National Institute for Health and Care Excellence

Health Technology Evaluation

Depemokimab for treating severe eosinophilic asthma in people 12 years and over ID6447
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	Asthma + Lung UK (patient)	The remit and approach taken to this evaluation seem appropriate. The age range (ages 12 and over) reflects the prescribing range for existing severe asthma biologics.	Thank you for your comment. No action required.
	AstraZeneca UK Ltd	AstraZeneca consider the proposed evaluation route to be appropriate.	Thank you for your comment. No action required.
	British Thoracic Society	Appropriate to evaluate this as a intervention for severe eosinophilic asthma. Six monthly dosing interval is novel in the context of currently available anti-IL5 biologic agents, so the proposed evaluation route is appropriate.	Thank you for your comment. No action required.
	GSK UK Ltd (company)	GSK agrees with appropriateness of evaluating the topic but proposes that it submits: • A cost-utility analysis (CUA) for people who have had 2 exacerbations in the previous year vs optimised standard therapy without biologics	Thank you for your comment. The committee will assess the technology in line with its marketing

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		• A cost-utility analysis (CUA) and a cost-comparison (CCA) for people who have had 3+ exacerbations in the previous year vs other biologics.	authorisation. The company will have the opportunity to justify its approach in the submission documents.
	Neonatal and Paediatric Pharmacy Group	Appropriate	Thank you for your comment. No action required.
	NHS England (Specialised Commissioning)	It is very appropriate to evaluate this topic as the technology offers additional benefits over and above those offered by the comparators.	Thank you for your comment. No action required.
Wording	Asthma + Lung UK	The draft remit is appropriate.	Thank you for your comment. No action required.
	AstraZeneca UK Ltd	N/A	No action required.
	British Thoracic Society	Yes.	Thank you for your comment. No action required.
	GSK UK Ltd (company)	Current draft scope wording To appraise the clinical and cost effectiveness of depemokimab within its marketing authorisation for severe eosinophilic asthma in people 12 years and over	Thank you for your comment. The evaluation objective has been updated to align

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		Proposed final scope wording To appraise the clinical and cost-effectiveness of depemokimab within its marketing authorisation for severe asthma with an eosinophilic phenotype in people aged 12 years and over who are inadequately controlled on medium- to high-dose inhaled corticosteroids (ICS) plus another asthma controller. Rationale GSK requests the wording of the remit to align with its anticipated market authorisation.	with the anticipated marketing authorisation.
	Neonatal and Paediatric Pharmacy Group	Appropriate	Thank you for your comment. No action required.
	NHS England (Specialised Commissioning)	Yes	Thank you for your comment. No action required.
Additional comments on the draft remit	Asthma + Lung UK	Timing issue: Ensuring equitable, timely access to biologic therapies for all eligible patients with severe asthma is crucial to improving health outcomes. However, the relative urgency of this evaluation is diminished by the current challenges within the NHS in delivering existing approved treatments to all who qualify.	Thank you for your comment. No action required.
	AstraZeneca UK Ltd	N/A	No action required.

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	British Thoracic Society	Timing issue: This agent has similar efficacy to other anti-IL5 biologics and therefore is unlikely to lead to significant improvements in asthma outcomes on an individual patient basis. However, there is a huge potential benefit from a severe asthma service delivery perspective. It is estimated that less than a sixth of severe asthma patients who would benefit from a biologic agent have access to treatment (NHSE BlueTeq data, 2021). Barriers to access identified by the AAC Asthma Biologics Working Group include patient factors (e.g. geographical distance from a specialist centre) and service factors (e.g. lack of capacity to carry out patient assessments in specialist centres). Depemokimab's prolonged dosing interval could help to overcome these barriers and improve access to treatment. Therefore, we suggest that a relatively short time frame for evaluation is justified.	Thank you for your comment. No action required.
	GSK UK Ltd (company)	Timing issue: GSK believes there is a significant unmet need in current NHS practice for people with severe asthma who have experienced two exacerbations in the previous year, as there are no other biologic treatments recommended by NICE in this population. Notably, the vast majority (85%) of the trial population in depemokimab's key trials (SWIFT 1 and 2) included patients with two exacerbations, highlighting how depemokimab addresses this critical unmet need. (ClinicalTrials.gov, 2024; ClinicalTrials.gov, 2024; Jackson et al., 2024) Additionally, depemokimab is also the only long-acting biologic with a twice-yearly dosing regimen. While the potential benefit of twice-yearly dosing of depemokimab quality of life via adherence can be confirmed through real-world studies, evidence from other therapeutic areas suggests positive outcomes. Publications have reported that patients transitioning to less frequent injections across various conditions, including growth hormone deficiency (GHD), experienced increased convenience and satisfaction,	Thank you for your comment. NICE aims to publish final guidance for all new technologies within 90 days of receiving marketing authorisation.

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		higher adherence rates, fewer adverse events, and improved quality of life (Loftus et al.2022). Additional comments: The treatment pathway in clinical practice in the UK is expected to be significantly updated in line with depemokimab's expected MHRA marketing authorisation and SWIFT 1 and 2 clinical trial evidence (see points below).	
	Neonatal and Paediatric Pharmacy Group	Timing issue: Very timely	Thank you for your comment. No action required.
	NHS England (Specialised Commissioning)	Timing issue: The timing of the evaluation should be aligned with ongoing evaluations at a global level to ensure equity of access to patients in England.	Thank you for your comment.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Asthma + Lung UK	The draft scope is comprehensive and detailed, though it needs amendment. The asthma prevalence figure included is 21 years out of date. Asthma + Lung UK estimates that there are 7.2 million people with asthma in the UK and recommends that this more accurate figure be included in the scope. The scope doesn't include a prevalence figure for severe asthma and should be amended to do so; around 200,000 people in the UK have severe asthma.	Thank you for your comment. We have updated the figures of asthma incidence and added information about the long-term

