National Institute for Health and Care Excellence

Health Technology Evaluation

Mepolizumab for maintenance treatment of uncontrolled chronic obstructive pulmonary disease with raised blood eosinophils ID1237

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	GlaxoSmithKline UK	GSK considers it appropriate for mepolizumab to be referred to NICE for appraisal. A single technology appraisal route is suitable. Subject to the ongoing dupilumab NICE evaluation, a cost-comparison appraisal could be considered.	Thank you for your comments. No action is needed.
	Asthma + Lung UK	Yes, we believe the evaluation route is appropriate.	Thank you for your comment. No action is needed.
	AstraZeneca UK	AstraZeneca consider the proposed evaluation route to be appropriate.	Thank you for your comment. No action is needed.
Wording	GlaxoSmithKline UK	To align with the wording in the MHRA license submission, GSK suggests the wording of the remit is adjusted to the following:	Thank you for your comment, we have amended the wording to " To appraise the

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		"To appraise the clinical and cost effectiveness of mepolizumab within its marketing authorisation for treating patients with chronic obstructive pulmonary disease (COPD) with an eosinophilic phenotype."	clinical and cost effectiveness of mepolizumab within its marketing authorisation for maintenance treatment of chronic obstructive pulmonary disease with raised blood eosinophils (eosinophilic phenotype)."
	Asthma + Lung UK	Yes, the wording is appropriate.	Thank you for your comment. No action is needed.
	Association of Respiratory nurses (ARNS)	Yes [the wording of the remit reflects the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider]	Thank you for your comment. No action is needed.
	AstraZeneca UK	The appropriate patient population for this appraisal are patients with moderate-to-severe chronic obstructive pulmonary disease (COPD), with high exacerbation risk despite being on triple inhaled therapy, that is, a long-acting muscarinic antagonist (LAMA) in combination with a long-acting beta-2 agonist (LABA) and an inhaled corticosteroid (ICS), or on dual inhaled therapy, that is, LABA in combination with a LAMA, if ICS was contraindicated. High exacerbation risk should be defined as exacerbation history of ≥2 moderate or ≥1 severe within the last year, as per MATINEE inclusion criteria. The wording of the remit should reflect the population to be appraised, in line with the pivotal trial MATINEE.	Thank you for your comments, we have amended the wording to "To appraise the clinical and cost effectiveness of mepolizumab within its marketing authorisation for maintenance treatment of chronic obstructive pulmonary disease with raised blood eosinophils (eosinophilic phenotype)."

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		AstraZeneca, therefore, kindly request the wording to be updated accordingly.	Mepolizumab will only be evaluated within its marketing authorisation.
Timing issues	GlaxoSmithKline UK	COPD affects approximately 3 million people in the UK (of which 2 million are undiagnosed), is the second leading cause of emergency admissions and accounts for around 1.4 million GP consultations annually.[1] The management of COPD has been shown to have a substantial impact on NHS resources, with annual direct healthcare costs of COPD in England estimated to increase from £1.5 billion in 2011 to £2.32 billion in 2030.[2] Specifically, the annual direct healthcare costs of moderate and severe COPD exacerbations in England is estimated to increase from £0.6 billion in 2011 to over £1 billion in 2030.[2] In the UK, COPD mortality rate has been estimated at 1,503 per 100,000.[3] Approximately 8% of COPD patients are estimated to die during a hospitalisation caused by an exacerbation, with up to 16% estimated to die within 90 days of a hospitalised exacerbation and 40-50% die within 5 years of a first severe exacerbation.[4,5] In the treatment of acute COPD exacerbations, current treatment options include inhaled bronchodilators, corticosteroids, antibiotics and supportive care such as supplementary oxygen.[6,7] Accessibility of biologic therapies that reduce exacerbation rates is of high urgency to patients and the NHS. 1. Prevalence and incidence, Background information, Chronic obstructive pulmonary disease NICE. Available from: https://cks.nice.org.uk/topics/chronic-obstructive-pulmonary-disease/background-information/prevalence-incidence/	Thank you for your comments. This topic has been scheduled into the work programme and NICE aims to provide timely guidance to the NHS. No action is needed.

