National Institute for Health and Care Excellence

Health Technology Evaluation

Efgartigimod for treating generalised myasthenia gravis ID4003

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	Argenx	We consider this an appropriate topic for NICE evaluation via the Single Technology Appraisal (STA). There is an unmet need for effective targeted treatment options for generalised myasthenia gravis (gMG) and timely appraisal by NICE will be key to ensuring that patients are able to access efgartigimod as soon as possible.	Comment noted. No action needed.
	Muscular Dystrophy UK	It is timely and appropriate for this topic to be evaluated by NICE.	Comment noted. No action needed.
Wording	Argenx	The wording of the proposed remit should be revised to reflect the currently anticipated licensed indication which is expected to be treatment of gMG in the acetylcholine receptor antibody positive population (AChR-Ab seropositive population) as add-on therapy.	Comment noted. Following discussion at the scoping workshop, the remit has not been updated and remains "to appraise the clinical and cost effectiveness

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			of efgartigimod within its marketing authorisation for treating generalised myasthenia gravis".
	Muscular Dystrophy UK	The wording is appropriate	Comment noted. No action needed.
Timing Issues	Argenx	There are currently no treatment options recommended by NICE for gMG, a condition which causes causing debilitating and potentially life-threatening muscle weakness.1 Current treatment relies on medicines that are mostly unlicensed, can take a long time to become effective, and are associated with long-term side-effects and tolerability issues.1 There is an urgent unmet need for targeted therapy for gMG which has demonstrated clinical and cost-effectiveness. Reference 1. NIHRIO Health Technology Briefing [13458] Efgartigimod for treating generalised myasthenia gravis. Sept 2021	Comment noted. No action needed.
	Muscular Dystrophy UK	There is an urgency to this evaluation, to ensure that Efgartigimod can be accessed by patients as close to the date of marketing authorisation as possible.	Comment noted. No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Argenx	We would recommend including within the background information that around 80% people with myasthenia will progress to generalised myasthenia gravis (gMG) within two years.1 Reference 1. NIHRIO Health Technology Briefing [13458] Efgartigimod for treating generalised myasthenia gravis. Sept 2021)	Comment noted. The background section of the scope has been updated to reflect this.
	Genetic Alliance UK	We have been informed by our members, Muscular Dystrophy UK, that Efgartigimod is seen to be an additional treatment to standard of care treatment for generalised myasthenia gravis, not a replacement for standard of care treatment.	Comment noted. No action needed.
	Muscular Dystrophy UK	This is accurate.	Comment noted. No action needed.
Population	Argenx	The population should be revised to reflect the currently anticipated licensed indication: treatment of gMG in the AChR-Ab seropositive population as add-on therapy.	Comment noted. Following discussion at the scoping workshop, the population has not been updated and remains as adults with generalised myasthenia gravis.
Subgroups	Argenx	No suggested subgroups	Comment noted. No action needed.
	Muscular Dystrophy UK	The population are defined appropriately. We do not feel that any groups should be considered separately.	Comment noted. No action needed.

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Comparators	Argenx	Yes, we consider the comparators listed in the scope to be the standard treatments currently used in the NHS. We do not consider eculizumab to be a relevant comparator. Eculizumab has not been appraised by NICE and consequently does not have a NICE recommendation for use in gMG. While licensed for use in a subset of people with refractory gMG in patients who are anti-acetylcholine receptor (AChR) antibody-positive, it is not routinely used and hence does not form part of standard treatment in the NHS. In addition, the licensed indication for eculizumab is restricted to a population in later subsection of the treatment pathway (i.e. refractory patients) as compared to the population that included in efgartigimod study.	Comment noted. Following discussions at the scoping workshop, eculizumab has not been included as a comparator and has been removed from the stakeholder matrix.
	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.	Comment noted. No action needed.
Outcomes	Argenx	The outcomes listed are broadly appropriate. However, we consider that to best capture health benefits an additional outcome measure considering time to clinically meaningful improvement would be beneficial. In the pivotal study, QMG was a key secondary outcome and we would suggest that this should also be included. We do not consider hospitalisation an appropriate outcome measure as this is likely to be ill-defined and may reflect varied aspects of the condition – for example hospitalisation could be for life-threatening myasthenic crisis or for symptom control which is less severe. For these reasons hospitalisation data were not collected within the efgartigimod clinical trials. Mortality data are not available, as data on mortality were not collected in the clinical trial programme.	Comment noted. Following discussions at the scoping workshop, the outcome measures have been updated to include improvement in myasthenia gravis and time to clinically meaningful improvement. Mortality and hospitalisations remain as relevant outcomes.