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		The draft scope discusses the use of steroid tablets – oral corticosteroids (OCS) – as 'standard' or maintenance therapy for treating severe asthma without acknowledging the side effects associated with OCS use. Side effects can include osteoporosis and steroid-induced diabetes, among others, and patients are at increased risk from just one course of OCS. The language of the draft scope should be amended to reflect the risks of these side effects, their potential impact on patients, and the actual difference between achieving condition control through optimised biologics as opposed to OCS reliance.	side effects associated with oral corticosteroids.
	AstraZeneca UK Ltd	AstraZeneca has two comments on the wording: 1. "Severe eosinophilic asthma is a subset of the condition that is associated with high levels of eosinophils and recurrent exacerbations". a. AstraZeneca would propose the addition of "and recurrent use of oral corticosteroids and inhaled corticosteroids at high doses". i. We would also request wording to highlight the burden of recurrent corticosteroid use and consequently, emphasise the key treatment goal of corticosteroid reduction. b. AstraZeneca would propose adding wording to clarify that severe eosinophilic asthma is a phenotype of severe asthma – not a subset of asthma. 2. "Eosinophilic nasal polyps may also be present". a. AstraZeneca acknowledges that nasal polyps can be present in severe asthma patients as can other comorbidities. As such, AstraZeneca recommend this sentence be removed to avoid ambiguity in the patient population as patients only suffering from nasal polyps (and not severe	Thank you for your comment. The aim of the background section is to provide a very brief summary of the disease area. We have added information about the long-term side effects associated with oral corticosteroids. Further information can be provided at the submission stage of the appraisal. The sentence relating to nasal polyps has been retained in the background section.

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		asthma) would be out of scope for this appraisal and will require a separate appraisal.	Nasal polyps are a phenotype associated with severe eosinophilic asthma. The committee will assess the technology in line with its marketing authorisation.
	British Thoracic Society	Minor amendments to wording are suggested as below. • "If control is inadequate on an as-needed inhaler, or if the presentation is more severe at the point of diagnosis, people will be offered maintenance and reliever therapy with a single inhaler device." • "...people may take either a leukotriene receptor antagonist (LTRA) or a long-acting muscarinic receptor antagonist (LAMA), or both, in addition to moderate-dose MART." • "Severe asthma is associated with a high number of exacerbations treated with high dose oral corticosteroids. Some patients require daily oral steroids to gain asthma control. Both daily maintenance oral steroids and short courses of high dose steroids for exacerbations are associated with a substantial increase in morbidity" (In place of the current wording 'Some people take steroid tablets as maintenance therapy where symptoms are not well controlled despite other treatments.')	Thank you for your comments. The background section has been updated to reflect your comments.
	GSK UK Ltd (company)	Current draft scope wording Depemokimab (brand name unknown, GlaxoSmithKline UK Ltd) does not currently have a marketing authorisation in the UK for treating severe eosinophilic asthma. It is being studied in phase 3 clinical trials as add-on treatment for people 12 years and older with eosinophilic asthma. It is compared with placebo, mepolizumab and benralizumab.	Thank you for your comment. Additional information on the trial populations has been added. The aim of the background and

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		Proposed final scope wording Depemokimab (GSK3511294, brand name unknown, GSK) is a monoclonal antibody that targets interleukin-5 (IL-5). IL-5 plays a key role in the survival, maturation, and migration of eosinophils, which are central to the inflammatory process in eosinophilic asthma (Hussain et al., 2024). By binding to IL-5, depemokimab inhibits the survival of eosinophils, reducing airway inflammation and asthma exacerbations. Depemokimab is administered subcutaneously once every 26 weeks. GSK has applied for and is awaiting marketing authorisation in the UK for depemokimab for the treatment of severe asthma with an eosinophilic phenotype. Depemokimab has been studied in phase 3 clinical trials (SWIFT 1 & 2) compared to placebo as an add-on maintenance treatment for adult and adolescent patients aged 12 years and older with type 2 inflammation characterized by an eosinophilic phenotype, who are inadequately controlled on medium- to high-dose ICS plus another asthma controller. (ClinicalTrials.gov, 2024; ClinicalTrials.gov, 2024; Jackson et al., 2024). Rationale To include an up to date and accurate description of the intervention and regulatory status.	technology section is to provide a very brief summary of the disease area. Further information can be provided at the submission stage of the appraisal.
	Neonatal and Paediatric Pharmacy Group	Appropriate	Thank you for your comment. No action required.
	NHS England (Specialised Commissioning)	Accurate	Thank you for your comment. The aim of the background and technology section is to provide a very brief

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		Should include information on the technology: depemokimab dosing schedule, route of administration	summary of the disease area. Further information can be provided at the submission stage of the appraisal.
Population	Association of Respiratory Nurses (ARNS)	Yes	Thank you for your comment. No action required.
	Asthma + Lung UK	The population is appropriate.	Thank you for your comment. No action required.
	AstraZeneca UK Ltd	N/A	No action required.
	British Thoracic Society	Yes	Thank you for your comment. No action required.
	GSK UK Ltd (company)	Current draft scope wording People 12 years and over with severe eosinophilic asthma Proposed final scope wording People aged 12 years and over with severe asthma with an eosinophilic phenotype who are inadequately controlled on medium- to high-dose inhaled corticosteroids (ICS) plus another asthma controller.	Thank you for your comment. This has been updated.