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		2. McLean S, Hoogendoorn M, Hoogenveen R. et al. Projecting the COPD population and costs in England and Scotland: 2011 to 2030. Sci Rep 6, 31893 (2016). https://doi.org/10.1038/srep31893 3. Gayle A, Axson E, Bloom C. Mortality rates of COPD Patients in UK Electronic Health Records (Clinical Practice Research Datalink). European Respiratory Journal Vol 52 Issue suppl 62 2012. 4. NHS England. 2014. Overview of potential to reduce lives lost from Chronic Obstructive Pulmonary Disease. [online]. Available from: https://www.england.nhs.uk/wpcontent/uploads/2014/02/rm-fs-6.pdf 5. Suissa S, Dell'Aniello S, Ernst P. Long-term natural history of chronic obstructive pulmonary disease: severe exacerbations and mortality. Thorax 2012;67:957-963. 6. Acute exacerbations, Management, Chronic obstrustive pulmonary disease NICE. Available from: https://cks.nice.org.uk/topics/chronic-obstructive-pulmonary-disease/management/acute-exacerbation/ 7. Acute exacerbation of chronic obstructive pulmonary disease, BMJ best practice. Available from: https://bestpractice.bmj.com/topics/en-gb/3000086/treatment-algorithm#	
	Asthma + Lung UK	This evaluation should be viewed as urgent, due to the huge burden caused by COPD exacerbations on the NHS. COPD exacerbations account for one in eight UK hospital admissions. There is a higher incidence of severe COPD exacerbations during the winter. COPD is estimated to account for 1.8 million annual hospital bed days in the UK, with 620,000 occurring during the winter period. Treatments that are available, namely double or triple inhaler therapy, are often not used effectively, and still leave many patients highly limited by symptoms of cough sputum and breathlessness, as well as acute attacks. This has contributed to the high demands on the NHS in primary care through to emergency care, where these patients often end up, particularly in winter.	Thank you for your comments. This topic has been scheduled into the work programme and NICE aims to provide timely guidance to the NHS. No action is needed.

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		This evaluation may provide a new treatment option to help keep these patients well at home thereby reducing the burden on them and on the health service. In the clinical trial, mepolizumab decreased the annualised frequency by 20% compared to the placebo. Reducing the number of COPD exacerbations will be vital to addressing the annual NHS winter crisis. For this to happen, patients experiencing multiple exacerbations annually must have access to new and effective treatments, such as mepolizumab.	
	Association of Respiratory nurses (ARNS)	Due to rising prevalence, ASAP	Thank you for your comments. This topic has been scheduled into the work programme and NICE aims to provide timely guidance to the NHS. No action is needed.
	AstraZeneca UK	Between 30% and 50% of patients with COPD experience at least one exacerbation per year.[1] Exacerbations increase the risk of patients experiencing severe cardiopulmonary events such as myocardial infarctions and heart failure. These events lead to hospitalisation and premature mortality – thereby placing a significant cost burden on the NHS and reducing the quality of life in these patients. Therefore, optimal treatment to reduce the risk of and prevent exacerbations in patients are of utmost urgency to alleviate the economic burden of COPD on the NHS and improve patient outcomes. 1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8901192/	Thank you for your comments. This topic has been scheduled into the work programme and NICE aims to provide timely guidance to the NHS. No action is needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	GlaxoSmithKline UK	The information in the draft scope with respect to the background, prevalence and treatment of COPD is generally accurate. However, there is a lack of emphasis on the impact exacerbations have on the patient and disease progression. Up to 40% of patients with COPD have a type 2 inflammation as an underlying pathology.[8-10] Type 2 inflammation contributes to a self-perpetuating cycle of exacerbations.[11-13] COPD exacerbations can increase the chance of hospitalisation, increases the risk of mortality, CV events and contributes to disease progression whilst increasing the risk of future exacerbations. As COPD progresses, exacerbations are more likely to occur resulting in poorer health status and an accumulation of tissue damage.[14-18] Recurrent exacerbations results in worsening symptoms and quality of life with increased rates of hospitalisation and ED visits.[13,19] Severe exacerbations are a leading cause of morbidity and mortality for patients with COPD and can occur in clusters with decreasing time between each subsequent exacerbation.[5] Up to 16% of patients with COPD are estimated to die within 90 days of a hospitalised exacerbation and 40-50% of patients with COPD die within 5 years of their first severe exacerbation.[4,5] The prevention of exacerbations is therefore key in the long-term management of COPD as supported by the 2025 GOLD report.[14] We kindly request that the background information is updated to reflect the importance of the prevention of exacerbations on future exacerbations, worsening disease progression, and mortality. 8. Yousuf A, Ibrahim W, Greening NJ, Brightling CE. T2 Biologics for Chronic Obstructive Pulmonary Disease. J Allergy Clin Immunol Pract. 2019 May-Jun;7(5):1405-1416. doi: 10.1016/j.jaip.2019.01.036. PMID: 31076058.	Thank you for your comment. We have updated the background section with information on the relevance of exacerbations in COPD.

