National Institute for Health and Care Excellence

Single Technology Appraisal

Zilucoplan for treating antibody positive generalised myasthenia gravis [ID4008]

Response to stakeholder organisation comments on the draft remit and draft scope

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 and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	UCB Pharma (manufacturer)	We believe that this topic is suitable for evaluation by NICE and that the Single Technology Appraisal is the most appropriate route for the evaluation of zilucoplan.	Thank you for your comment. No changes to the draft scope required
	Muscular Dystrophy UK	It is timely and appropriate for this topic to be evaluated by NICE.	Thank you for your comment. No changes to the draft scope required
	Myaware	This evaluation is welcomed and the evaluation route is appropriate from the perspective of a patient group.	Thank you for your comment. No changes to the draft scope required

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Wording	UCB Pharma (manufacturer)	The wording of the remit is appropriate.	Thank you for your comment. No changes to the draft scope required
	Muscular Dystrophy UK	The wording is appropriate.	Thank you for your comment. No changes to the draft scope required
	Myaware	Yes [wording is appropriate]	Thank you for your comment. No changes to the draft scope required
Timing Issues	UCB Pharma (manufacturer)	A UK marketing authorisation for zilucoplan is anticipated [redacted]. As such, the evaluation will need to start promptly in order for NICE to issue timely guidance at or close to the expected marketing authorisation and launch date.	Thank you for your comment. NICE aims to publish guidance within 6 months of marketing authorisation. This topic will be scheduled into the technology appraisals program.
	Muscular Dystrophy UK	There is an urgency to this evaluation, to ensure that Zilucoplan can be accessed by patients as close to the date of marketing authorisation as possible.	Thank you for your comment. NICE aims to publish guidance within 6 months of marketing authorisation. This topic will be scheduled into

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			the technology appraisals program
	Myaware	The urgency is relative to any other rare disease, particularly where there has not been a great deal of development in therapeutic options. New treatments are welcomed, and myasthenia is not a disease where 'one size fits all', so diversity in medication options is greatly welcomed and encouraged.	Thank you for your comment. NICE aims to publish guidance within 6 months of marketing authorisation. This topic will be scheduled into the technology appraisals program

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	UCB Pharma (manufacturer)	The background section provides a largely accurate description of mild generalised myasthenia gravis (gMG) and myasthenic crises. However, a significant proportion of people with gMG are classified as having moderate to severe disease on a chronic basis and we believe it is important to reflect the full spectrum of the patient population in the scope. gMG presents heterogeneously with patients experiencing a variety of symptoms that fluctuate in both severity and frequency. It is estimated that the vast majority of people with gMG are being treated with corticosteroids on a chronic or long-term basis. Nevertheless, a significant proportion of patients with chronic, moderate-severe gMG do not achieve satisfactory disease control despite current standard of care and are considered treatment-resistant.	Thank you for your comment. The background section is intended to give a brief overview of the condition and current treatment options. The committee will consider the appropriate treatment pathway for this evaluation. No changes to the draft scope required.

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		Moreover, there is no mention of exacerbations that might require rescue medication, for example, people experiencing frequent and significant relapses, or people who continue to demonstrate active disease despite maximal treatment with standard of care options (Farrugia ME and Goodfellow JA (2020) A Practical Approach to Managing Patients With Myasthenia Gravis—Opinions and a Review of the Literature. Front. Neurol. 11:604. doi: 10.3389/fneur.2020.00604). Although not routinely commissioned other than for acute exacerbations or crises, there is evidence that some IVIg/PLEx is used to treat people with gMG on a chronic basis in the NHS in England. (NHS England (2021) Commissioning Criteria Policy for the use of therapeutic immunoglobulin (Ig) England, 2021). Accordingly, there is a need for additional treatment options that can meet the wide spectrum of needs of people with chronic moderate to severe gMG and lessen the steroid burden.	
	Genetic Alliance UK	People living with myasthenia gravis often have multiple medications to take in order to manage their condition. It is important to acknowledge that a complex treatment regime can be burdensome, difficult to adhere to and may impact daily activities and therefore quality of life.	Thank you for your comment. The background section is intended to give a brief overview of the condition and current treatment options. The committee will consider the appropriate treatment pathway for this evaluation. No changes to the draft scope required.

