National Institute for Health and Care Excellence

Single Technology Appraisal

Rozanolixizumab for treating antibody positive generalised myasthenia gravis [ID5092]

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 rozanolixizumab. Rozanolixizumab may be a suitable candidate for the proportionate approach, but this will be dependent on the outcome of other ongoing NICE HTAs for generalised myasthenia gravis (gMG).	Thank you for your comment. At the current time there is no technology appraisal guidance for treatments for myasthenia gravis. No changes to the draft scope required.
	Association of British Neurologists (ABN)	STA is overall appropriate for this drug.	Thank you for your comment. No changes to the draft scope required

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	Myaware	This evaluation is appropriate based on target population and route of assessment.	Thank you for your comment. No changes to the draft scope required
Wording	UCB Pharma (manufacturer)	The wording of the remit is appropriate. Specifically, rozanolixizumab is expected to be indicated for the treatment of [redacted]	Thank you for your comment. No changes to the draft scope required
	Association of British Neurologists (ABN)	Yes; it is reasonable. Lacks detail / figures on the impact of the drug on reduction of need and use of other immunosuppressive drugs including: • Cumulative steroid dose and side effects • IVIG (expensive and limited resource) • PLEX (difficulty with access, potential complicaitons, expensive and onerous manpower and infrastructure) Also objective impact on the hospital admissions and their consequences; importantly also on the impact on QOL of patients and NHS services. The potential for subcutaneous self delivery of this medication at home may have meaningful impact on QoL in some patients previously reliant of frequency admissions for maintenance therapy. The introduction would benefit from a sentence on the 10-20% of MG patients who remain refractory (ongoing disabling symptoms) despite optimal immunosuppression. And also the high risk status of a myasthenic crisis, the risk of death from bulbar and respiratory weakness, the risk associated with	Thank you for your comment. The committee will consider any relevant impacts on the treatment pathway in the evaluation. Health-related quality of life will be considered in the analysis. The committee will also consider any relevant subgroups if evidence allows. The scope has been updated to state that there will be some people who have ongoing disabling symptoms despite

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		prolonged supportive care in the ITU setting. Highlighting the potential impact of a more effective, molecule specific therapy in these settings.	optimal immunosuppression. No changes to the draft scope required.
	Myaware	It does, and it would be interesting to see a thorough review of the economic benefit of subcutaneous administration compared to intravenous	Thank you for your comment. No changes to the draft scope required
Timing Issues	UCB Pharma (manufacturer)	A European marketing authorisation for rozanolixizumab is anticipated in [redacted]. The date for UK approval is currently unknown but would normally be expected in or around [redacted] assuming timelines for the new MHRA international recognition framework are aligned with the target dates stated in the EC Decision Reliance Procedure (67 days following EC CHMP opinion). There are currently no other treatments licensed specifically for the treatment of MuSK antibody-positive gMG and thus there is a high unmet need for treatment options for this patient population. As such, the evaluation will need to start promptly in order for NICE to issue timely guidance at or close to the expected UK 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 programme.
	Association of British Neurologists (ABN)	Non-urgent, though should be timely.	Thank you for your comment. NICE aims to publish guidance within 6 months of marketing

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			authorisation. This topic will be scheduled into the technology appraisals program
	Myaware	There is relative urgency to the NHS because treatments for myasthenia gravis are sincerely lacking in diversity. This is especially true when considering treatments that do not produce significant side effects or perform poorly when controlling symptoms. In addition, there are few treatments that selectively target autoantibodies against muscle-specific tyrosine kinase (MuSK).	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
Other comments	Association of British Neurologists (ABN)	Any additional comments on the draft remit 1) considering how this drug, and other potential new MG drugs will be used (e.g. add on or single, chronic or as induction) and how they could be integrated in the current therapeutic algorithms for Ab positive MG in near future, 2) allowing the use of the drug by experts, under an appropriate scheme, to gain real world experience in clinical practice, important to enhance the experience gained through clinical trials, and possibly identifying extra benefits or even risks. 3) encouraging the pharma / sponsors to provide detailed information about non-responders in the trials (info usually not very clear in the main publications)	Thank you for your comments. The committee will consider the treatment pathway for MG. The committee will assess the clinical evidence provided. No changes to the draft scope required.

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 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. MG 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. 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. 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). There is an unmet need based on currently available treatment strategies. Traditional non-steroidal immunosuppressant therapies (all of which are unlicensed for gMG) may be slow to achieve maximum effect, are not always effective and may be associated with significant side effects. Licensed treatments for MG are either due to be appraised by NICE or are not currently recommend. Their place in the treatment pathway is yet to be determined but	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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		may be most likely used in the refractory setting. None of them are licensed for MuSK antibody-positive disease. Accordingly, there is a need for additional treatment options that can meet the wide spectrum of needs of people with chronic moderate to severe [redacted] and lessen the burden of corticosteroids.	
	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. How treatments are administered, for example intravenously or subcutaneously, may also contribute to the complexity and overall burden of treatment therefore should be taken into consideration when comparing treatments.	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.
	Association of British Neurologists (ABN)	Overall seems accurate.	Thank you for your comment. No changes to the draft scope required.