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		9. Singh D, Kolsum U, Brightling CE, Locantore N, Agusti A, Tal-Singer R; ECLIPSE investigators. Eosinophilic inflammation in COPD: prevalence and clinical characteristics. Eur Respir J. 2014 Dec;44(6):1697-700. doi: 10.1183/09031936.00162414. Epub 2014 Oct 16. PMID: 25323230. 10. Narendra DK, Hanania NA. Targeting IL-5 in COPD. Int J Chron Obstruct Pulmon Dis. 2019 May 16;14:1045-1051. doi: 10.2147/COPD.S155306. PMID: 31190789; PMCID: PMC6529620. 11. Wedzicha JA, Seemungal TA. COPD exacerbations: defining their cause and prevention. Lancet. 2007 Sep 1;370(9589):786-96. doi: 10.1016/S0140-6736(07)61382-8. PMID: 17765528; PMCID: PMC7134993. 12. Halpin DMG, Decramer M, Celli BR, Mueller A, Metzdorf N, Tashkin DP. Effect of a single exacerbation on decline in lung function in COPD. Respir Med. 2017 Jul;128:85-91. doi: 10.1016/j.rmed.2017.04.013. Epub 2017 Apr 24. PMID: 28610675. 13. Hurst JR, Vestbo J, Anzueto A, Locantore N, Müllerova H, Tal-Singer R, Miller B, Lomas DA, Agusti A, Macnee W, Calverley P, Rennard S, Wouters EF, Wedzicha JA; Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) Investigators. Susceptibility to exacerbation in chronic obstructive pulmonary disease. N Engl J Med. 2010 Sep 16;363(12):1128-38. doi: 10.1056/NEJMoa0909883. PMID: 20843247. 14. GOLD. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2025 report. Available at: https://goldcopd.org/2025-gold-report/ [accessed November 2024]; 15. Miravitlles M, Ribera A. Understanding the impact of symptoms on the burden of COPD. Respir Res. 2017 Apr 21;18(1):67. doi: 10.1186/s12931-017-0548-3. PMID: 28431503; PMCID: PMC5399825. 16. Doneva M, Petrova G, Petrova D, Kamusheva M, Petkova V, Tachkov K, Pencheva V, Georgiev O. Chronic obstructive pulmonary disease exacerbations and progression in relation to ambient air pollutants exposure. J Thorac Dis. 2019 Jun;11(6):2490-2497. doi: 10.21037/jtd.2019.05.50. PMID: 31372286; PMCID: PMC6626810.	

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		17. MacNee W. Pathogenesis of chronic obstructive pulmonary disease. Proc Am Thorac Soc. 2005;2(4):258-66; discussion 290-1. doi: 10.1513/pats.200504-045SR. PMID: 16267346; PMCID: PMC2713323. 18. Qureshi H, Sharafkhaneh A, Hanania NA. Chronic obstructive pulmonary disease exacerbations: latest evidence and clinical implications. Ther Adv Chronic Dis. 2014 Sep;5(5):212-27. doi: 10.1177/2040622314532862. PMID: 25177479; PMCID: PMC4131503.	
	Asthma + Lung UK	We believe that the background information must highlight how there is currently a huge unmet need for COPD patients and that the majority of people living with COPD are not being provided with essential basic care. Asthma + Lung UK's 2024 'Life with a Lung Condition' survey revealed that only 10% of COPD patients in England reported receiving the 5 fundamentals of COPD care (smoking cessation, vaccination, pulmonary rehabilitation, personalised self-management plan, and optimising treatment for co-morbidities). That means 9 out of 10 people with COPD are not receiving the care they need. Only 56% of COPD patients in the annual survey reported being offered smoking cessation support, a critical intervention to stop the progression of the disease. In addition, only 32% of patients reported that they had been offered a course of pulmonary rehabilitation, one of the most cost-effective interventions for COPD. The background information section must also cover the significant health inequalities associated with COPD and how the poorest COPD patients are being left behind. Those from the poorest 10% of households are 4.7 times more likely to die from COPD compared to the 10% most affluent households. While mepolizumab will not overcome all causes of health inequalities, they can encourage the optimisation of the COPD treatment pathway for patients, thereby ensuring everyone receives the basic care they need, and those that need additional treatments, like mepolizumab, can receive them.	Thank you for your comments. The background section is intended to be a brief overview of the disease area. We have noted your comment in the equality impact form (EIA). This will be considered by the committee.

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	Association of Respiratory nurses (ARNS)	Informal I believe the latest number of deaths is 21,000 per year GOV.UK. Office for Health Improvement and Disparities. Official Statistics. INteractive Health Atlas of Lung conditions in England (INHALE). March 2023 update. https://fingertips.phe.org.uk/profile/inhale/data#page/	Thank you for your comment. The latest figure given on that link for 2023 is 26,827, so this has been amended to 'nearly 27,000'.
	AstraZeneca UK	AstraZeneca suggests the following addition to the background information presented within the draft scope: • Expansion on the unmet need, including: o COPD-related morbidity Number of patients continuing to exacerbate despite maximal inhaled therapy (including rescue OCS use)	Thank you for your comment. The background section is intended to be a brief overview of the disease area. Where relevant, stakeholders are welcome to submit evidence or information for the committee's consideration during appraisal. No action is needed.
	Chiesi	Chiesi would like to highlight that the treatment pathway proposed for the management of COPD patients is based upon the NICE guideline NG115, which was last updated in July 2019. Healthcare professionals will now increasingly look to the GOLD report for guidance on the treatment pathway for COPD patients given this is updated on a yearly basis. This now details that ICS+LABA+LAMA (triple therapy) should be used in place of an ICS+LABA should an inhaled corticosteroid be indicated. Further detail should also be provided of the mepolizumab eligible COPD cohort, including specification of Type 2 inflammation characterised by raised blood eosinophil count.	Thank you for your comments. We have updated the background section in light of the comment.