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		Rationale GSK would like the population to reflect the anticipated marketing authorisation.	
	Neonatal and Paediatric Pharmacy Group	Yes	Thank you for your comment. No action required.
	NHS England (Specialised Commissioning)	This is not fully clear- how is severe eosinophilic asthma defined? Definition should include - uncontrolled disease (ongoing exacerbations needing oral corticosteroids) despite optimised treatment including high dose ICS	Thank you for your comment. The population has been updated to reflect the population in the marketing authorisation
Subgroups	Asthma + Lung UK	No comment	No action required.
	AstraZeneca UK Ltd	AstraZeneca would request a cutoff being specified for the subgroup “baseline eosinophil levels” and “frequent oral corticosteroid treatment”.	Thank you for your comment. The company is invited to justify the thresholds used in its analyses, such as clinical significance, available data, or those used in previous technology appraisals. Exclusion of these subgroups or inclusion

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			of additional subgroups should also be justified in the submission.
	British Thoracic Society	The recommended subgroups are appropriate.	Thank you for your comment. No action required.
	GSK UK Ltd (company)	**Current draft scope subgroups** • baseline eosinophil levels • baseline fractional exhaled nitric oxide levels • people who require maintenance oral corticosteroid treatment (mOCS) • people who require frequent oral corticosteroid treatment **Proposed final scope subgroups** • Patients not requiring mOCS o History of exacerbations per year – 2 only and 3+ exacerbations in the previous year. o Baseline eosinophil levels ▪ EOS ≥150/µL ▪ EOS ≥300/µL o Baseline ICS level ▪ High dose ICS ▪ Mid dose ICS **Rationale** Currently, all biologics are indicated for patients with 3+ exacerbations in the previous year or those on mOCS.	Thank you for your comment. Where evidence allows, analysis of subgroups noted in the scope should be provided. The company should justify any omissions or additional subgroups in its submission. The number of exacerbations in the previous year has been added.

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		Around 95% of the SWIFT trial population were on not on mOCS [redacted] Additionally, 85% of the patients in SWIFT 1 and 2 had a history of 2 exacerbations in the previous year. Since clinical criteria in the UK for the existing biologics recommended in severe asthma are based on numbers of exacerbations, it would be relevant to explore a subgroup analysis based on the history of exacerbations. In the SWIFT trials, 15% of the population had 3+ exacerbations. Given that IL-5 biologics are well-established in clinical practice for this population and there is sufficient data available for the analysis, GSK believes it is a relevant subgroup. **Lastly, there is no available data from SWIFT 1 and 2 to support baseline fractional exhaled nitric oxide (FeNO) levels.**	
	Neonatal and Paediatric Pharmacy Group	Those who have had asthma exacerbations. Consider those individuals that would have difficulty in adhering to other biologics either due to needle phobia or other issues as this medication allows twice yearly administration compared to fortnightly or monthly administration.	Thank you for your comment. The incidence of exacerbations in the previous year has been added. Difficulty taking other treatments may be considered an equalities issue and has been added to the Equality impact assessment. Further information about this can be provided at the

Section	Consultee/ Commentator	Comments [sic]	Action
			submission stage of the appraisal.
	NHS England (Specialised Commissioning)	These are adequate.	Thank you for your comment. No action required.
Comparators	Association of Respiratory Nurses (ARNS)	Yes	Thank you for your comment. No action required.
	Asthma + Lung UK	The draft scope includes all six biologics currently licensed for treating severe asthma. This is an appropriate set of comparators. Comment is not made, however, as to the poor availability of existing biologics. Treatment of severe asthma is hampered by woeful access rates among eligible patients, with a national average of 17% and some ICBs reaching only 2% biopenetration. The draft scope discusses the use of steroid tablets – oral corticosteroids (OCS) – as standard or maintenance therapy for treating severe asthma but does not highlight the side effects associated with OCS use. Side effects can include osteoporosis and steroid-induced diabetes, among others, and patients are at increased risk from one course of OCS. The language of the draft scope should be amended to reflect the risks of these side effects, their potential impact on patients, and the actual difference between achieving condition control through optimised biologics as opposed to OCS reliance.	Thank you for your comment. Information about the long-term side effects associated with oral corticosteroids has been added to the background section. The aim of the comparator section is to provide an inclusive list of relevant comparators. Further information can be provided at the submission stage of the appraisal.
	AstraZeneca UK Ltd	N/A	No action required.

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	British Thoracic Society	The comparators are appropriate with no omissions.	Thank you for your comment. No action required.
	GSK UK Ltd (company)	**Current comparators** For people for whom biologics are indicated or suitable according to NICE guidance, in addition to standard therapy: • Tezepelumab • Reslizumab • Benralizumab • Mepolizumab • Dupilumab • Omalizumab For people for whom currently available biologics are not indicated or suitable: • Optimised standard therapy without biologics **Proposed comparators** **1.** In patients not requiring mOCS and with a history of 2 exacerbations a year: • Optimised standard therapy without biologics **2.** In patients with a history of 3+ exacerbations a year: **2.a.** Baseline eosinophil levels 150-300/µL • Tezepelumab (in addition to optimised standard therapy) (NICE, 2023) • Dupilumab (in addition to optimised standard therapy) (NICE, 2021) **2.b.** Baseline eosinophil levels 300+ /µL • Mepolizumab (in addition to optimised standard therapy) (NICE, 2021)	Thank you for your comment. The comparators have been retained as those listed in the scope are intended to be broad. A strong and clear rationale should be provided for excluding any comparators from the evidence submission. The most appropriate comparator(s) will be discussed in more detail during the appraisal and by the committee, with input from the company submission and clinical experts.

