38.8% for spesolimab	77.6% for BAC, 38.8% for spesolimab
>1% people having spesolimab have ICU admissions with 50% relative reduction vs BAC if no data to inform	[redacted]% for BAC, 0% for spesolimab	11.5% for BAC, 5.75% for spesolimab (EAG corrected error)

ACM, appraisal committee meeting; BAC, best available care; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; ICU, intensive care unit; SEE, structured expert elicitation; UK, United Kingdom

Cost-effectiveness results

All ICERs are reported in PART 2 slides

because they include confidential prices

Company and EAG base case: spesolimab is dominant against BAC

Company and EAG scenarios: spesolimab is dominant against BAC in all scenarios except those assuming spesolimab reduces inpatient rates by 0%, 5% and 10% compared with BAC

N.B dominant treatments are less costly and produce more QALYs than the dominated comparator

NICE

BAC, best available care; ICER, incremental cost effectiveness ratio; QALY, quality adjusted life year

Scenarios provided at consultation

Company scenarios		
1	Treatment of recurrent flares different to initial flares	a) For people having BAC, b) For people having spesolimab
2	Active flare at end of time horizon	12.37% of patients in both arms
3	Hospitalisation with spesolimab	30% reduction in a) inpatient b) ICU admissions
4	Efficacy of BAC	SEE exercise (severe flares)
5	Proportion of inpatients on BAC	Based on literature (most severe flares)
6	Length of stay for ICU with mechanical ventilation	Not capped
EAG scenarios		
1	Active flares by end of time horizon	For BAC: a) 12.37%, For spesolimab: a) 5.7%, b) 12.37%, c) 20%
3	Cost of ciclosporin	£48.50 (NICE requested scenario)
4	Efficacy of BAC: GPPGA pustulation subscore of 0 or 1	a) Effisayil 1 (first week) + Effisayil 1 historical cohort b) Effisayil 1 (first week) + SEE exercise (81%moderate/ 19% severe) c) SEE exercise (45% moderate/ 55% severe) d) SEE exercise (81% moderate/ 19% severe)
9	Efficacy of BAC: GPPGA pustulation subscore of 0	a) SEE exercise (81% moderate/ 19% severe) b) Effisayil 1 (first week) + SEE exercise (81% moderate/ 19% severe)
10	% inpatients with spesolimab	a) 77.6% (0% reduction) b) 73.7% (5% reduction), c) 69.84% (10% reduction), d) 62.08% (20% reduction), e) 54.32% (30% reduction)
11	% in ICU with spesolimab	a) 0%, b) 5%, c) 10%, d) 15%, e) [redacted]

BAC, best available care; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; ICU, intensive care unit; SEE, structured expert elicitation

Key issues

Issue
Has the company correctly implemented a 2nd GPP flare in the model? Is it plausible that: • Equal proportion of people have a day 8 dose of spesolimab for non-response? • Equal rates of 2nd flares for spesolimab and BAC? • Identical treatments used to treat GPP flares with no reduction in efficacy for subsequent flares?
• Has the company appropriately modelled the proportion of inpatient and ICU admissions with spesolimab? • Do the company's costs and resource use for hospital visits have face validity?
Should a mortality benefit be included for spesolimab?
Would waning of effect be expected with use of spesolimab as an acute treatment for recurrent flares over a person's lifetime?
Given the 12-week time horizon, are there any other uncaptured benefits for spesolimab?
Should any recommendation: • be limited to the population informing the evidence? • include a definition of GPP flares and response? • consider the rarity of the condition?
Should managed access be considered?

GPP, generalised pustular psoriasis, ICU, intensive care unit

Spesolimab for treating generalised pustular psoriasis flares [ID3963]