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	Myaware	This background information is accurate and forms a reasonable picture of myasthenia gravis. There could be mention of those who produce autoantibodies for LRP-4, however.	
Population	UCB Pharma (manufacturer)	NICE should appraise rozanolixizumab in line with the anticipated population description in the marketing authorisation.	Thank you for your comment. NICE will appraise rozanolixizumab within its marketing authorisation.
	Association of British Neurologists (ABN)	Yes; reiterate seropositive MG (Abs against AChR or MuSK).	Thank you for your comment. No changes to the draft scope required.
	Myaware	Yes [Is appropriate].	Thank you for your comment. No changes to the draft scope required.
Subgroups	UCB Pharma (manufacturer)	NICE should appraise rozanolixizumab in line with the anticipated population description in the marketing authorisation.	Thank you for your comments. NICE will assess results for any relevant subgroups.
	Myaware	The two subgroups, adults with autoantibodies for the AChR and MuSK are appropriate. Treatments targeting these could prove to be cost effective as they could alleviate the need for broader, less effective medications that can be clinically detrimental with time.	Thank you for your comments. NICE will assess results for any

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			relevant subgroups if the evidence allows.
	Association of British Neurologists (ABN)	Indications (Current +considerations): 1. Patients who do not respond to standard immunosuppression, or have serious side effects or complications, or do not tolerate it. 2. Severe disease at the onset, or those that at any stage are severely affected (e.g. in ITU, +/- ventilated), with indication for PLEX or IVIg, but unavailable or contraindicated or at risks. Rozanolixizumab is likely to benefit these patients (rapid onset mechanism of action), simple delivery (SC) and therefore accessible and may have favourable risk profile to IVIg or PLEX in some individuals. 3. Patients who require frequent hospital admissions and /or regular or frequent acute rescue therapy (IVIG or PLEX).	Thank you for your comments. The subgroup of adults with severe myasthenia gravis needing intravenous immunoglobulin or plasma exchange has been added to the scope. The committee will consider the relevant subgroups if evidence allows. No changes to the draft scope required.
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	Two of the comparators stated in the draft scope are described as 'subject to a NICE ongoing appraisal', therefore they are not widely available. As far as we understand, the definition of a comparator is a technology that is routinely used in the NHS, therefore we have concerns that these comparators appear to be outside of the usual definition of a comparator.	Thank you for your comments. The comparators in the NICE scope include those which are current

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		We understand that there may be circumstances that are appropriate to use technologies that are currently being assessed by NICE as a comparator but we would appreciate an overview of how decisions about expanding the definition of a comparator are made, and a discussion with the patient community as to the potential risks and benefits of using comparators outside of the definition and when it may be appropriate to do so. Otherwise, we fear this may lead to an inconsistency and inequality between appraisals. 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.	standard of care or may be recommended by NICE during the evaluation of the technology being scoped. Typically when considering whether to include a comparator subject to NICE evaluation it would need to be plausible that a recommendation for the comparator technology could made at least 3 months ahead of the first committee meeting for the scoped technology.
	Association of British Neurologists (ABN)	Comparators listed included (standard immunosuppression, efgartigimod (subject to NICE evaluation), ravulizumab (subject to NICE evaluation) are correct. However, others need to be added: - Zilucoplan (subject to NICE evaluation) - Rituximab (or its biosimilar) should be mentioned as not yet seen as a standard immunosuppression); it is under a commissioning policy (NHSE) - Even if included in standard immunosuppression, IVIG and PLEX deserve a separate note as comparators (particular value based on cost savings with these two particular interventions)	Thank you for your comments. Zilucoplan was added to list of comparators (subject to NICE evaluation). Rituximab was explicitly added to the description of standard of care

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		- With long-term effect, I consider including thymectomy as comparator (impact on steroid dependence)	without rozanolixizumab. A potential subgroup of people with severe myasthenia gravis needing intravenous immunoglobulin has been added to the scope.
	Myaware	Yes [appropriate].	Thank you for your comments. 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. 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.	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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Outcomes	UCB Pharma (manufacturer)	The outcomes listed are appropriate and broadly align with the post-referral scopes for other NICE technology appraisals in this therapy area.	Thank you for your comment. No changes to the draft scope required.
	Genetic Alliance UK	Clarity on how 'time to clinically meaningful improvement' will be measured would be appreciated.	Thank you for your comment. No changes to the draft scope required.
	Myaware	The outcomes listed are appropriate. It will be interesting to see how clinically meaningful improvement will be measured compared to improvement in myasthenia gravis.	Thank you for your comment. The committee will consider the evidence presented on steroid use. No changes to the draft scope required.
	Association of British Neurologists (ABN)	They are appropriate but vague and incomplete. 1. More myasthenia specific outcome measures • QMG and MGADL scores as specific measures of disease severity; • MGFA-PIS as measure of post intervention status (good summary of level of improvement) 2. Steroid sparing effects, specifically the steroid dose reduction, and subsequent reduction in steroid side effects.	Thank you for your comments. The outcomes listed in the draft scope are not exhaustive and the committee will assess all evidence presented. It is anticipated that the specific measure for each outcome will be determined during the