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		It is worth clarifying that as of 2024 data, there are nearly 1.2 million people diagnosed with COPD, not 1.2 million new diagnoses in 2024.	
Population	GlaxoSmithKline UK	The MATINEE trial did not include patients for who ICS was not appropriate. GSK suggests the wording is adjusted to the following: “Adults with COPD with an eosinophilic phenotype who have uncontrolled disease on optimised inhaled therapy.”	Thank you for your comment, we have amended the wording to “Adults with uncontrolled COPD with raised blood eosinophils (eosinophilic phenotype).”
	Asthma + Lung UK	A clinical definition of moderate and severe COPD is included (‘FEV1 less than 79% predicted normal and severe COPD is defined as FEV1 less than 50% predicted normal.’) and is correct. And whilst moderate and severe COPD based on FEV1 is clear, other severity factors from trial population will need to be considered around eligibility – the appropriate threshold level of eosinophil count, breathlessness, quality of life, symptom scores (e.g. CAT score) as well as exacerbation frequency, hospitalisation history and the presence of other medical problems.	Thank you for your comments. Where relevant and appropriate, subgroups may be considered by the committee if evidence allows. No action is needed.
	Association of Respiratory nurses (ARNS)	No - frequency of exacerbation within previous 12 months is too vague	Thank you for your comment. Where relevant and appropriate, subgroups may be considered by the committee if evidence allows. No action is needed.
	AstraZeneca UK	The appropriate patient population for this appraisal are patients with moderate-to-severe chronic obstructive pulmonary disease (COPD), with high	Thank you for your comments, we have

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		exacerbation risk despite being on triple inhaled therapy, that is, a long-acting muscarinic antagonist (LAMA) in combination with a long-acting beta-2 agonist (LABA) and an inhaled corticosteroid (ICS), or on dual inhaled therapy, that is, LABA in combination with a LAMA, if ICS was contraindicated. High exacerbation risk should be defined as exacerbation history of ≥2 moderate or ≥1 severe within the last year, as per MATINEE inclusion criteria. The wording should reflect the population to be appraised, in line with the pivotal trials MATINEE. AstraZeneca, therefore, kindly request the wording to be updated accordingly.	amended the wording to "Adults with uncontrolled COPD with raised blood eosinophils (eosinophilic phenotype)."
	Chiesi	The population should align with that of the trial population from the MATINEE study designed to identify those patients who could benefit most from Mepolizumab: Adults with COPD at least 40 years of age, with a blood eosinophil count of ≥300 cells per microlitre (evidence of Type 2 inflammation), on a background treatment regimen of ICS+LABA+LAMA triple therapy (unless LABA or LAMA contraindicated), with a steroid equivalent dose of at least 500mcg fluticasone propionate or equivalent per day.[1,2] Chiesi also question whether it would be relevant to consider the population eligible for Mepolizumab only after a trial of PDE4 inhibitor given the significant cost and administration differences between PDE4 inhibitors and biologics. [1] Clinicaltrials.gov; NCT04133909	Thank you, we have amended the wording to "Adults with uncontrolled COPD with raised blood eosinophils (eosinophilic phenotype)."

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		[2] GSK press release, Sept 2024: GSK announces positive results from phase III trial of Nucala (mepolizumab) in COPD | GSK	
Subgroups	GlaxoSmithKline UK	The patient population in the MATINEE trial was informed by the preceding METREX and METREO studies. The MATINEE trial has demonstrated mepolizumab's efficacy in reducing exacerbation rates across a broad spectrum of patients reflective of those who would benefit from a biologic therapy in clinical practice, including those with eosinophils greater than or equal to 300 cells per microlitre with and without symptoms of chronic bronchitis, in different stages of COPD disease severity (GOLD 2-4), a wide range of modified Medical Research Council (mMRC) scores (0-4), and experienced at least two or more moderate COPD exacerbations or at least one severe COPD exacerbation in the previous 12 months. Subgroups related to severity of COPD may be considered if the evidence allows, however GSK do not believe that the other subgroups suggested in the scope will be relevant in this appraisal. GSK would like to note that the MATINEE trial recruited patients with and without symptoms of chronic bronchitis. Approximately 32% of patients in MATINEE did not have symptoms of chronic bronchitis at baseline. The inclusion criteria of the BOREAS and NOTUS trials for dupilumab specified a patient-reported history of signs and symptoms of chronic bronchitis (chronic productive cough) for 3 months in the year up to screening in the absence of other known causes of chronic cough. The subgroup of patients in the mepolizumab trials with symptoms of chronic bronchitis at baseline would be an important subgroup to consider in a potential comparison with dupilumab.	Thank you for your comments. Where relevant and appropriate, subgroups may be considered by the committee if evidence allows. The scope has been updated in light of the comment regarding chronic bronchitis.
	Asthma + Lung UK	Patients with comorbidities, and what comorbidities may exclude someone. Patients who still smoke. Patients who exacerbate very frequently and/or have frequent hospitalisations	Thank you for your comments. The list of possible subgroups is not intended to be exhaustive in the scope. Where appropriate and