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		• Benralizumab (in addition to optimised standard therapy) (NICE, 2019) • Tezepelumab (in addition to optimised standard therapy) (NICE, 2023) • Reslizumab (in addition to optimised standard therapy) (NICE, 2017) • Dupilumab (in addition to optimised standard therapy) (NICE, 2021) **Rationale** The appropriate comparators differ across populations, depending on the number of exacerbations and eosinophil levels. GSK has outlined a clear set of comparators above, based on current marketing authorisations, NICE guidance, and clinical practice in the UK. Additionally, GSK believes that omalizumab (NICE, 2013) is not a relevant comparator for the following reasons: • *Different Mechanisms of Action:* Omalizumab is an anti-IgE antibody, targeting allergic pathways without direct eosinophil depletion. • *Patient Population:* Omalizumab is primarily used for allergic asthma with elevated IgE, not necessarily characterized by high eosinophils. • *Clinical Efficacy in asthma with eosinophilic phenotype* Omalizumab has limited evidence in patients with eosinophilic asthma without significant allergic components.	
	Neonatal and Paediatric Pharmacy Group	Consider those individuals that would have difficulty in adhering to other biologics either due to needle phobia or other issues as this medication allows twice yearly administration compared to fortnightly or monthly administration.	Thank you for your comment. Difficulty with adherence to other treatments may be considered an equalities issue and

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			have been included in the Equality impact assessment. Further information about this can be provided at the submission stage of the appraisal.
	NHS England (Specialised Commissioning)	Yes	Thank you for your comment. No action required.
Outcomes	Association of Respiratory Nurses (ARNS)	Health-related quality of life – Could a psychological specific outcome be considered?	Thank you for your comment. Health-related quality of life will be captured using Quality Adjusted Life Years (QALYs) as outlined in the NICE reference case. Further data and information can be provided at the submission stage of the appraisal.
	Asthma + Lung UK	As depemokimab is the first asthma biologic injection to be given once every 6 months there must be adequate emphasis placed on detailed scrutiny regarding long-term tolerability and the onset of possible side effects; and more importantly how side effects are to be managed. All other biologics can be stopped if there are reactions, however, once injected this biologic would potentially be circulating within the patient for 6 months.	Thank you for your comment. The aim of the outcomes section is to provide a very brief list of key outcomes and

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		The language used in this section should be amended. All exacerbations have the potential to be fatal, and each exacerbation indicates poor condition control, suggesting the patient is at risk of further exacerbations and death. Asthma + Lung UK suggests this alternative wording for the second bullet point: • "incidence of exacerbations, including those which require unscheduled contact with healthcare professionals or hospitalisation"	is not exhaustive. The company will have the opportunity to justify its considerations of the outcomes in its submission. We have removed "clinically significant" before "exacerbations" from the outcomes section.
	AstraZeneca UK Ltd	N/A	No action required.
	British Thoracic Society	The suggested outcomes are appropriate and will capture the main risks and benefits of treatment. Reduction of inhaled corticosteroid dose would be an important outcome to evaluate if the evidence allows for this.	Thank you for your comment. Reduction of inhaled corticosteroid dose has not been added but the company can include this outcome if evidence allows. Use or dose of oral corticosteroid is included as an outcome.
	GSK UK Ltd (company)	GSK is aligned with the outcomes listed. The key clinical outcomes in the SWIFT 1 & 2 trials are: • Annualized rate of clinically significant	Thank you for your comment. The company will have the opportunity to justify the

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		exacerbations over 52 weeks (primary outcome) • Change from baseline in Asthma Control Questionnaire-5 (ACQ-5) score at Week 52 • Change from baseline in St. George's Respiratory Questionnaire (SGRQ) total score at Week 52 • Change from baseline in in pre-bronchodilator forced expiratory volume in one second (FEV1) at Week 52 • Annualized rate of exacerbations requiring hospitalization and/or Emergency Department (ED) visit over 52 weeks	inclusion/exclusion of any outcomes in its submission.
	Neonatal and Paediatric Pharmacy Group	Adherence to twice yearly administration vs fortnightly or monthly administrations.	Thank you for your comment. The company will have the opportunity to include additional outcomes in its submission (where evidence allows).
	NHS England (Specialised Commissioning)	Yes Our patient with lived experience notes that although the document mentions quality-adjusted life years (QALY) and thinks it's also important to emphasise real-world patient benefits beyond just reducing exacerbations. Improvements in daily function, fatigue levels, hospital visit frequency, and overall mental health are crucial factors in determining how impactful a treatment is. If any preliminary data on these aspects exist, including them would be valuable. They acknowledge that this may be due to the fact that depemokimab is still in clinical trials and certain details may not yet be available. However, if any preliminary data or expected positioning in the treatment pathway could be	Thank you for your comment. Aspects of health-related quality of life, such as improvements in daily function, fatigue levels and mental health will be captured using Quality Adjusted Life Years (QALYs) as outlined in the NICE

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		included, they believe it would provide valuable context to both clinician and patient.	reference case. Further data and information can be provided at the submission stage of the appraisal. The company will have the opportunity to justify its considerations of the outcomes in its submission.
Equality	Asthma + Lung UK	The draft remit makes no comment as to the potential accessibility of depemokimab, nor any comment on the existing access issues with the severe asthma biologics that are currently licensed for use. Asthma + Lung UK hears from thousands of people with lung conditions, including those with asthma and severe asthma. We know that disparate access to essential treatments like biologic therapies compounds healthcare inequalities and drives poor patient outcomes. Access to severe asthma biologics is low nationally, and abysmal in places, with some ICBs having as few as 2% of eligible patients initiated. Those on the lowest incomes are most likely to have poorer outcomes, resulting in part from poorer access to good care. This is in part driven by disparate access to severe asthma centres which perpetuates the postcode lottery that defines respiratory care in the UK. As a result, people with severe asthma may have to travel hours and incur costs to access appointments and essential care which can be remarkably difficult given the condition's severity and impact. We know that asthma's severity is often disregarded and that barriers to accessing care can be ignored; one supporter told us that "people think you look ok. But you're really struggling."	Thank you for your comment. This has been included in the Equality impact assessment.