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		3. Reduction in the use of IVIG / PLEX • Reduction in IVIg spend • Reduction in PLEX exchanges(including staffing costs) • Reduction in hospital days • Reduction in complications 4. Reduction ITU length of stay, duration of ventilatory support 5. Reduction / independence of SSA 6. Ability to go back to the education / school &university, reduce dependency from family or carers, do sports, work productively, have children, have other health problems resolved (able to have non-urgent operations done). 7. Mortality may be measured, but this is usually caused by multiple factors. This could be considered, however, in a familiar scenario – elderly patients with severe MG (crises) where an admission to ITU/ventilation can sometimes be problematic; (decision making based on age, severity of the condition and multiple morbidities and potential to survive). Using this drug in this acute situation, could make a great difference, including avoiding ITU or, if still needed, being easily taken to ITU and having higher chance of quicker recovery, reducing death as well.	appraisal. No changes to the draft scope required.

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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	In principle, there are no equality concerns. However, if such drugs are going to be approved, there must be a straightforward way for all eligible patients who might benefit to access the treatments. Therefore, the neurology community, as well others who see possibly more severe MG patients – e.g. respiratory, infectious diseases - should be fully informed of the indication and accessibility to the drug. The role of patient associations in disseminating accurate information to patients will be vital to improve accessibility and equality. If to be delivered via expert centres, these will need to be geographically distributed with equity and also require appropriate supporting resources (human and financial): • to facilitate prompt access to review • for appropriate screening/ monitoring (clinical response, other outcome measures and complications) • Education and training • Out of hospital (clinical nurse specialist) support – especially if home delivered regular maintenance use	Thank you for your comment. The committee will consider all relevant equality issues. No changes to the draft scope required.

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	Myaware	There is a concern that there are geographic inequalities in access to clinical trials or new therapeutics. It would be good to see this considered and a framework introduced to try and overcome this during the scope.	Thank you for your comment. The committee will consider all relevant equality issues. No changes to the draft scope required.
Questions for consultation	UCB Pharma (manufacturer)	**1. Is the population defined appropriately?** NICE should appraise rozanolixizumab in line with the anticipated population description in the marketing authorisation. At the present time, it is anticipated that rozanolixizumab will be indicated in Europe and the UK [redacted]. **2. Would rozanolixizumab be used as an add-on to the current NHS standard care for generalised myasthenia gravis? If so, which treatments would rozanolixumab be added on to?** [redacted].	Thank you for your comments. NICE will appraise rozanolixizumab 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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		[redacted] **3. Where do you consider rozanolixizumab will fit into the existing care pathway for antibody-positive generalised myasthenia gravis?** We anticipate that rozanolixizumab will be used [redacted]. [redacted] **4. Would rozanolixizumab be used after a corticosteroid if it has not worked well enough?** Yes, it could be considered if the patient required additional therapy, or treatment escalation due to worsening symptoms. **5. Would rozanolixizumab be used after azathioprine if it has not worked well enough?** Yes, it could be considered if the patient required additional therapy, or treatment escalation due to worsening symptoms.	

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		6. Would rozanolixizumab be used after alternative immunosuppressants (including mycophenolate mofetil, methotrexate, ciclosporin and rituximab) have not worked well enough? Yes, it could be considered if the patient required additional therapy, or treatment escalation due to worsening symptoms. **7. Are there any subgroups of people in whom rozanolixizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?** • **For example, people with mild, moderate or severe weakness of muscles other than the eye based on Myasthenia Gravis Foundation of America (MGFA) Class?** • **For example, people with autoantibodies against acetylcholine receptor (AChR) or autoantibodies against muscle-specific kinase (MuSK)?** UCB is not aware of any subgroups that should be considered separately. **8. Would rozanolixizumab be a candidate for managed access?** At this point in time, we do not anticipate that rozanolixizumab will be a candidate for managed access. **9. Do you consider that the use of rozanolixizumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Yes. Generalised myasthenia gravis is a rare condition and collecting robust quality of life data and patient-reported outcomes can be challenging.	

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		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 are fully captured by EQ-5D, for example, the ocular improvements associated with treatment, or some mental health aspects associated with gMG. For these reasons, it is anticipated that a QALY calculation based on EQ-5D data may not capture all the health-related benefits of rozanolixizumab treatment specific to patients and carers living with this rare condition. In addition, the expected impact of rozanolixizumab treatment on steroid use/sparing; IVIg-sparing and the potential opportunity to free up IVIg resources for other conditions; the 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. **10. 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. 11. **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.** We do not believe that the wording of the draft remit or scope need adjusting to address NICE's equality aims. However, the typographical error in this consultation question ('zilucoplan' instead of 'rozanolixizumab') should be corrected prior to publication on the NICE website.	

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		12. Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts. Not applicable. 13. **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 believe that the Single Technology Appraisal is the most appropriate route for the evaluation of rozanolixizumab. Rozanolixizumab may be a suitable candidate for the proportionate approach, but this will be dependent on the outcome of other ongoing NICE HTAs for generalised myasthenia gravis(gMG).	

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

Argenx
Novartis