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	Muscular Dystrophy UK	The information is accurate.	Thank you for your comment. No changes to the draft scope required.
	Myaware	The background is accurate, but could also mention LRP4 antibodies which are present in around 2% of MG cases. (Lazaridis and Tzartos (2020), Front. Immunol)	Thank you for your comment. The pivotal trial for zilucoplan included the requirement of “Positive serology for acetylcholine receptor (AChR) autoantibodies”. Therefore, no changes to the draft scope required.
Population	UCB Pharma (manufacturer)	NICE should appraise zilucoplan in line with the anticipated population description in the marketing authorisation.	Thank you for your comment. NICE will appraise zilucoplan within its marketing authorisation.
	Muscular Dystrophy UK	The population is defined appropriately.	Thank you for your comment. No changes to the draft scope required.
	Myaware	The population is defined appropriately.	Thank you for your comment. No changes

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			to the draft scope required.
Subgroups	UCB Pharma (manufacturer)	We are not aware of any relevant sub-groups at this time.	Thank you for your comments. NICE will assess results for any relevant subgroups.
	Muscular Dystrophy UK	The population are defined appropriately. We do not feel that any groups should be considered separately.	Thank you for your comments. NICE will assess results for any relevant subgroups.
Comparators	UCB Pharma (manufacturer)	We believe that all relevant comparators have been included in the draft scope.	Thank you for your comment. No changes to the draft scope required.
	Genetic Alliance UK	The comparators stated in the draft scope may not be fair comparators as they are both subject to a NICE evaluation and are therefore currently not widely available to patients in the UK. We have been informed by the patient organisation Myaware that these treatments are being accessed by a small number of patients via an Early Access to Medicine Scheme (EAMS). It is also important to note that having multiple treatment options for the same condition improves patient care and outcomes. Our current understanding as to why some people respond better to some medications than others is still developing therefore having multiple options means that patients can find the best treatment option for them.	Thank you for your comments. The comparators in the NICE scope include those which are current standard of care or may be recommended by NICE during evaluations which are ongoing. No changes to the draft scope required.

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	Muscular Dystrophy UK	It is important to consider whether this treatment should be used in addition to the current standards of care rather than a replacement. It would provide additional clarity to reiterate this within the scope.	Thank you for your comment. The committee will consider any evidence presented on the use of the technology within the treatment pathway. No changes to the draft scope required.
	Myaware	Two of the listed comparitors (Efgartigimod and Ravulizumab) are currently undergoing NICE appraisals. Myaware is aware these medications have been made available on EAMS and wonder whether there are plans for Zilucoplan to apply for this scheme as well. This would ensure fair access in comparison to the three treatments.	Thank you for your comments. The comparators in the NICE scope include those which are current standard of care or may be recommended by NICE during evaluations which are ongoing. No changes to the draft scope required.
	Alexion Pharma UK	We do not consider it appropriate that efgartigimod and ravulizumab have been included as comparators in the draft scope. As laid out in the NICE Methods Manual, the scope aims to identify “all relevant comparators that are established practice in the NHS.” As neither efgartigimod nor ravulizumab is used in the NHS for the treatment of patients with gMG, we do not consider either product to be an appropriate comparator in this appraisal.	Thank you for your comments. The comparators in the NICE scope include those which are current standard of care or may be recommended by

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		While both products are currently subject to ongoing NICE appraisals, there is no certainty that either will be reimbursed for use in the NHS. Given currently published appraisal timelines, should NICE recommend reimbursement for either product, the earliest they would be available would be late 2023.	NICE during evaluations which are ongoing. No changes to the draft scope required.
Outcomes	UCB Pharma (manufacturer)	The outcomes listed are appropriate and broadly align with the final scopes for other NICE technology appraisals in this therapy area. We would suggest adding “time to clinically meaningful improvement” as an outcome. This aligns with the final scope for the efgartigimod evaluation (Efgartigimod for treating generalised myasthenia gravis. NICE technology appraisal [ID4003]).	Thank you for your comment. The outcomes section in the draft scope is not exhaustive and the committee can consider outcome data provided. The scope has been updated to include “time to clinically meaningful improvement” has been added to the outcome section in the scope.
	Muscular Dystrophy UK	Yes, ensuring that the mental health aspects within the health-related quality of life (for patients) outcomes are explicitly reviewed. The physical, psychological and financial benefits of this treatment to carers/families of people living with MG should be considered in the appraisal. Changes in burden of treatment regime if Zilucoplan is intended to replace current standard treatments for MG.	Thank you for your comment. No changes to the draft scope required.