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			evidence allows, the committee may consider other subgroups. No action is needed.
	Association of Respiratory nurses (ARNS)	What severity of COPD? How many exacerbations to be eligible	Thank you for your comment. Where relevant and appropriate, subgroups may be considered by the committee if evidence allows. No action is needed.
	Chiesi	Chiesi agree with the subgroups suggested. It is particularly important to consider those with type 2 inflammation with a high blood eosinophil count, given it could be expected that mepolizumab would be more clinically and cost-effective here, than in the whole COPD population.	Thank you for your comment. No action is needed.
Comparators	GlaxoSmithKline UK	Roflumilast and azithromycin are not relevant comparators for this appraisal. Clinical experts consulted by GSK as well as the clinical experts in the dupilumab NICE appraisal have confirmed that: • Roflumilast is very rarely used in clinical practice in the UK due to its adverse event profile and tolerability issues. One of the clinical experts at the first dupilumab appraisal committee meeting stated that roflumilast is currently only prescribed for about 37 people in England. • Azithromycin is used in a different population of COPD patients. COPD patients with chronic infections respond to azithromycin as the pathophysiological process is not eosinophilic driven.	Thank you for your comments. We have removed roflumilast and azithromycin from the comparators list.

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		The relevance of dupilumab as a comparator is subject to the ongoing NICE appraisal (ID6235).	
	Asthma + Lung UK	We believe that roflumilast and azithromycin should be excluded from the comparator list. Azithromycin targets bacterial infections and therefore targets different symptoms from mepolizumab. There is very little patient population overlap between azithromycin and mepolizumab. In the NICE 2019 guidelines, azithromycin is only recommended to patients who are non-smokers and experience fewer than 4 exacerbations per year. In addition, azithromycin lacks clinical evidence in patients with uncontrolled and Type 2 COPD inflammation. Clinicians have told us there is also limited overlap between who roflumilast is recommended for and the target population for mepolizumab. Roflumilast has a range of adverse side effects, including diarrhoea, weight loss and depressive mood. Only 5% of eligible patients were prescribed. We have heard from clinicians that only 37 people in England are currently being prescribed roflumilast. Therefore, we believe that it's not appropriate to include roflumilast as a comparator.	Thank you for your comments. We have removed roflumilast and azithromycin from the comparators list.
	Association of Respiratory nurses (ARNS)	Yes [the comparators listed are considered to be the standard treatments currently used in the NHS with which the technology should be compared]	Thank you for your comment. We have removed roflumilast and azithromycin from the comparators list.
	AstraZeneca UK	AstraZeneca consider the comparators to be appropriate and an exhaustive list.	Thank you for your comment. We have removed roflumilast and azithromycin from the comparators list.
	Chiesi	Chiesi agrees that Roflumilast is a relevant comparator. Given the upcoming UK pipeline of PDE4 inhibitors which will be available in an inhaled	Thank you for your comments. We have

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		formulation,[1] and therefore expected to be associated with an improved safety profile – it is important to consider the population eligible for Mepolizumab only after a trial of a PDE4 inhibitor given the significant cost and administration differences between PDE4 inhibitors and biologics. NICE have recently published negative draft guidance for Dupilumab, therefore this would not be considered to be a standard treatment currently used in the NHS.[2] [1] Clinicaltrials.gov; NCT04636801, NCT04636814 [2] NICE draft guidance GID-TA11246	removed roflumilast and azithromycin from the comparators list. Dupilumab is included subject to NICE evaluation, for which final guidance has not yet been published.
Outcomes	GlaxoSmithKline UK	Given the importance of preventing exacerbations in this patient population, GSK would also like to highlight an additional relevant outcome to the scope that has been captured in the MATINEE trial and is of relevance to patients and the NHS: frequency of exacerbations resulting in a hospitalisation and/or emergency department visit. It is important to highlight that biologics are not bronchodilators and primarily impact exacerbations. Lung function is a less relevant outcome for the target population of COPD patients that would be treated with biologics due to mucus impaction that occurs in the disease process. This has been confirmed through consultations with clinicians who have stated that exacerbation frequency is the most relevant outcome to consider when prescribing biologic therapies in COPD. This outcome has been captured over a 104-week time period in the MATINEE trial.	Thank you for your comments. We have updated the outcomes list to include exacerbations leading to hospitalisation.
	Asthma + Lung UK	All listed outcomes are appropriate; however to capture all health related benefits, other outcomes could also be considered: • Frequency of moderate/severe exacerbations should include exacerbations resulting in hospitalisation	Thank you for your comments. We have updated the outcomes list to include