Supplementary appendix

NICE National Institute for Health and Care Excellence

Decision problem

Link to main slides: Summary of appraisal

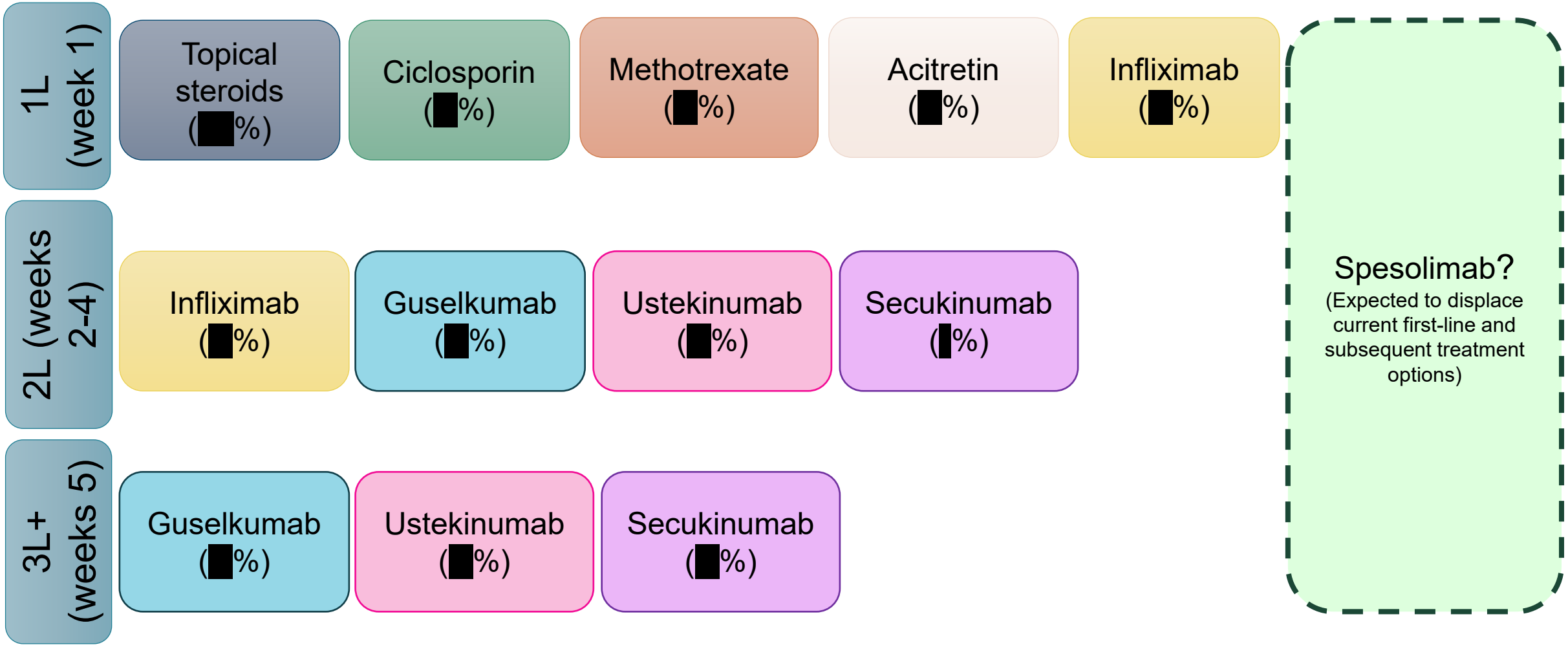
PICO from scope

	Final scope	Company	EAG comments
Population	Adult patients with generalised pustular psoriasis presenting with flares	Adult patients with GPP presenting with flares	Clinical evidence drawn from a narrower population than defined in the NICE scope and the company's decision problem as the company's pivotal trial, Effisayil 1, only included adult patients with GPP experiencing moderate-to-severe intensity flares
Intervention	Spesolimab	Spesolimab	The intervention matches the NICE scope and in the pivotal Effisayil 1 trial, the licensed dose of spesolimab was used.
Comparators	Established clinical management without spesolimab which may include: Systemic non-biological therapies such as ciclosporin Biological therapies (such as TNF-alpha inhibitors, IL-17 and IL-23 family inhibitors)	Established clinical management without spesolimab	EAG note that the comparator in the economic model is not fully aligned with the NICE scope and company definition of the decision problem

ACM, appraisal committee meeting; BAC, best available care; GPP, generalised pustular psoriasis; IL-17, Interleukin-17; TNF, tumour necrosis factor

Treatment pathway for GPP flares

Link to main slides: Summary of appraisal



- Which treatments reasonably reflect the standard of care for moderate-to-severe GPP flares in the NHS?

1L, first-line; 2L, second-line; 3L+, third- or later-line; GPP, generalised pustular psoriasis

Scoring for the GPPGA

Score	Erythema	Pustules	Scaling
0 (clear)	Normal or post-inflammatory hyperpigmentation	No visible pustules	No scaling or crusting
1 (almost clear)	Faint, diffuse pink, or slight red	Low-density occasional small discrete pustules (noncoalescent)	Superficial focal scaling or crusting restricted to periphery of lesions
2 (mild)	Light red	Moderate-density groups discrete small pustules (noncoalescent)	Predominantly fine scaling or crusting
3 (moderate)	Bright red	High-density pustules with some coalescence	Moderate scaling or crusting covering most or all lesions
4 (severe)	Deep fiery red	Very-high-density pustules with pustular lakes	Severe scaling or crusting covering most or all lesions

Each component is graded separately and then the average composite mean score is used to produce a total GPPGA score

Mean composite score	Total GPPGA score	Description
0	0	Clear
> 0 to < 1.5	1	Almost clear
≥ 1.5 to 2.5	2	Mild
≥ 2.5 to 3.5	3	Moderate
≥ 3.5	4	Severe

GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; GPPASI, Generalised Pustular Psoriasis Area and Severity Index.

Sources of evidence

Link to main slides: Summary of appraisal

Source	Details
Effisayil 1 trial	• Company-sponsored, multi-centre, randomised, double-blind phase II study of spesolimab versus placebo for the treatment of adult patients with GPP flares of moderate-to-severe intensity • Provides evidence fully relevant to this appraisal and informs the economic model • provides a direct comparison between the intervention and the comparator
Effisayil 1 historical cohort	• In the absence of an indirect treatment comparison to inform the economic model the company used data from the Effisayil 1 historical cohort • Retrospective study that provides data on the characteristics and clinical course of past GPP flares • Study did not report on which medications were received for the three categories of flare or the treatment composition for individual flares
SEE	• Carried out by the company to identify treatments used in the UK to treat GPP flares and the efficacy and safety profiles of the current treatments • Two rounds of elicitation (one individual round and one group round) • Modelling the treatments indicated by the UK experts as part of the SEE exercise is a reasonable approach • EAG considers the SEE exercise estimates to reflect UK reality more closely and to be aligned with the modelled comparator treatments (which were elicited by the same experts)

GPP, Generalised Pustular Psoriasis; SEE, Structured expert elicitation

Key clinical trial Effisayil 1 (n=53)