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	Muscular Dystrophy UK	Yes, ensuring that the mental health aspects within the health-related quality of life (for patients and carers) outcomes are explicitly reviewed.	Comment noted. No action needed.
Equality	Argenx	Not applicable	Comment noted. No action needed.
	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.	Comment noted. No action needed.
Other considerations	Muscular Dystrophy UK	We recommend that the following questions are also addressed: Do you consider that the use of Efgartigimod 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?	Comment noted. No action needed.
Questions for consultation	Argenx	<u>Place in the existing treatment pathway</u> We anticipate that efgartigimod will provide an additional treatment option for patients diagnosed with MG who have symptoms of generalised muscle weakness consistent with Myasthenia Gravis Foundation of America (MGFA) class II or more and who are AChR antibody positive as an add-on to standard therapy. In the absence of a UK-specific classification system the MGFA system is well-recognised.	Comment noted. No action needed.

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		Efgartigimod is not expected to be used to treat the emergency situation of myasthenic crisis (MGFA class V) <u>Innovative potential</u> There are currently no NICE recommended products for gMG. As previously described, current treatment options are aimed at symptom control, generally take a significant time to work and are associated with long-term side-effects and significant tolerability issues. Despite current therapies, many patients with gMG continue to be affected by substantial disease burden, and experience symptoms and morbidities that negatively impact their quality of life. Approximately 90% of patients with gMG are unable to maintain normal muscle strength without medication.[1,2] Furthermore, 10% to 15% of patients are refractory to available treatments.[3,4] There is a significant unmet need for effective targeted therapies for people with gMG. Efgartigimod is a first in class antibody fragment specifically developed to target the underlying mechanism of gMG by blocking FcRn (a protein in cells which helps prevent IgG breakdown). By binding to FcRn at the same site as endogenous IgG and thereby blocking its action, efgartigimod allows IgGs (including the pathogenic autoantibodies causing the disruption to normal nerve and muscle function) to be broken down and more quickly removed from the body. It is a reduced size compared to full-length antibodies to facilitate smaller dosing volumes and increased tissue penetration. Efgartigimod therefore represents an innovative and targeted approach to addressing the unmet need in gMG and if licensed and recommended for use could offer the NHS a step change in treatment options for gMG. <u>Health-related benefits</u>	Comment noted. No action needed.

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		We consider that the main health-related benefits are likely to be included within the QALY calculation. <u>Barriers to adoption</u> We do not anticipate any barriers to adoption of this technology. The diagnosis and treatment of gMG are well-established and treatment with efgartigimod will not require changes to the existing NHS treatment pathway or services. References 1. Grob D, Brunner N, Namba T, Pagala M. Lifetime course of myasthenia gravis. Muscle Nerve. 2008;37(2):141-149. 2. Sanders DB, Wolfe G, Benatar M, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology. 2016;87(4):419-425 3. Silvestri NJ, Wolfe GI. Treatment-refractory myasthenia gravis. J Clin Neuromuscul Dis. 2014;15(4):167-178. 4. Suh J, Goldstein JM, Nowak RJ. Clinical characteristics of refractory myasthenia gravis patients. Yale J Biol Med. 2013;86(2):255-260	Comment noted. No action needed. Comment noted. No action needed.
Additional comments on the draft scope	CSL Behring	Request that 'CSL Behring UK (plasma exchange)' is changed to 'CSL Behring UK (human immunoglobulin, plasma exchange	Comment noted. The stakeholder matrix has been updated to reflect this.

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

CSL Behring UK