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	AstraZeneca UK Ltd	N/A	No action required.
	British Thoracic Society	No apparent equality issues identified.	Thank you for your comment. No action required.
	GSK UK Ltd (company)	GSK is not currently aware of any equality issues relating to the proposed remit and scope.	Thank you for your comment. No action required.
	Neonatal and Paediatric Pharmacy Group	Consider CYP or individuals with needle phobia as an alternative treatment to current biologics treatments that are administered fortnightly or monthly.	Thank you for your comment. This has been included in the Equality impact assessment.
	NHS England (Specialised Commissioning)	We do not consider that the draft remit and scope would exclude or impact adversely on any of these groups of people.	Thank you for your comment. No action required.
Other considerations	Asthma + Lung UK	NA	No action required.
	AstraZeneca UK Ltd	N/A	No action required.
	British Thoracic Society	We would welcome the inclusion of specific reference to women of child-bearing potential in view of the prolonged duration of action.	Thank you for your comment. This has been added to the

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			Equality impact assessment.
	GSK UK Ltd (company)	The treatment pathway for patients with severe asthma receiving biologics before depemokimab, has required patients to have had 3+ exacerbations or be on mOCS. No biologic is recommended in patients who experienced 2 exacerbations yearly. In contrast, the SWIFT trials for depemokimab included a large proportion (85%) of patients who had 2 exacerbations and 95% were not on mOCS. [redacted] This marks a significant shift, offering a biologic treatment option for patients with 2 or more exacerbations who are not on mOCS. (ClinicalTrials.gov, 2024; ClinicalTrials.gov, 2024; Jackson et al., 2024)	Thank you for your comment. The committee will assess the technology in line with its marketing authorisation. The company will have the opportunity to justify its positioning in the submission.
	Neonatal and Paediatric Pharmacy Group	Consider healthcare utilisation costs in terms of attendance for injections – and though most will go onto homecare, the first couple of injections are always in hospital for training. Consider the number of homecare deliveries for other biologics, currently only allowed 2 -3 monthly due to wastage and also fridge space, therefore approximately4-6 deliveries per year. A twice yearly medication would only require one delivery cost per year.	Thank you for your comment. The NICE reference case specifies that all costs incurred by the NHS should be included in the cost effectiveness analyses. The company will have the opportunity to justify its considerations of the relevant administration methods and

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			associated costs in its submission.
	NHS England (Specialised Commissioning)	None	No action required.
Questions for consultation	Association of Respiratory Nurses (ARNS)	Will the intervention be used to treat the same population as the comparator(s)? YES	Thank you for your comment. No action required.
	Asthma + Lung UK	***Will the intervention be used to treat the same population as the comparator(s)?*** Depemokimab will be used to treat much the same population as its comparators. Depemokimab is an ultra-long-lasting IL-5-targeting biologic It can be used to treat eosinophilic severe asthma with similar application to current IL-5-targeting biologics mepolizumab, reslizumab, and benralizumab. ***Which treatments are the most relevant comparators for depemokimab? Are there any other relevant comparators that have not been included in the scope?*** The draft scope includes all six biologics currently licensed for treating severe asthma. This is an appropriate set of comparators. ***Which comparators are used in the same place in the treatment pathway as depemokimab? Have there been any major changes to the treatment pathway recently? If so, please describe.***	Thank you for your comment. No action required.

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		All comparators are used in the same place within the treatment pathway as depemokimab would be for adults and children aged 12-17. ***Which treatments are the most relevant comparators for people aged 12-17?*** Tezupelumab, Dupilumab, and Omalizumab as each is licensed for ages 12 and above (with Omalizumab suitable for those aged 6 and over). ***Where do you consider depemokimab will fit into the existing care pathway for severe eosinophilic asthma?*** Depemokimab will fit into the same place as currently licensed biologics for adults and children aged 12-17. To optimise depemokimab's use – and that of all other severe asthma biologics – more must be done to better identify and refer appropriate patients more quickly as per the AAC Consensus Pathway. ***Please select from the following, will depemokimab be:*** *C. Prescribed in secondary care with routine follow-up in secondary care* ***Do you consider that the use of depemokimab results in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?*** The key health-related benefit – beyond condition control – of depemokimab is the reduced or eliminated need for oral corticosteroids (OCS). Reduction of	Further data and information can be provided at the submission stage of the appraisal. The company

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		OCS use is associated with lifetime cost savings that should be reflected in QALY calculations and improved health outcomes.	will have the opportunity to justify its considerations of the outcomes in its submission.
	AstraZeneca UK Ltd	**Q1. Will the intervention be used to treat the same population as the comparator(s)?** Depemokimab is expected to be utilised for treating individuals aligned with the patient profiles from the SWIFT-1 and SWIFT-2 trials, in accordance with its marketing authorisation, specifically for those aged 12 years and older who have severe eosinophilic asthma. Phenotyping plays a crucial role in severe asthma, aiding in the identification of relevant comparators within the evaluated population. As noted above, specifying a cutoff for the subgroup related to "baseline eosinophil levels" would also assist in determining the suitable population for this treatment. **Q2. Which treatments are the most relevant comparators for depemokimab? Are there any other relevant comparators that have not been included in the scope?** AstraZeneca believes the comparator list to be appropriate and exhaustive. The most relevant comparators will depend on the reimbursed population. **Q3. Which comparators are used in the same place in the treatment pathway as depemokimab? Have there been any major changes to the treatment pathway recently? If so, please describe.** The expectation is that the assessment for, and initiation of, depemokimab should be consistent with the current treatment pathway for other, approved,	Thank you for your comment. The company will have the opportunity to justify any exclusion of these subgroups or inclusion of additional subgroups in its submission. Thank you for your comment. No action.