Link to main slides: Summary of appraisal

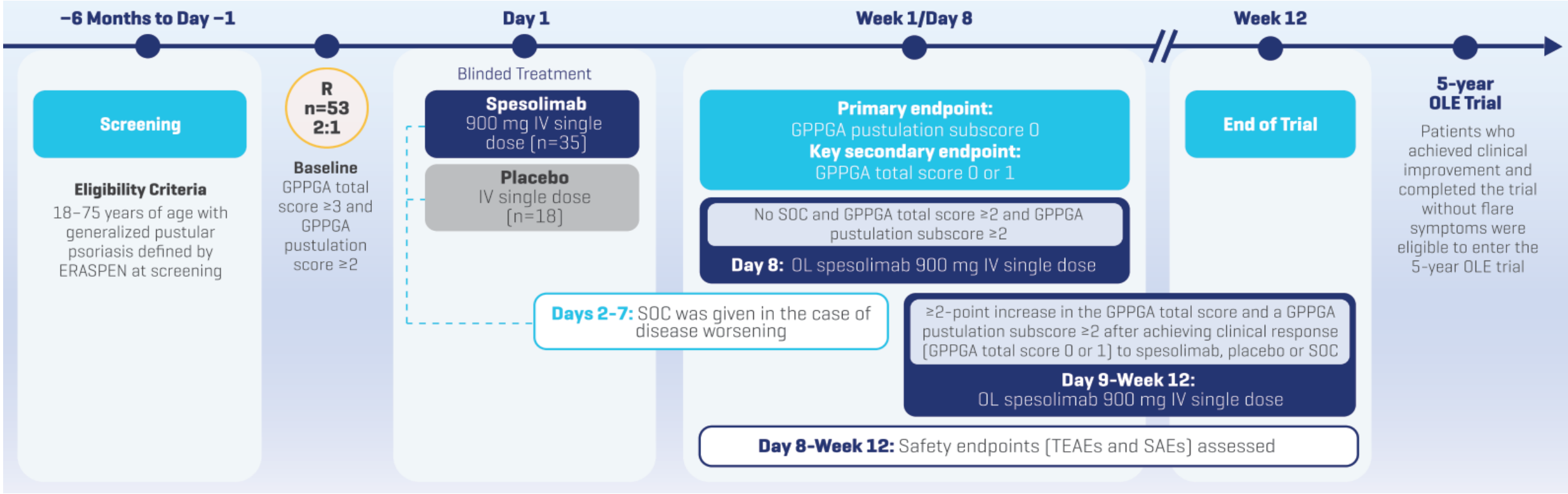
Design	Multi-centre, randomised, double-blind phase II study
Population	• GPPGA score of at least 3 (moderate) • Presence of fresh pustules (new appearance or worsening of existing pustules) • GPPGA pustulation sub score of at least 2 (mild) • At least 5% of body surface area covered with erythema (redness of skin or mucous membranes) and presence of pustules
Intervention	Spesolimab
Comparator(s)	Placebo
Duration	12 weeks
Primary outcome	GPPGA pustulation subscore of 0 at week 1
Key secondary outcomes	GPPGA total score of 0 or 1 at week 1
Exploratory endpoints	GPPASI score, pain VAS, PSS and FACIT-Fatigue
Locations	Europe, North America, North Africa, and Asia
Outcome used in model	GPPGA pustular subscore of 0 or 1 (represents flare resolution)

NICE

ERASPEN, European Rare And Severe Psoriasis Expert Network; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy – Fatigue Scale; GPP, generalised pustular psoriasis; GPPGA , Generalised Pustular Psoriasis Physician Global Assessment; GPPASI, Generalised Pustular Psoriasis Physician Global Assessment; PSS, Psoriasis Symptom Scale; VAS, Visual Analogue Scale

Effisayil 1 Trial design

Link to main slides: Summary of appraisal



Four post-hoc groups where the original randomised ITT set is split
Patients randomised to spesolimab who received,
• either 1 dose (day1) or 2 doses (day 1 and day 8), n=35
• 1 dose (day 1), n=23
• 2 doses (day 1 and day 8), n=12
Patients randomised to placebo who received
• spesolimab (day 8), n=15

GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; IV, intravenous infusion; OL, open-label; OLE, open-label extension; SD, single dose; SoC, standard of care.

RECAP

Effisayil 1 baseline characteristics

Characteristic	Spesolimab (n = 35)	Placebo (n = 18)
Age, mean years (SD)	43.2 (12.1)	42.6 (8.4)
Female, n (%)	21 (60)	15 (83)
GPPGA total score, n (%)		
3 (moderate)	28 (80)	15 (83)
4 (severe)	7 (20)	3 (17)
GPPGA pustulation subscore — n (%)		
2 (mild)	6 (17)	5 (28)
3 (moderate)	16 (46)	7 (39)
4 (severe)	13 (37)	6 (33)
Median GPPASI total score (IQR)	27.4 (15.5–36.8)	20.9 (12.0–32.0)
Median DLQI score (IQR)	19.5 (16–25)	19.5 (14–24)
Median pain VAS score (IQR)	79.8 (70.5–87.8)	70.0 (50.0–89.4)
Median PSS score (IQR)	11.0 (9–12)	10.5 (9–11)

DLQI, Dermatology Life Quality Index; GPPASI, Psoriasis Area and Severity Index for Generalised Pustular Psoriasis; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; IQR, interquartile range; n, number; PSS, Psoriasis Symptom Scale; SD, standard deviation; VAS, Visual Analogue Scale.

Link to main slides: Summary of appraisal

Key outcomes from Effisayil 1 (n=53)

Spesolimab is more effective than placebo at all endpoints

	Spesolimab (N=35)	Placebo (N=18)
Primary outcome		
GPPGA subscore score of 0 or 1, n/N (%) at week 1	20/35 (57.1%)	2/18 (11.1%)
Risk difference percentage points	46.0	
Key secondary outcomes		
Time to first achievement of GPPGA total score of 0 or 1	• Rapid onset of skin clearance as early as day 3 (N=2) and day 8 (N=17) • 88% reached GPPGA total score of 0 to 1 (clear or almost clear skin) with a single dose of spesolimab by week 1 (day 8).	
Score change from baseline at week 1 (in pain VAS, FACIT-Fatigue, DLQI, PSS)	• Median: spesolimab group [redacted] MCID for the pain VAS score (a [redacted] points, MCID is a decrease of =>30 points), and that the placebo group [redacted] MCID for the PSS score. • Mean: improvements in PROs from baseline. The mean score change from baseline were all above the MCID thresholds for each PRO by week 1 in the spesolimab arm.	
EQ-5D	By week 1, the group initially randomised to spesolimab achieved EQ-5D median score change from baseline [redacted], surpassing the [redacted]	

Risk difference percentage points: difference between the risk of an outcome in the exposed group and the unexposed group, expressed as a percentage. DLQI, Dermatology Life Quality Index; GPPASI, Psoriasis Area and Severity Index for Generalised Pustular Psoriasis; FACIT, Functional Assessment of Chronic Illness Therapy; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; MCID, Minimal Clinically Important Difference; n, number; PRO, patient reported outcome; PSS, Psoriasis Symptom Scale; N, number; VAS, Visual Analogue Scale.

