National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Tezepelumab for treating severe asthma

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Wording	AstraZeneca	Yes this wording accurately reflects the clinical and cost effectiveness issues surrounding this product	Comment noted. No changes to the scope are needed.
	Novartis Pharmaceuticals UK	Yes the wording reflects the remit.	Comment noted. No changes to the scope are needed.
	British Thoracic Society	Yes	Comment noted. No changes to the scope are needed.
	Asthma UK and British Lung Foundation	Yes	Comment noted. No changes to the scope are needed.

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Timing Issues	AstraZeneca	We consider this appraisal to be urgent as Tezepelumab will allow patients who are currently not eligible for treatment with a biologic access to this innovative medicine.	Comment noted. NICE aims to provide draft guidance to the NHS within 6 months from the date when marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action needed.
	Novartis Pharmaceuticals UK	No comments.	-
	British Thoracic Society	Despite the availability and use of other advanced treatments for asthma (omalizumab, mepolizumab, reslizumab and benralizumab), some patients with severe asthma continue to experience exacerbations, which can be severe and life-threatening. Therefore, there is a clinical need for additional treatment options, for this group of patients.	Comment noted. NICE aims to provide draft guidance to the NHS within 6 months from the date when marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action needed.

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	Asthma UK and British Lung Foundation	Severe asthma is the most debilitating and life-threatening form of asthma, which is expected to impact around 200,000 people in the UK. Currently, around 60,000 people with severe asthma are eligible for existing biologic treatments, which leaves 140,000 people with no other option that to bounce in and out of hospital or take toxic oral steroids, which have nasty side effects including mood swings, diabetes and osteoporosis. People with severe asthma are also at increased risk of serious illness and death from COVID-19. Getting people onto the right treatments, such as biologics, may help reduce this risk. The importance of starting people on biologic treatments to protect them from COVID-19 is reiterated in the NICE rapid guideline.	Comment noted. NICE aims to provide draft guidance to the NHS within 6 months from the date when marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	AstraZeneca	There are some points to address below.	Comment noted. No changes to the scope are needed.
	Novartis Pharmaceuticals UK	No comments.	-
	British Thoracic Society	The information presented is accurate. However, it would be helpful to include that despite the availability of biologic therapies, many patients continue to experience asthma exacerbations associated with considerable morbidity. A recent publication from the UK Severe Asthma Registry (Jackson et al Thorax 2020) showed that about a third of patients did not fulfil criteria to receive any	Thank you for your comments. The background section is intended to provide a brief summary of the condition. More details

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		of the currently available biologics, indicating that there is a clinical need for treatments for this group of patients.	on the disease and its complications will be discussed during the appraisal. No action needed.
	Asthma UK and British Lung Foundation	It is accurate; however, it could further stress the impact that having to take oral steroids can have on people with asthma. People with severe asthma can become caught in a vicious cycle of emergency trips to hospital, intensive care, and regular doses of strong oral corticosteroids (OCS) tablets or injections. These tablets can stop the symptoms, but they have devastating side effects on physical and mental health, from kidney and bone damage to insomnia and suicidal thoughts. [references not included – please see the consultation response]	Thank you for your comments. The background section is intended to provide a brief summary of the condition. More details on the disease and its complications will be discussed during the appraisal. No action needed.
The technology/ intervention	AstraZeneca	This is accurate	Comment noted. No changes to the scope are needed.
	Novartis Pharmaceuticals UK	No comments.	-
	British Thoracic Society	Yes	Comment noted. No changes to the scope are needed.

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	Asthma UK and British Lung Foundation	Yes, biologics must still be taken with standard preventative therapy	Comment noted. No changes to the scope are needed.
Population	AstraZeneca	It is anticipated that the marketing authorization will have an age limit of people 12 years or older	Comment noted, the population definition was updated accordingly.
	Novartis Pharmaceuticals UK	Based on the population from the pivotal trial NAVIGATOR, tezepelumab is expected for use in adult and adolescents with severe uncontrolled asthma. This should be clearly stated in the population.	Comment noted, the population definition was updated to specify people 12 years or older.
	British Thoracic Society	Yes Patients with blood eosinophil count ≥0.3 x10^9/L and patients with blood eosinophil count ≤0.3 x10^9/L	Comment noted. No changes to the scope are needed. Please note, the population definition was updated to specify people 12 years or older.