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		• Symptom control should include breathlessness/MRC dyspnoea score • Health related quality of life should include exercise capacity/ability to undertake daily activity • Acceptability of drug in lifestyle (e.g. do patients want to travel to get drug administered by HCP? Are patients happy to self-inject? Are the services delivering this drug accessible and acceptable to patients?) • Impact on comorbidities. • Cumulative oral steroid dose and/or reduction of steroid use must also be listed in outcomes. In the UK, an estimated 44% of COPD patients rely upon long-term OCS use.[i] Patients taking high-dose ICS inhalers are at a higher risk of increased side effects, especially oral candidiasis, dysphonia, pneumonia, and osteoporosis. Long-term ICS use is associated with a 52% increase in the likelihood of developing osteoporosis, so many COPD patients will suffer from bone density loss.[ii] For asthma patients, the Initiation of biologics allows patients to reduce their oral corticosteroids (OCS) use safely. A multinational study published in 2023 found that 92% of patients receiving a biologic treatment were able to safely reduce their OCS use, while six in ten were able to stop all use completely.[iii] We believe a key benefit of mepolizumab is its potential to reduce COPD patients' OCS use and the related side effects and should therefore be considered an outcome.	exacerbations leading to hospitalisation. Other outcomes are covered broadly by the existing categories. NICE scopes do not specify particular scales or instruments to avoid excluding clinical trials that use scales or instruments not specified in the scope.
	Association of Respiratory nurses (ARNS)	should include hospitalisation	Thank you for your comments. We have updated the outcomes list to include exacerbations leading to hospitalisation.

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	AstraZeneca UK	AstraZeneca consider the outcomes to be appropriate.	Thank you for your comment. No action is needed.
	Chiesi	Chiesi agree that the outcomes listed are appropriate to consider.	Thank you for your comment. No action is needed.
Equality	GlaxoSmithKline UK	Individuals from socioeconomically disadvantaged backgrounds with multiple comorbidities are disportionately impacted by COPD and are consequently at higher risk of experiencing exacerbations and hospitalisations.[20,21] Consideration should be given to the impact and importance that a well tolerated and effective treatment in reducing exacerbations will have on these patients and on reducing inequalities. 19. Williams PJ, Cumella A, Philip KEJ, Laverty AA, Hopkinson NS. Smoking and socioeconomic factors linked to acute exacerbations of COPD: analysis from an Asthma + Lung UK survey: BMJ Open Respiratory Research 2022;9:e001290. 20. Westerik JA, Metting EI, van Boven JF, Tiersma W, Kocks JW, Schermer TR. Associations between chronic comorbidity and exacerbation risk in primary care patients with COPD. Respir Res. 2017 Feb 6;18(1):31. doi: 10.1186/s12931-017-0512-2. PMID: 28166777; PMCID: PMC5294875.	Thank you for your comments. We have noted your comment in the equality impact form (EIA). This will be considered by the committee.
	Asthma + Lung UK	It does not appear that this draft remit and scope could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed. By defining eligibility by the need for basic COPD care to have been optimised, access to the drug will depend on this being available. We know that basic care is very poorly delivered in COPD (to less than 20% of patients).	Thank you for your comments. We have noted your comment in the equality impact form (EIA). This will be considered by the committee.

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		This includes the availability of a quality assured spirometry test. Whilst this is essential to diagnose COPD, we know these tests are not available everywhere and are not always performed to the required level of accuracy. Some locations will be unable to provide this test, or have long waiting lists, which will mean delays for certain populations to accessing drug simply due to their postcode. This requirement may also be limiting to those without the physical ability to do a spirometry test. The use of CT scanning is likely to be useful in assessing for comorbidities such as lung cancer and bronchiectasis, but again access to these tests may be a limiting factor in access to the drug as well as the consequences of having a comorbidity that will impact suitability for dupilamab. People from the poorest 10% of households are more than two and a half times more likely to have COPD than someone from the most affluent 10% of households. [iv] Therefore, the committee must consider that mepolizumab has the potential to address health inequalities by improving outcomes and quality of life for COPD patients from the most deprived households.	
Other considerations	GlaxoSmithKline UK	Clinician insights demonstrate the value of the MATINEE data in that it treated patients for up to 104 weeks, thereby enhancing the long-term data and safety profile of mepolizumab. Furthermore, mepolizumab has over 400,000 patient years of exposure globally from launch (Q4 2015) to 2023 across multiple indications, including severe asthma.[22] Mepolizumab has been shown to be well tolerated, with demonstrable patient adherence to the 4-weekly dosing schedule, and an established safety profile across real-world studies and RCTs.[22-30] 21. GlaxoSmithKline. Post marketing mepolizumab exposure data. Data on File; REF-234396	Thank you for your comments. The evidence for mepolizumab in COPD will be considered during the evaluation. No action is needed.