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		severe asthma biologics (initiated under the management of specialists in tertiary care). **Q4. Which treatments are the most relevant comparators for people aged 12-17?** The relevant comparators for people aged 12-17 are listed below and the populations in which they are relevant comparators are provided: 1. tezepelumab: people 12 years and over, who have had 3 or more exacerbations in the previous year, or having maintenance oral corticosteroids 2. omalizumab: severe persistent confirmed allergic IgE-mediated asthma in people 6 years and older, who need continuous or frequent treatment with oral corticosteroids (defined as 4 or more courses in the previous year) 3. dupilumab: people 12 years and over, who have a blood eosinophil count of 150 cells per microlitre or more and fractional exhaled nitric oxide of 25 parts per billion or more and has had at least 4 or more exacerbations in the previous 12 months, and the person is not eligible for mepolizumab, reslizumab or benralizumab, or has asthma that has not responded adequately to these biological therapies. **Q5. Where do you consider depemokimab will fit into the existing care pathway for severe eosinophilic asthma?** Considering the long-acting mechanism of depemokimab that permits dosing every 6 months, there are evidence gaps, and further clarification is required on several aspects:	Thank you for your comment. Further data and information can be

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		• Efficacy o The efficacy for depemokimab, as reported in the SWIFT-1 and SWIFT-2 trials, were similar to those of other IL-5 biologics for severe eosinophilic asthma. However, no statistically significant quality of life benefit was identified compared with placebo, leaving it unclear how the 6-month dosing schedule will affect patients' quality of life over a prolonged period. • Stopping criteria o Biologics for severe asthma have specific stopping criteria based on response (e.g., a minimum of 50% reduction in exacerbations or reduction in oral corticosteroid dose within 6 months); hence, it is expected that similar criteria will be applied to depemokimab. However, due to the 6-month dosing schedule and limited interactions with healthcare providers, it remains unclear how monitoring and implementation of these criteria will take place. • Safety o Due to the 6-month dosing schedule, it is uncertain how any adverse events related to depemokimab will be addressed, as patients will not have regular interactions with their healthcare provider, and the medication will already be administered for a fixed period. • Monitoring o As noted above, there is uncertainty in the monitoring of response, subsequently leading to stopping criteria. o No evidence has been provided for the "run-in" period of depemokimab; therefore, patients should not be transitioned to other biologics without supporting evidence for such a switch. o Management of severe asthma often involves clinicians initiating oral corticosteroid tapering or adjusting inhaled corticosteroid doses; however, it is	provided at the submission stage of the appraisal. The company will have the opportunity to justify its considerations of the outcomes in its submission.

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		unclear how these adjustments will occur given the limited patient interactions. • If/when to switch to Homecare o Typically, severe asthma biologics are initiated in tertiary care, with routine follow-up. Once patients have achieved adequate control of their disease and can be discharged from a specialist's care, patients move on to administering severe asthma biologics at home (Homecare). o However, given the long-acting nature of depemokimab, it is unclear whether: These patients should be initiated onto Homecare. Of note, currently, the majority of severe asthma biologic patients are managed by industry-funded homecare services which free up NHS capacity and have a positive impact on patients' quality of life by providing an "in-home" service which means reduced time and cost of travel to hospital appointments. When would it be appropriate to do so How would they be monitored • Unmet need o There are currently 6 severe asthma biologics available as treatment options in the UK – of which 3 are for severe eosinophilic asthma (mepolizumab, benralizumab and reslizumab). The rationale for bringing depemokimab as an alternative treatment option is not fully clear, given the uncertainty on several implementation aspects, as outlined above and the additional complexity of initiating and monitoring a long-acting intervention. **Q6. Please select from the following, will depemokimab be:**	

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		A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details): As noted in Qn 3, the expectation is that assessment for, and initiation of, depemokimab should be consistent with the current treatment pathway for other, approved, severe asthma biologics (initiated under the management of specialists in tertiary care). **Q7. For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** As noted in Qn 5, typically, severe asthma biologics are initiated in tertiary care, with routine follow-up. Once patients have achieved adequate control of their disease and can be discharged from a specialist's care, patients move on to administering severe asthma biologics at home (Homecare). However, given the long-acting nature of depemokimab, it is unclear whether: • These patients should be initiated onto Homecare • When would it be appropriate to do so • How would they be monitored	

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		Q8. Do you consider that the use of depemokimab result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? A long-acting mechanism of action presents the following limitation that must be considered: if a patient experiences side effects or insufficient efficacy that necessitates discontinuing depemokimab, the cost incurred for the six-month period becomes a sunk cost that cannot be recovered.	Thank you for your comment. No action required
	British Thoracic Society	**Will the intervention be used to treat the same population as the comparator(s)?** Depemokimab targets the same severe asthma patient populations as other biologics (all listed as comparators). The phase IIIa trials SWIFT-1 and SWIFT-2 included people with severe asthma and frequent exacerbations (2 minimum in last 12 months) despite medium-to high-dose inhaled corticosteroids plus additional controller medication – similar to criteria used in RCTs for comparators. There is heterogeneity in the T2 biomarker thresholds on which access to current biologic therapies for severe asthma are based in the UK (for example, blood eosinophils >150 cells/μL for Dupilumab, >300 cells/μL for Mepolizumab, and no blood eosinophil threshold for Tezepelumab), so the intervention will likely be used to treat populations that compare to current anti-IL5/R populations, rather than a wider cohort treated with any biologic agent for severe asthma. **Which treatments are the most relevant comparators for Depemokimab? Are there any other relevant comparators that have not been included in the scope?**	Thank you for your comment.