Supporting data for generalisability of Effisayil 1 to NHS population

PLUM study: observational cohort study aiming to identify genes influential in development of GPP, related immune pathways and responses to treatment in 110 people with GPP

Demographic data for UK patients with GPP from PLUM study

	n	%age
With GPP	110	
Average age (recruitment)		56.3
Gender (Female)	73	66%
% White	92	84%
% Asian	16	15%
Average PGA		3.7
Average ppPASI		8.9
Average DLQI		11
Prior UV Therapy	12	11%
Average age of onset		42.1
Average BMI		29.7

	Biologics		Systemics	
Prior treatments	n	%	n	%
0	62	56%	31	28%
1	25	23%	40	36%
2	12	11%	25	23%
3	8	7%	13	12%
4	2	2%	1	1%
5	0	0%	0	0
6	1	1%	0	0

Twelves et al. 2019: observational cohort study evaluating clinical and genetic features of pustular psoriasis in 863 unrelated patients (251 people with GPP)

Phenotype characteristics of GPP by country, Twelves, et al. 2019

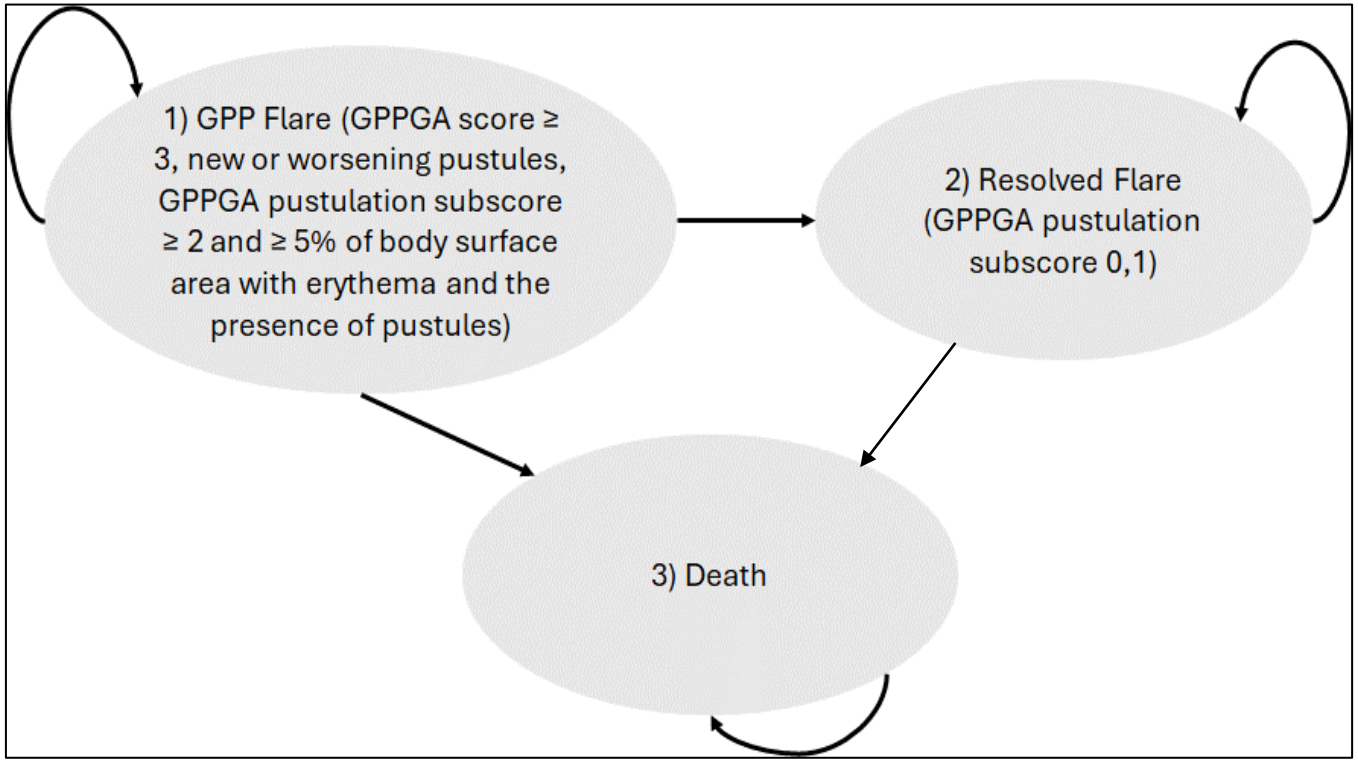
	Sex		PV (psoriasis vulgaris) status		Age of onset (yrs)
Cohort	Female	Male	PV	No PV	Mean
UK/Ireland	27 (75%)	9 (25%)	16 (42%)	17 (44%)	31.8
Malaysia	90 (68%)	41 (31%)	102 (77%)	29 (22%)	33.3
Egypt	21 (41%)	30 (59%)	4 (8%)	47 (92%)	27.9

Psoriasis vulgaris is the most common form of psoriasis and often occurs concurrently with other forms. BMI, body mass index; DLQI, Dermatology Life Quality Index; GPP, generalised pustular psoriasis; ppPASI, Psoriasis Area and Severity Index for Generalised Pustular Psoriasis; PGA, Physician's Global Assessment, n, number; N, number; UK, United Kingdom; UV, ultraviolet. Link to main slides: consultation comments

Link to main slides: Summary of appraisal

Company's model overview

- Markov model, three health states:
  1. GPP flare (defined as per Effisayil 1 trial: GPPGA score ≥ 3, new or worsening pustules, GPPGA pustulation subscore ≥ 2 and ≥ 5% of body surface area with erythema and the presence of pustules). Everyone begins in this health state
  2. Resolved flare (GPPGA pustulation subscore 0, 1)
  3. Death



Model features:
Time horizon: 12 weeks
Cycle length: daily

Note: No comparative evidence beyond week 1 and company uses data from Effisayil 1 historical cohort to inform cost-effectiveness modelling of comparator arm beyond week 1

Further details on variables applied in economic model and key model inputs

NICE

BAC, best available care; GPP, generalised pustular psoriasis; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment.