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	Asthma UK and British Lung Foundation	Current biologics are only effective in Type 2 (T2) asthma. This type of asthma is driven by inflammation of the airways linked to eosinophils. However, there is an unmet need for those with non-T2 asthma. This type of asthma is driven by other, sometimes poorly understood mechanisms, and characterised in some cases by neutrophilic airway inflammation or paucigranulocytic airway inflammation (normal levels of both eosinophils and neutrophils). Non-T2 asthma is, broadly, more common in patients with adult onset asthma, in particular women and in asthma driven by obesity, air pollution, smoking and viral or bacterial infections. Because of the mechanistic pathway Tezepelumab targets it may also be an effective treatment for non-T2 asthma. We know that severe asthma disproportionately affects women and that they have a higher rate of asthma attacks and hospital admissions. However, the reasons for this are still largely unknown and this population has so far not been considered independently in terms of both research and treatment. It is pertinent that we start to better understand and treat severe asthma in women. The government has recently launched a call for evidence for the Women's Health Strategy, highlighting that now is the time to start considering the impact and treatment of severe asthma on women. [references not included – please see the consultation response]	Comments noted. No changes to the scope are needed. Please note, the population definition was updated to specify people 12 years or older. For completeness, we have added your comment that that severe asthma disproportionately affects women to the EIA from.
Comparators	AstraZeneca	The comparators are appropriate. Optimised standard therapy for patients not eligible for biologics would consist of high dose ICS/LABA ± OCS. This is reflected in the key regulatory trial for Tezepelumab (NAVIGATOR) as patients in both treatment arms received background treatment of medium-high dose ICS-LABA ± OCS± controller	Comments noted. No changes to the scope are needed.

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	Novartis Pharmaceuticals UK	The listed comparators are all currently used to treat severe asthma. There are several distinct pathological endotypes within severe asthma including allergic and non-allergic eosinophilic asthma. A monoclonal antibody against thymic stromal lymphopoietin (TLSP) is likely to work by inhibition of the TSLP enzyme which is involved in the non-allergic eosinophilic inflammatory pathway. (Papi et al, *Lancet* 2018; 391: 783–800) Mepolizumab, Benralizumab and reslizumab are therefore the most likely relevant comparators.	Comments noted. No changes to the scope are needed.
	British Thoracic Society	Yes	Comment noted. No changes to the scope are needed.
	Asthma UK and British Lung Foundation	Yes, our understanding is that bronchial thermoplasty is rarely used in practice and so is not a relevant comparator. It should also be noted that just because someone is eligible for current biologics it does not mean that they will work for them.	Comments noted. No changes to the scope are needed.
Outcomes	AstraZeneca	Yes. The outcomes are appropriate; and will capture the most important benefits and harms of the technology.	Comments noted. No changes to the scope are needed.
	Novartis Pharmaceuticals UK	The most important outcome measures in severe asthma, which are often used as the primary endpoint in trials, are exacerbation rate and forced expiratory volume in 1 second (FEV1), i.e. lung function. Asthma control and quality of life measures are also important measures that capture health benefits. The outcomes listed in the draft scope are relevant to capturing the most important health related benefits of the technology.	Comments noted. No changes to the scope are needed.

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	British Thoracic Society	Yes	Comment noted. No changes to the scope are needed.
	Asthma UK and British Lung Foundation	Yes. Our research has shown quality of life to be the most important outcome to people with severe asthma. [references not included – please see the consultation response]	Comments noted. No changes to the scope are needed.
Economic analysis	AstraZeneca	The time horizon for the economic analysis will be a lifetime perspective.	Comment noted. No changes to the scope are needed.
	Novartis Pharmaceuticals UK	No comments.	-
	Asthma UK and British Lung Foundation	We agree that the time horizon should be sufficiently long enough to reflect differences in costs and outcomes and in particular the long-term consequences of taking oral steroids. It has been shown that *four or more* courses of oral steroids in a year is associated with significantly greater odds of a person developing osteoporosis, hypertension, obesity, type 2 diabetes, gastrointestinal ulcers/bleeds, fractures, and cataracts. In fact, one study has shown that cumulative exposures, equivalent to just four courses of oral steroids over a lifetime, are associated with adverse outcomes. Therefore, the side effects of courses of steroids over someone's lifetime need to be adequately represented within the economic analysis. [references not included – please see the consultation response]	Comments noted. No changes to the scope are needed.
Equality and Diversity	AstraZeneca	No equality matters are identified.	Comment noted. No changes to the scope are needed.

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	Novartis Pharmaceuticals UK	No comments.	-
	British Thoracic Society	No	Comment noted. No changes to the scope are needed.
	Asthma UK and British Lung Foundation	No	Comment noted. No changes to the scope are needed.
Other considerations	AstraZeneca	None	Comment noted. No changes to the scope are needed. Please note, the scope was updated to include subgroups by baseline fractional exhaled nitric oxide levels.

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	Novartis Pharmaceuticals UK	Novartis agree that if the evidence allows, the following subgroups should be considered: • baseline eosinophil levels • Baseline fractional exhaled nitric oxide (FenO) levels • people who require maintenance oral corticosteroid treatment • people who require frequent oral corticosteroid treatment.	Comment noted. The scope was updated accordingly.
Innovation	AstraZeneca	Yes. Tezepelumab is innovative; and represents a step-change in its potential to make a significant impact on health-related benefits for asthma patients who are not currently eligible for treatment with biologics. Tezepelumab works by blocking TLSP which is activated earlier in the inflammatory pathway than eosinophils or allergic markers and therefore Tezepelumab works on a wider population than agents which block eosinophils directly.	Comments noted. No changes to the scope are needed.
	Novartis Pharmaceuticals UK	No comments.	-
	British Thoracic Society	Yes, the technology is innovative in its potential to make a significant and substantial impact Yes the technology has the potential to result in significant and substantial health-related benefits that may not necessarily be included in the QALY calculation	Comments noted. No changes to the scope are needed.