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		As above, the most relevant comparators are Mepolizumab, Benralizumab and Reslizumab, given the similar target (IL-5 pathway) and clinical profile (severe eosinophilic asthma). We have not identified any omissions. **Which comparators are used in the same place in the treatment pathway as Depemokimab? Have there been any major changes to the treatment pathway recently? If so, please describe.** All listed comparators are used in the same place in the treatment pathway i.e., where a severe asthma patient with evidence of type 2 inflammation remains inadequately controlled despite high-dose inhaled corticosteroid plus an additional controller. Evidence for clinical response to biologic agents at different T2 biomarker thresholds has accumulated since licensing of some comparators, and we would expect the consultation to carefully consider the biomarker criteria for access to Depemokimab. Depemokimab may represent an option to reduce dosing frequency in patients with severe eosinophilic asthma already established on current biologic agents. There is no direct comparator for use in this context. The NIMBLE study, evaluating the safety and efficacy of switching patients from Mepolizumab or Benralizumab to Depemokimab, will provide valuable evidence toward this indication. Which treatments are the most relevant comparators for people aged 12-17? Similar to adults, Mepolizumab is felt to be the most relevant comparator for people aged 12-17. We strongly highlight that in the SWIFT-1/2 trials only 30 of 732 patients completing treatment, were adolescents aged 12–17 years, with just 15 receiving Depemokimab. The reported efficacy and safety findings are based on the assumption that adult trial outcomes can be generalized to adolescents. Many paediatric severe asthma clinicians question this and feel that children and adolescents should not be viewed as ‘little adults’. Unlike	The committee will consider any uncertainties around the clinical data.

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		Depemokimab, biologics such as Dupilumab have robust data from dedicated large paediatric trials. Severe asthma is heterogeneous, and it remains uncertain whether the disease pathophysiology in adolescence mirrors that in adults. **Where do you consider Depemokimab will fit into the existing care pathway for severe eosinophilic asthma?** 1. As a first-line biologic therapy for patients with severe eosinophilic asthma with inadequate response to high dose inhaled corticosteroids and an additional controller. 2. For patients who are established responders to Mepolizumab or Benralizumab, to reduce injection frequency (twice-yearly injections compared to monthly or bi-monthly). 3. Specific populations including those with adherence issues, geographical barriers or needle phobia, on the basis of the less frequent dosing schedule. **Please select from the following, will Depemokimab be:** C. Prescribed in secondary care with routine follow-up in secondary care For both adults and adolescents, Depemokimab will require secondary care prescribing and follow-up, at least in the initial period. For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. Comparators are also prescribed in the specialist severe asthma centre setting. **Would Depemokimab be a candidate for managed access?**	

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		Given that there are already treatment options for this patient population we do not feel that managed access would be necessary, either for adults or adolescents. **Do you consider that the use of Depemokimab result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** For adults, reduced healthcare resource utilisation due a lower frequency of treatments should be considered. This could have an important impact on health inequality. In specific populations such as those unable to adhere to monthly dosing schedules, Depemokimab treatment could reduce the burden of emergency healthcare visits. There is no certainty with regards to adolescents due to the limited evidence base.	Difficulty with adherence has been added to the Equality impact assessment.
	GSK UK Ltd (company)	**1. Question:** Will the intervention be used to treat the same population as the comparator(s)? **1. Response:** Currently, all biologics are recommended for patients with 3+ exacerbations or those on maintenance oral corticosteroids (mOCS) with no biologic recommended in patients with 2 exacerbations who are not on mOCS. In contrast, the vast majority of participants in the depemokimab SWIFT trials experienced 2 exacerbations (85%) and were not on mOCS (95%). Depemokimab will provide a biologic treatment option for people living with severe asthma who experience 2 or more exacerbations per year and are not on mOCS. (ClinicalTrials.gov, 2024; ClinicalTrials.gov, 2024; Jackson et al., 2024)	Thank you for your comments.

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		2. Question: Which treatments are the most relevant comparators for depemokimab? Are there any other relevant comparators that have not been included in the scope? **2. Response:** The appropriate comparators vary across different populations, depending on exacerbations and eosinophil levels. Below, GSK has provided below a clear set of comparators based on clinical trial populations considering the current marketing authorisations, NICE guidance, and clinical practice in the UK. **1.** In patients not on mOCS and with a history of 2 exacerbations a year: • Optimised standard therapy without biologics **2.** In patients with a history of 3+ exacerbations a year: **2.a.** Baseline eosinophil levels 150-300 /µL • Tezepelumab (in addition to optimised standard therapy) (NICE, 2023) • Dupilumab (in addition to optimised standard therapy) (NICE, 2021) **2.b.** Baseline eosinophil levels 300+ /µL • Mepolizumab (in addition to optimised standard therapy) (NICE, 2021) • Benralizumab(in addition to optimised standard therapy) (NICE, 2019) • Tezepelumab (in addition to optimised standard therapy) (NICE, 2023) • Reslizumab (in addition to optimised standard therapy) (NICE, 2017) • Dupilumab (in addition to optimised standard therapy) (NICE, 2021) **3. Question:** Which comparators are used in the same place in the treatment pathway as depemokimab? **3. Response:**	

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		See response from GSK to the previous question. Appropriate comparators depend on the updated current treatment pathway and populations, based on mOCS use and number of yearly exacerbations 2 or 3+, as laid out above. **4. Question:** Have there been any major changes to the treatment pathway recently? If so, please describe. **4. Response:** The 2024 GINA guidelines recommend the use of low dose mOCS only as a last resort, due to their serious cumulative long-term side effects (GINA 2024, Graham et al.2024). The depemokimab SWIFT trial population aligns with this guidance, as the vast majority of the population (95%) was not on mOCS, [redacted] This means patients not on mOCS, with 2+ exacerbations, will have an RCT-based option of a biologic therapy (ClinicalTrials.gov, 2024; ClinicalTrials.gov, 2024). As a result, GSK proposes that the updated treatment pathway in UK clinical practice be sequentially split based on mOCS use and then number of exacerbations (2 or 3+). **5. Question:** Which treatments are the most relevant comparators for people aged 12-17? **5. Response:** In addition to the expected marketing authorisation for Depemokimab, Dupilumab, Omalizumab, and Tezepelumab are the only biologics currently recommended by NICE for this population. The same considerations or appropriateness of comparators depending on the updated current treatment	