Company's model overview at ACM2

Link to main slides: Summary of appraisal

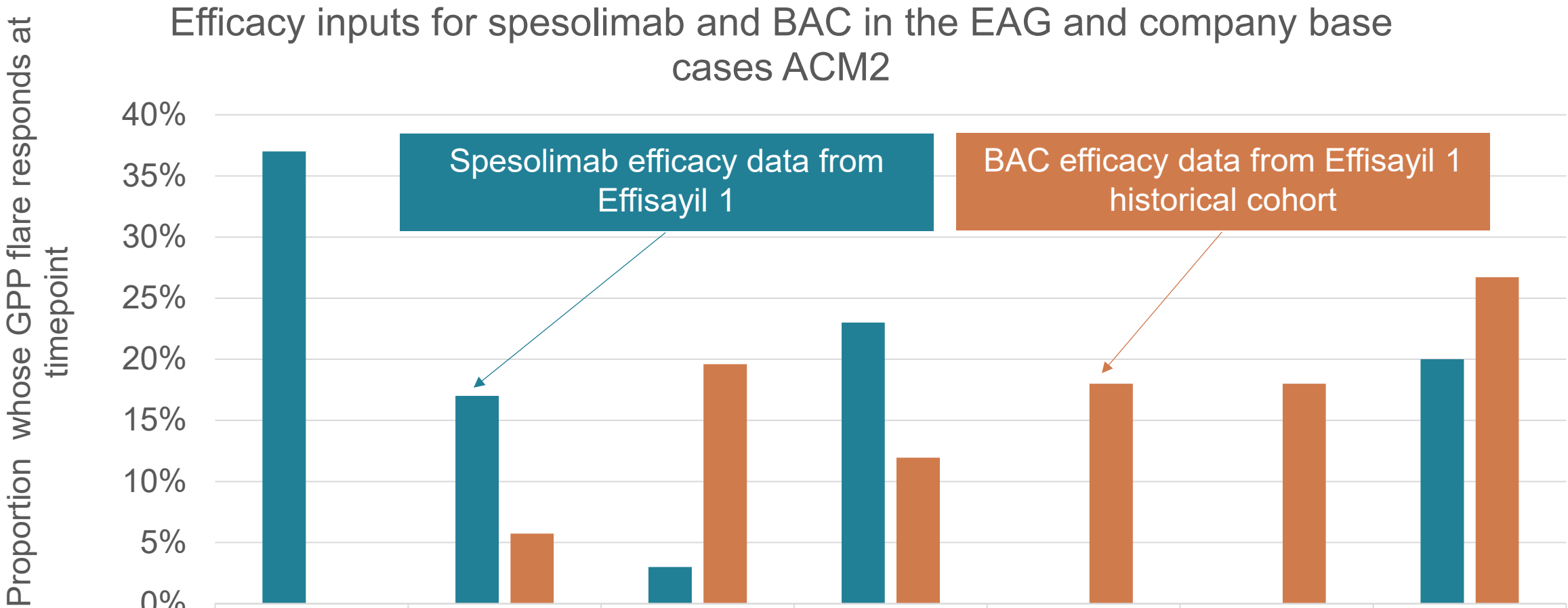
Model parameters	Source
Baseline characteristics	• Patients with mean age 43 years in both groups; 67.90% females – Effisayil 1 trial
Response to treatment: spesolimab and AE incidence	Effisayil 1
Response to treatment: BAC	Effisayil 1 trial historical cohort
Mortality	French SNDS study (Viguier et al., 2024)
Utilities	• Health state utilities: Effisayil 1 trial • AE disutilities: literature (Sullivan et al., 2011 and Stevenson et al., 2016)
Cost and HCRU:	
Intervention and comparators' costs and resource use	Drug costs: Monthly Index of Medical Specialties and the electronic Market Information Tool Resource use: NHS reference costs 2020/21 (published 2022)
Structured expert elicitation – HCRU for a GPP flare	Six English dermatologists, with experience treating GPP patients at specialist centres
Health state unit costs & resource use	Unit Costs of Health and Social Care, 2023,
AE unit costs and resource use	National schedule of NHS costs 2020/2021.
Miscellaneous unit costs & resource use	Georghiou et al. 2014.

AE, adverse event; BAC, best available care; GPP, generalised pustular psoriasis; HCRU, health care resource use; SNDS, French National Health System database