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		22. Electronic Medicines Compendium. 2025. Nucala 100 mg solution for injection in pre- filled pen, Summary of Product Characteristics. [online] Available from: Nucala 100 mg solution for injection in pre-filled pen - Summary of Product Characteristics (SmPC). 23. Pilette C, Canonica GW, Chaudhuri R, Chupp G, Lee FE, Lee JK, Almonacid C, Welte T, Alfonso-Cristancho R, Jakes RW, Maxwell A, Price RG, Howarth P. REALITI-A Study: Real-World Oral Corticosteroid-Sparing Effect of Mepolizumab in Severe Asthma. J Allergy Clin Immunol Pract. 2022 Oct;10(10):2646-2656. doi: 10.1016/j.jaip.2022.05.042. Epub 2022 Jun 24. PMID: 35753668. 24. Khurana S, Brusselle GG, Bel EH, FitzGerald JM, Masoli M, Korn S, Kato M, Albers FC, Bradford ES, Gilson MJ, Price RG, Humbert M. Long-term Safety and Clinical Benefit of Mepolizumab in Patients With the Most Severe Eosinophilic Asthma: The COSMEX Study. Clin Ther. 2019 Oct;41(10):2041-2056.e5. doi: 10.1016/j.clinthera.2019.07.007. Epub 2019 Aug 22. PMID: 31447130. 25. Bel EH, Wenzel SE, Thompson PJ, Prazma CM, Keene ON, Yancey SW, Ortega HG, Pavord ID; SIRIUS Investigators. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. N Engl J Med. 2014 Sep 25;371(13):1189-97. doi: 10.1056/NEJMoa1403291. Epub 2014 Sep 8. PMID: 25199060. 26. Ortega HG, Liu MC, Pavord ID, Brusselle GG, FitzGerald JM, Chetta A, Humbert M, Katz LE, Keene ON, Yancey SW, Chanez P; MENSA Investigators. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med. 2014 Sep 25;371(13):1198-207. doi: 10.1056/NEJMoa1403290. Epub 2014 Sep 8. Erratum in: N Engl J Med. 2015 Apr 30;372(18):1777. doi: 10.1056/NEJMx150017. PMID: 25199059. 27. Navarrete Rouco M, Comella-Anaya L, Carballo N, et al4CPS-271 Adherence to mepolizumab and benralizumab in real clinical practice. European Journal of Hospital Pharmacy 2022;29:A117. 28. Harrison T, Canonica GW, Chupp G, Lee J, Schleich F, Welte T, Valero A, Gemzoe K, Maxwell A, Joksaite S, Yang S, Howarth P, Van Dyke MK. Real-world mepolizumab in the prospective severe asthma REALITI-A study: initial analysis. Eur Respir J. 2020 Oct 15;56(4):2000151. doi: 10.1183/13993003.00151-2020. PMID: 32817259; PMCID: PMC7559868.	

Section	Consultee/ Commentator	Comments [sic]	Action
		29. Han JK, Bachert C, Fokkens W, Desrosiers M, Wagenmann M, Lee SE, Smith SG, Martin N, Mayer B, Yancey SW, Sousa AR, Chan R, Hopkins C; SYNAPSE study investigators. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Respir Med. 2021 Oct;9(10):1141-1153. doi: 10.1016/S2213-2600(21)00097-7. Epub 2021 Apr 16. PMID: 33872587.	
	Chiesi	Consideration should be given to the method of administration of Mepolizumab (sub-cutaneous injection) and regular monitoring required compared to the other comparators listed, including those in development, and the challenges this may pose for patient use.	Thank you for your comments. Costs associated with method of administration will be captured in the economic modelling during this evaluation. If the model does not capture the quality of life impact associated with the method of administration, this may be considered as an uncaptured benefit. No action is needed.
Questions for consultation	GlaxoSmithKline UK	The pathway for administering biologic therapies to COPD patients in the UK is currently uncertain. It is anticipated that initially, mepolizumab in addition to other biologic therapies would be prescribed in secondary care with routine follow-up in secondary care. Routine follow-up may move to primary care once pathways and services are more established.	Thank you for your comments. No action is needed.
	Asthma + Lung UK	Where do you consider mepolizumab will fit into the existing care pathway for COPD?	Thank you for your comments. No action is needed.

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		We need some understanding of the volume of patients who may qualify for assessment for mepolizumab – this will require a pathway that covers primary care identification and referral, an assessment in secondary or tertiary care, and mechanism for drug initiation/delivery. Secondary care is appropriate, but capacity must be considered as mepolizumab (and other drugs like it) will need an increase in workload and therefore resource. It is essential that the pathway for accessing [mepolizumab] is not limited by only being available via tertiary care – as we have seen in the delivery of severe asthma biologics, this can create long delays between referral and drug initiation due to tertiary centre capacity, and geographical disparities in patients being able to access these centres.	
	AstraZeneca UK	**Please note AstraZeneca has only provided responses to questions for consultation here, where responses are not already captured in above sections.** **Is the intervention in the draft scope appropriate?** AstraZeneca would request updating the wording to “Mepolizumab as an add-on to triple inhaled therapy or dual therapy where ICS is not appropriate” **Where do you consider mepolizumab will fit into the existing care pathway for COPD?** Mepolizumab is likely to be an add-on to maintenance treatment, i.e. triple therapy or dual therapy if ICS is contra-indicated. **Do you consider that the use of mepolizumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** N/A	Thank you for your comments, we have amended the intervention wording to “Mepolizumab as an add-on to maintenance treatment.”