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		pathway (with mOCS use or not) and populations (number of yearly exacerbations 2 or 3+) will apply as above for this limited group of licensed comparators in this population. **6. Question:** Where do you consider depemokimab will fit into the existing care pathway for severe eosinophilic asthma? **6. Response:** In people aged 12 years and over with severe asthma characterized by an eosinophilic phenotype with 2+ exacerbations in the previous year and with an eosinophil count of ≥150 /µL **7. Question:** Please select from the following, will depemokimab be: A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details): **7. Response:** C. Prescribed in secondary care with routine follow-up in secondary care **8. Question** For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. **8. Response**	

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		Same as all comparator treatments. Prescribed in secondary care with routine follow-up in secondary care **9. Question:** Would depemokimab be a candidate for managed access? **9. Response:** No, depemokimab is not considered a candidate for managed access. **10. Question:** Do you consider that the use of depemokimab would result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? **10. Response:** GSK believes that the QALY calculation may not fully capture the value of depemokimab as the only long-acting biologic indicated for severe asthma patients with two exacerbations who currently have no access to biologics. Additionally, depemokimab offers the unique advantage of a twice-yearly dosing regimen, which could be particularly beneficial for patients with needle phobia or those who struggle with more frequent injections. This simplified dosing schedule has the potential to enhance treatment adherence and improve the overall patient experience (Loftus et al.2022), benefits that may not be adequately reflected in the QALY calculation. **11. Question** Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. **11. Response**	The company will have the opportunity to justify its considerations of the outcomes in its submission.

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		GSK intends to submit a cost-utility analysis (CUA) for severe asthma patients in line with the updated treatment pathway outlined above. This will include: [redacted] Additionally, GSK intends to submit a cost comparison (CCA) for patients with [redacted] As the only long-acting IL-5 inhibitor, depemokimab is also being evaluated in the ongoing NIMBLE non-inferiority trial (NCT04718389) (ClinicalTrials.gov, 2025). The study aims to assess the impact of switching patients previously treated with mepolizumab or benralizumab on disease control and safety in patients with severe asthma with eosinophilic phenotype.	
	Neonatal and Paediatric Pharmacy Group	In the economic health evaluation, please consider delivery costs and wastage as above	Thank you for your comment. The company will have the opportunity to justify its considerations on all costs at the submission stage of the appraisal.
	NHS England (Specialised Commissioning)	**1. Will the intervention be used to treat the same population as the comparator(s)?** Patients treated with the intervention may also be eligible for treatment with tezepelumab, reslizumab, benralizumab, mepolizumab, dupilumab or	Thank you for your comments. The aim of the comparator section is to

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		omalizumab. However, not all patients who are eligible for treatment with tezepelumab and omalizumab may be eligible for treatment with the intervention. Which treatments are the most relevant comparators for depemokimab? Are there any other relevant comparators that have not been included in the scope? Mepolizumab, benralizumab, maintenance oral corticosteroids. **2. Which comparators are used in the same place in the treatment pathway as depemokimab? Have there been any major changes to the treatment pathway recently? If so, please describe.** All comparators listed are used at the same point of the treatment pathway where depemokimab is expected to be used. **3. Which treatments are the most relevant comparators for people aged 12-17?** All except benralizumab and reslizumab (noting reslizumab not currently available/used). **4. Where do you consider depemokimab will fit into the existing care pathway for severe eosinophilic asthma?** Depemokimab has a unique dosing schedule- 6 monthly. No other currently available biologic offers this. The 6-monthly dosing schedule has many advantages, including fewer injections, fewer home care deliveries, no concern about adherence to biologic, no need to align travel with a monthly	provide an inclusive list of relevant comparators. Further information can be provided at the submission stage of the appraisal.

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		dosing schedule. In these scenarios depemokimab will be the most suitable biologic. **5. Please select from the following, will depemokimab be:** A. Prescribed in primary care with routine follow-up in primary care: NO B. Prescribed in secondary care with routine follow-up in primary care: NO C. Prescribed in secondary care with routine follow-up in secondary care: NO D. Other (please give details): specialist severe asthma clinics in secondary and tertiary care **6. For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** No the setting and follow-up will be the same as the comparators **7. Would depemokimab be a candidate for managed access?** No **8. Do you consider that the use of depemokimab result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Yes. There will be health-related benefits gained for reduced use of oral corticosteroids. These may not all be automatically included in a QALY calculation	The company will have the opportunity to justify its considerations of the outcomes in its submission.

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Additional comments on the draft scope	Association of Respiratory Nurses (ARNS)	Where do you see the follow up of management, treatment and measured outcomes after starting depemokimab to be? (Primary care, community care, secondary care…etc)	Thank you for your question. The company will have the opportunity to justify its considerations on the care pathway at the submission stage of the appraisal.
	Asthma + Lung UK	N/A. The provisional stakeholder list is appropriate and contains many key stakeholders.	Thank you for your comment. No action required.
	AstraZeneca UK Ltd	N/A	No action required.
	British Thoracic Society	None	No action required.
	GSK UK Ltd (company)	NA	
	NHS England (Specialised Commissioning)	No additional comments. The stakeholder list appears comprehensive.	Thank you for your comment. No action required.