Link to main slides: Modelling 2nd flares

Efficacy inputs at ACM2

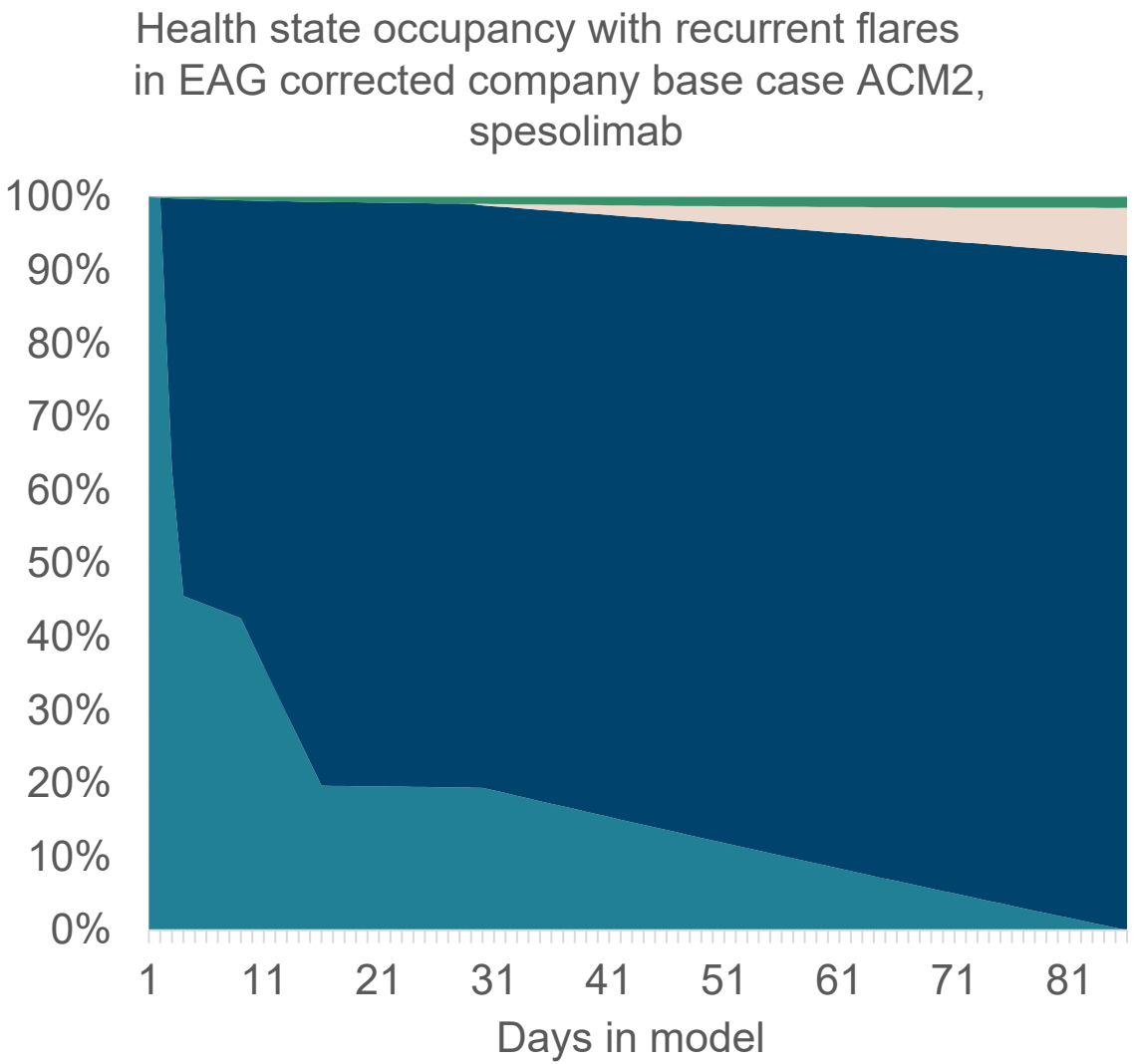
Higher proportion of people having early flare resolution with spesolimab vs BAC

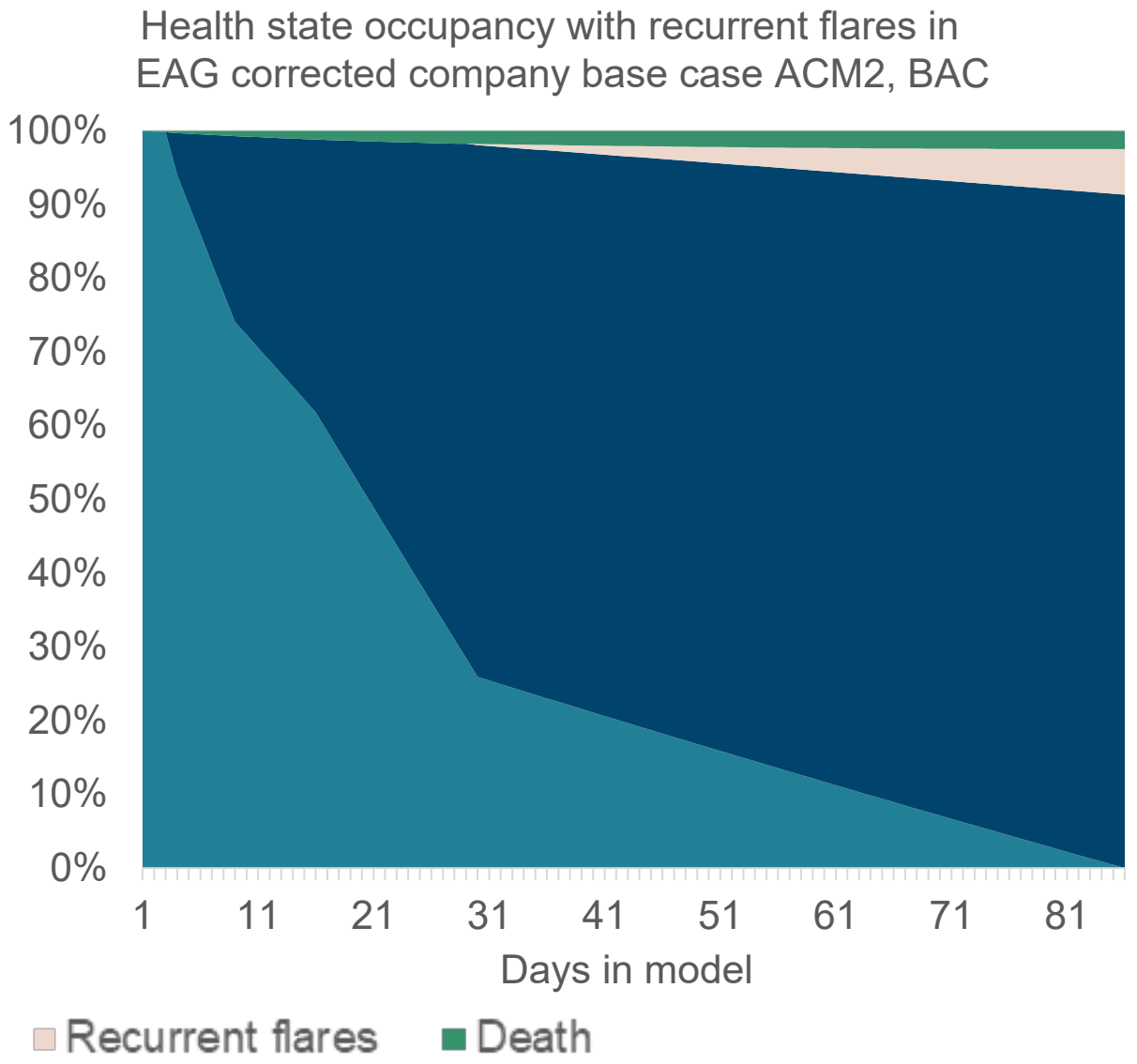


	Day 2	Day 3	Day 8	Week 2	Week 3	Week 4	Week 12
Spesolimab	37%	17%	3%	23%	0%	0%	20%
BAC	0%	6%	20%	12%	18%	18%	27%