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		Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. N/A	
	Chiesi	Where do you consider mepolizumab will fit into the existing care pathway for COPD? It is estimated that 60 – 80% of COPD patients do not present with evidence of Type 2 inflammation and the MATINEE study population for Mepolizumab is limited to patients with Type 2 inflammation.[1] In contrast, PDE4 inhibitors are not restricted to use in the Type 2 inflammation cohort. As such, under the current care pathway, Roflumilast (an oral PDE4 inhibitor) can be used in combination with ICS/LABA/LAMA (for people who had 2 or more exacerbations in the previous 12 months despite triple inhaled therapy). There is also an upcoming UK pipeline of inhaled PDE4 inhibitors for which ongoing phase III studies support their positioning as an add-on to triple therapy for exacerbating patients.[2, 3] These products will be available in an inhaled formulation, and therefore expected to be associated with an improved safety profile. We therefore propose that exacerbating patients on triple therapy should receive PDE4 inhibitors as an add-on treatment prior to Mepolizumab initiation due to the more complex method of administration (sub-cutaneous injection vs inhaled/oral route), likely higher cost and the anticipated need to involve secondary and tertiary care specialists in at least the first prescription of biologic agents, for Mepolizumab compared with PDE4 inhibitors.	Thank you for your comments. The committee will review all available evidence for mepolizumab. Stakeholders are welcome to present any evidence or information related to the intervention during the appraisal. No action is needed.

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		[1] MATINEE study, NCT04133909 Study Details | Mepolizumab as Add-on Treatment IN Participants With COPD Characterized by Frequent Exacerbations and Eosinophil Level | ClinicalTrials.gov [2] PILLAR study, NCT04636814 Study Details | A 52-week, Placebo- and Active- Controlled (Roflumilast, Daliresp® 500µg) Study to Evaluate the Efficacy and Safety of Two Doses of CHF6001 DPI (Tanimilast) as add-on to Maintenance Triple Therapy in Subjects With COPD and Chronic Bronchitis. (PILLAR) | ClinicalTrials.gov [3] PILASTER study, NCT04636801 Study Details | A 52-week, Placebo-controlled Study to Evaluate the Efficacy and Safety of 2 Doses of CHF6001 DPI (Tanimilast), as add-on to Maintenance Triple Therapy in Subjects With COPD and Chronic Bronchitis (PILASTER) | ClinicalTrials.gov Please select from the following, will mepolizumab 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): C. To ensure appropriate prescription of Mepolizumab in relevant COPD patients, prescribing should be initiated by experts experienced in treating COPD in secondary care, with routine follow-up required for monitoring of response and safety/adverse reactions also conducted by secondary care experts.	
Additional comments on the draft scope	GlaxoSmithKline UK	[no comment]	No action is needed.
	Asthma + Lung UK	Any additional comments on the draft scope Patient identification must also be considered (e.g. tool like SPECTRA): there will be a significant number of incorrectly diagnosed patients i.e. not COPD or have been diagnosed with inadequate spirometry who will need a full work up	Thank you for your comments. Where relevant and appropriate, identification and

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		by specialist care, however it is now unusual to do monitoring spirometry on COPD patients. This should be considered alongside the many thousands of people who could qualify for dupilumab and would need referring. This is a significant cost for the NHS, both from a systems and drug cost perspective, even before new clinics are created and staffed and including new capacity for spirometry. These patients will also need following up by specialist clinics. Lessons to be learned from severe asthma biologics (See Consensus pathway for managing uncontrolled asthma in adults)	diagnosis of COPD in the NHS may be considered by the committee. Stakeholders are welcome to present any evidence or information related to the intervention during the appraisal. No action is needed.
	Association of Respiratory nurses (ARNS)	Is there enough date to undertake an accurate QALY calculation	Thank you for your comment. The quality and quantity of available data to undertake a robust cost effectiveness analysis will be considered as part of the evaluation. No action is needed.

[i] Price D, et al, 'Disease burden for patients with COPD receiving maintenance therapy, Journal of Respiratory Critical Care, (201:53), 2022. Accessed here.
[ii] Janson, C., Lisspers K., *et al, Osteoporosis and fracture risk associated with inhaled corticosteroid use among Swedish COPD patients: the ARCTIC study* European Respiratory Journal (2021).Accessed here
[iiiiii] Jackson, D., Heaney, L., Humbert, M. et al, "*Reduction of Daily maintenance inhaled corticosteroids in patients with severe asthma treated with benralizumab*." The Lancet. 2023; 304:271-281.

[iv] *British Lung Foundation. 2021. Failing on the fundamentals: Insights from those living with chronic obstructive pulmonary disease (COPD) around the UK. British Lung Foundation. Accessed here (October 2022). PP. 14-15.*