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	Myaware	Myaware understands Zilucoplan has the potential to reduce steroid intake. It would be an ideal benefit for MG patients if this became an achievable outcome.	Thank you for your comment. The committee will consider the evidence presented on steroid use. No changes to the draft scope required.
Equality	UCB Pharma (manufacturer)	We do not believe that the wording of the draft remit or scope need adjusting to address NICE's equality aims.	Thank you for your comment. No changes to the draft scope required.
	Muscular Dystrophy UK	It is important to ensure that no patient has to travel excessive distances to receive the treatment given the level of disability that many will face.	Thank you for your comment. The committee will consider all relevant equality issues. No changes to the draft scope required.
	Myaware	We are aware that there is an evident 'postcode lottery' when it comes to being given the chance to take part in early access schemes, such as EAMS. As mentioned before, if Zilucoplan looks to emulate the pathway of its comparators, it is most likely that those who live in areas where there is a centre for excellence of myasthenia research that they will be given the chance of early access. It would be good to see other areas given this chance, so more people with myasthenia could benefit.	Thank you for your comment. The committee will consider all relevant equality issues. No changes to the draft scope required.

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Questions for consultation	UCB Pharma (manufacturer)	**1. Is the population defined appropriately?** NICE should appraise zilucoplan in line with the anticipated population description in the marketing authorisation. At the present time, it is anticipated that zilucoplan will be indicated in Europe and the UK [redacted]. **2. Would zilucoplan be used as an add-on to the current NHS standard care for generalised myasthenia gravis?** [redacted]. **3. Where do you consider zilucoplan will fit into the existing care pathway for antibody-positive generalised myasthenia gravis?** We anticipate that zilucoplan will be used [redacted]. **4. Have all relevant comparators for zilucoplan been included in the scope?** As noted above, we believe that all relevant comparators for zilucoplan have been included in the scope.	Thank you for your comments. NICE will appraise zilucoplan within its marketing authorisation. The committee will consider the appropriateness of the EQ-5D and will assess any evidence provided on this matter. Please see relevant responses above to other comments.

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		5. **Are there any subgroups of people in whom zilucoplan is expected to be more clinically effective and cost effective or other groups that should be examined separately? For example, those based on Myasthenia Gravis Foundation of America (MGFA) Class?** **We are not aware of any such sub-groups at this point in time.** 6. **Are the outcomes listed appropriate?** The outcomes listed are appropriate and broadly align with the final scopes for other NICE technology appraisals in this therapy area. **We would suggest adding "time to clinically meaningful improvement" as an outcome. This aligns with the final draft scope for the efgartigimod evaluation (Efgartigimod for treating generalised myasthenia gravis. NICE technology appraisal [ID4003]).** **7. Would zilucoplan be a candidate for managed access?** At this point, we do not anticipate that zilucoplan will be a candidate for managed access. **8. Do you consider that the use of zilucoplan can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Generalised myasthenia gravis is a rare condition and collecting robust quality of life data and patient-reported outcomes can be challenging. Secondly, EQ-5D is a generic, rather than condition-specific, measure of health-related quality of life. As such, not all HRQoL aspects of gMG may be fully captured by EQ-5D, for example, the ocular improvements associated with treatment.	

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		For these reasons, it is anticipated that a QALY calculation based on EQ-5D data may not capture all the health-related benefits of zilucoplan treatment specific to patients and carers living with this rare condition. In addition, the positive impact of a sub-cutaneous administration option on patient burden/patient preference; and carer utilities/health-related quality of life are unlikely to be captured in the QALY calculation. **9. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** We are in the process of identifying appropriate data sources. 10. **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 zilucoplan will be licensed;** • **could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;** • **could have any adverse impact on people with a particular disability or disabilities.**	

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		We do not believe that the wording of the draft remit or scope need adjusting to address NICE's equality aims. 11. **Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.** **Not applicable.** **12. NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process.** We agree that this technology is appropriate for evaluation through the NICE Single Technology Appraisal process**.**	
	Muscular Dystrophy UK	We recommend that the following questions are also addressed: Do you consider that the use of Zilucoplan can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? Do you consider that there will be any barriers to adoption of this technology into practice?	Thank you for the comment. The committee will consider all relevant evidence. No changes to the draft scope required.

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

Argenx