ACM, appraisal committee meeting; BAC, best available care; GPP, generalised pustular psoriasis

Health state occupancy with recurrent flares, ACM2





ACM, appraisal committee meeting; BAC, best available care; GPP, generalised pustular psoriasis

Link to main slides: Modelling 2nd flares

Hospitalisation costs in the EAG corrected model

[redacted]

[redacted]

BAC, best available care; GPP, generalised pustular psoriasis; ICU, intensive care unit; MV, mechanical ventilation

Further company consultation comments

Link to main slides: Company's response to consultation

Committee requested	Company
Use or market share data for BAC treatments to verify SEE exercise	• No further data identified. • Note discrepancies between SEE exercise and clinical experts ACM1 (e.g. methotrexate or infliximab at first line) → SEE exercise more appropriate source for BAC composition as elicited via structured process from a larger sample of experts

ACM, appraisal committee meeting; BAC, best available care; SEE, structured expert elicitation

Key issue: BAC treatment effect

Link to main slides: Company's response to consultation

Company scenario uses values elicited for severe flares in SEE exercise for BAC efficacy

Background: BAC treatment effect at ACM1 informed by:

- Company: Effisayil 1 trial week 1 (week 1 in model), historical cohort Effisayil 1 (after week 1)
- EAG: Effisayil 1 trial week 1 (week 1 in model), SEE exercise (after week 1) (as limitations in historical cohort)

Committee conclusion: prefer Effisayil 1 historical cohort from day 0 as:

- week 1 Effisayil 1 data not generalisable to UK population, historical cohort aligns with population in trial.

Requested scenario using SEE exercise to inform BAC efficacy from Day 0.

Company: updated base case to committee's preferred assumption

Scenario: applies efficacy elicited from SEE exercise from people with 'severe flares' only

- Approach chosen as GPPGA scores from Effisayil 1 best match those in Wolf et al 2024 from flares clinically assessed as 'severe' (see supplementary appendix)

EAG comments: In SEE exercise, clinicians [redacted]

- Definitions used in the SEE exercise for severe and moderate flares unclear
- Company scenario where 100% have severe flares inappropriate → does not match population in Effisayil 1

Base case: historical cohort Effisayil 1 trial from day 0

Scenarios: SEE exercise using populations a) 81% GPPGA total score of 3 (moderate), 19% GPPGA score of 4 (severe) (best match to Effisayil 1 population) b) 45% moderate, 55% severe

ACM, appraisal committee meeting; BAC, best available care; GPP, generalised pustular psoriasis; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; UK, United Kingdom; SEE, structured expert elicitation

Link to main slides: Company's response to consultation

Key issue: BAC treatment effect

EAG provides scenarios with varying severities from the SEE exercise

Time to earliest response estimates from the SEE exercise to inform the efficacy of BAC

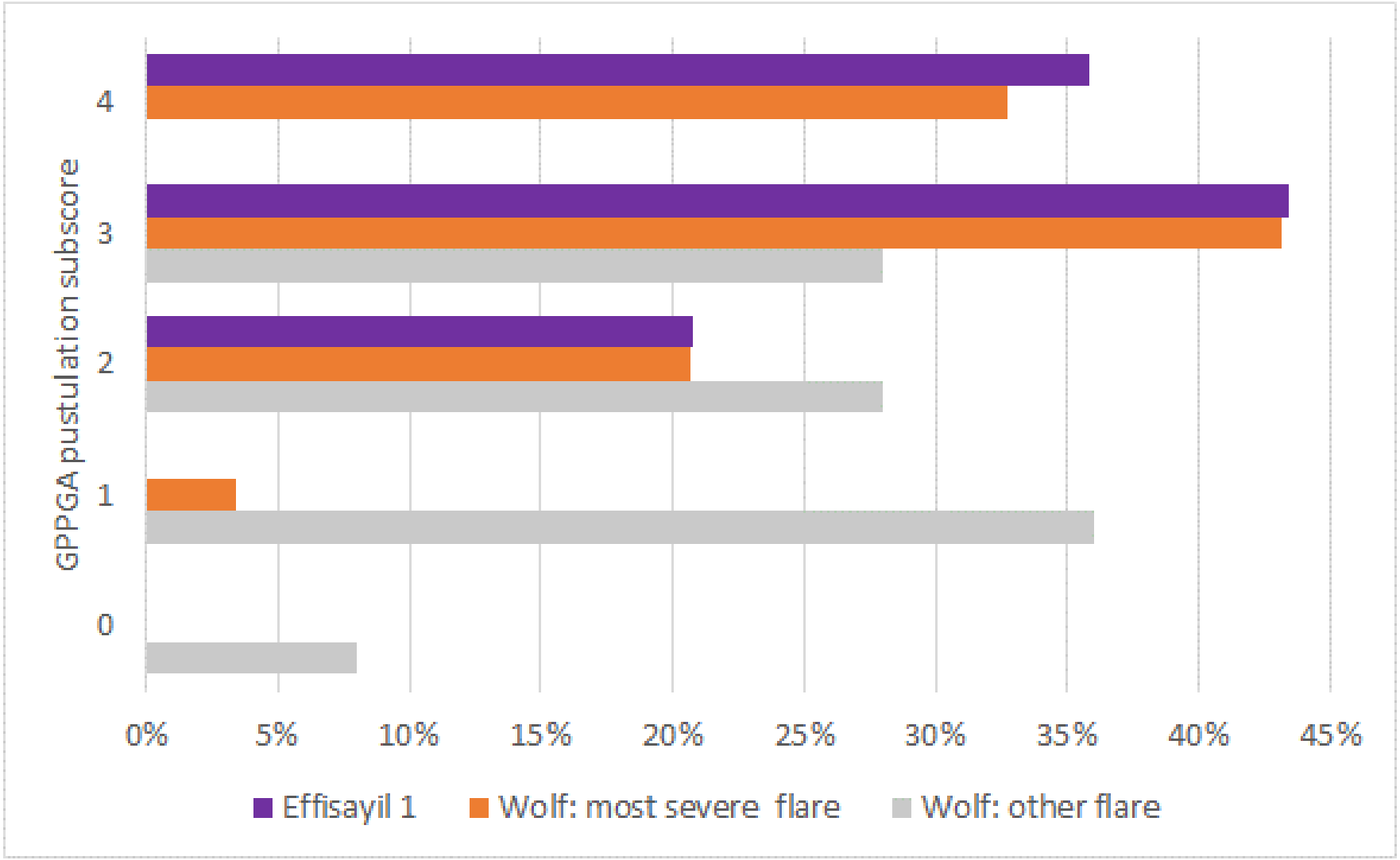
	Post-DG company scenario	ACM 1 EAG base case	ACM 1 EAG Scenario	Post-DG EAG scenario
Target GPPGA score	0 or 1	0 or 1	0	0 or 1
Population	100% severe	45% moderate, 55% severe	45% moderate, 55% severe	81% moderate, 19% severe
Proportion reaching target GPPGA score at timepoint:				
Day 2	[redacted]	[redacted]	[redacted]	[redacted]
Day 3	[redacted]	[redacted]	[redacted]	[redacted]
Day 8	[redacted]	[redacted]	[redacted]	[redacted]
Week 2	[redacted]	[redacted]	[redacted]	[redacted]
Week 3	[redacted]	[redacted]	[redacted]	[redacted]
Week 4	[redacted]	[redacted]	[redacted]	[redacted]
Week12	[redacted]	[redacted]	[redacted]	[redacted]