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	Asthma UK and British Lung Foundation	Yes, Tezepelumab targets a different mechanistic pathway to existing biologic treatments for severe asthma. It has the potential to treat the non-T2 population that currently have no other safe alternative and may work for those who have not been successful on current biologics. Our report 'Asthma still kills' outlines the unmet need for people with non-T2 asthma. [references not included – please see the consultation response]	Comments noted. No changes to the scope are needed.
Questions for consultation	AstraZeneca	Where do you consider tezepelumab will fit into the existing NICE pathway, asthma? Tezepelumab will fit into the existing NICE asthma pathway within the 'difficult or severe asthma' patient category under the 'asthma management' section. It will fit into the treatment algorithm alongside other biologics but also in patients who currently do not have access to biologics.	Comment noted. No changes to the scope are needed.
	Novartis Pharmaceuticals UK	**Which treatments are considered to be established clinical practice in the NHS for treating severe asthma that is inadequately controlled by standard therapy?** The therapies listed in the draft scope are considered established clinical practice. **Have all relevant comparators for tezepelumab been included in the scope? In particular:** • **Is omalizumab a relevant comparator?** Please see Comparators section above. Omalizumab is recommended in patients with severe **allergic** asthma. As omalizumab was not considered a relevant comparator in the appraisal of benralizumab (TA565), it is not expected to be seen as a relevant comparator for tezepelumab. **Are the outcomes listed appropriate?** The listed outcomes are appropriate.	Comments noted. Tezepelumab is a treatment for severe asthma including allergic asthma so no changes to list of comparators were made. The scope has been amended to include subgroups by baseline fractional exhaled nitric oxide levels, if evidence allows.

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		Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom tezepelumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? In addition to the subgroups listed, fractional exhaled nitric oxide (FeNO) levels should also be examined as it is plausible that outcomes would differ based on this factor. **Where do you consider tezepelumab will fit into the existing NICE pathway, asthma?** Please see comparator section above. Tezepelumab is likely to be included in the treatment pathway at a similar place to treatments for severe asthma. **Do you consider that the use of tezepelumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?** It is not believed that tezepelumab will result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation.	
	British Thoracic Society	**Questions for consultation** Which treatments are considered to be established clinical practice in the NHS for treating severe asthma that is inadequately controlled by standard therapy? Have all relevant comparators for tezepelumab been included in the scope? In particular:	Comments noted. The scope has been amended to include subgroups by baseline fractional exhaled nitric

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		• Is omalizumab a relevant comparator? All currently available biologics are being used as comparators and therefore omalizumab should be included • Is bronchial thermoplasty a relevant comparator? No Which other treatments for severe asthma will tezepelumab be used in combination with? Inhaled steroids, long-acting beta-2 agonists, LAMAs, theophyllines, macrolide therapy, oral steroids Are the outcomes listed appropriate? Yes Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom tezepelumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? It is more clinically effective in patients with raised FeNO and blood eosinophils Where do you consider tezepelumab will fit into the existing NICE pathway, asthma? Advanced therapies (alongside the other asthma biologics) NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope: • could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which tezepelumab will be licensed; No • could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by	oxide levels, if evidence allows.

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		making it more difficult in practice for a specific group to access the technology; No • could have any adverse impact on people with a particular disability or disabilities. No Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts. Do you consider tezepelumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? Do you consider that the use of tezepelumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits. To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly. No barriers to adoption as severe asthma centres have set up biologics pathways and this will fit alongside the other biologics. A minor barrier may be if it cannot be self-administered at home and most patients self-administer their own biologic. NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of	

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		appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction). NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made. • Would it be appropriate to use the cost comparison methodology for this topic? • Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators? Yes • Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant? Yes • Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year? SOURCE trial (steroid sparing effect of Tezepelumab): due publication soon [references not included – please see the consultation response]	

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	Asthma UK and British Lung Foundation	To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly. Yes, Asthma UK's research has shown that only 18% of people with suspected severe asthma are referred according the British Thoracic society's guidelines. Currently, there are no NICE guidelines for severe asthma or criteria for when someone should be referred. Our analysis has also shown that 3/4 of people eligible for current biologics are still missing out. The Accelerated Access Collaborative's rapid uptake programme is going someway to help improve this, however we still urgently need NICE guidelines for severe asthma so health care professionals are aware of the services and treatment available and know when to refer.	

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

- Sanofi
- Teva