ACM, appraisal committee meeting; BAC, best available care; DG, draft guidance; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; SEE, structured expert elicitation

Key issue: BAC treatment effect

GPPGA pustulation sub scores by evidence source

Link to main slides: Company's response to consultation



BAC, best available care; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; SEE, structured expert elicitation

Link to main slides: Modelling 2nd flares

Recap: Effisayil 1 historical cohort

Background ACM1

- Effisayil 1 historical cohort used at ACM1 to inform model after week 1 (n=53) → same cohort of as Effisayil 1 trial and provides data on the characteristics and clinical course of past GPP flares
- Treatments in BAC arm of company's model beyond week 1 obtained from SEE exercise
- Historical cohort lacked GPPGA pustulation subscore data (0 or 1), using time to pustular clearance as a proxy
- No standard definition for typical, most severe and longest flares, based on investigator interpretation
- Company used patient demographic and flare data from POLARIS and SCRIPTOR RWE to assess representativeness of historical cohort to England, cautioning against cross-source comparisons due to differing definitions and methods
- Patients with incident GPP in POLARIS study (mean age 57.3, SD 19.0) and [redacted]
- Ethnic distributions varied between POLARIS, SCRIPTOR and Effisayil 1 trial due to locations
- Comparisons for other characteristics were limited by missing or inconsistently reported data

EAG comments

- SEE is lower quality evidence source compared to RWE for estimating BAC efficacy
- Explore assumption of using SEE exercise and Effisayil 1 trial for GPPGA subscore of 0 or 1 in scenarios
- Use of biologic treatments in Effisayil 1 historical cohort, seems lower than might be expected in NHS
- Concerns about how well flares and treatments received for flares represent current BAC in England

ACM, appraisal committee meeting; BAC, best available care; GPP, Generalised Pustular Psoriasis; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; RWE, real-world evidence; SEE, structured expert elicitation; SD, standard deviation

Overview of key model

How the technology is modelled to affect QALYs and Costs

Effect on QALYs	• The number of patients achieving a GPPGA pustulation subscore of 0 or 1 is different between spesolimab and BAC, which determines the proportion moving into the resolved flare health state and results in considerable QALY differences • The number of patients hospitalised in each arm. As the number of patients hospitalised on spesolimab is half that of the comparator arm, the QALY difference is significant • The number of patients admitted to ICU in the spesolimab arm, which further increases the QALY difference between the two arms • The rate of adverse events, which is different between the arms although the impact in QALYs is minor
Effect on costs	• The number of patients achieving a pustulation subscore of 0 or 1, hospitalised and admitted to the ICU in each arm • The different adverse events that arise with the different medications in each arm, although the impact on costs is minor • The different acquisition and administration costs for spesolimab and the medications in best available care
Effect on life years	• The number of people who die is different between spesolimab and BAC as linked to the number of people in ICU

Note: 12-week time horizon so long-term impact on costs, QALYs and life years uncertain

BAC, best available care; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment; ICU, intensive care unit; QALY, quality adjusted life-year

Data sources excluded by the company

Link to main slides: Inpatient and ICU rates

Source	Description	Company comments
Hospital episodes statistics (HES)	International Classification of Diseases (ICD)-10 code, L40.1, to identify patients admitted with primary diagnosis of GPP.	Inappropriate source of data for hospitalisations: • No data on admission rates as only from admitted patients • Doesn't detect GPP flare-ups, severity, or subsequent results. • Little information on procedures undertaken and treatments administered • Outpatient visit data only linked to 'Dermatology' but not specifically GPP → <5% visits contain diagnostic information. • Cannot link ICU data to GPP flare-ups.
Primary care data	Specific HES codes linked to primary care data to identify GPP flare-ups that didn't result in hospitalisation	• No patients identified using GPP-specific codes
BADBIR registry	UK and Ireland observational study assessing long term safety of biologic treatments for psoriasis. Records baseline GPP diagnosis and specific follow up outcomes	• Not possible to attribute hospital admissions to GPP/GPP flare, or determine number who avoided hospitalisation. • No data on ICU admissions.
Secure data environments	De-identified linked health and care dataset covering over 2.5 million people	• GPP coded under 'Pustular Psoriasis' code → inappropriate as does not differentiate GPP from other forms of pustular psoriasis

BAC, best available care; GPPGA, Generalised Pustular Psoriasis Physician Global Assessment