National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Eculizumab for treating refractory myasthenia gravis

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
Appropriateness	Alexion	Evaluation of eculizumab for anti- acetylcholine receptor (AChR) antibody positive refractory generalised myasthenia gravis (gMG) is appropriate under the highly specialised technologies (HST) programme, not the Standard Technology Appraisal (STA) programme. See Alexion response below for why eculizumab for this indication fulfils each of the seven HST prioritisation criteria.	The topic's suitability for HST was fully considered as part of the scoping process, however it did not meet all of the HST criteria. In summary: • The target population is not distinct for clinical reasons. • The condition is managed in a large number of centres and is not delivered

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			as a highly specialised service. • The population is uncertain and may be larger than that normally considered for HST. For more detail please refer to the Batch Scoping report on the Institute's website. The Department of Health has referred this topic for appraisal through the single technical appraisal process.
	Association of British Neurologists	It is reasonable for the company to seek NICE approval for normal commercial reasons. However, I am being asked to offer an assessment without access to the company's data and before any publication of the study results. Clinicians always wish to understand patient selection and the details of the results, and the definitions of statistical and clinical significance in determining the meaning of a clinical study. The translation of a finding to normal clinical practice is limited.	Comments noted. The aim of this consultation exercise is to scope the topic, rather than trying to establish the clinical and cost-effectiveness of the technology. The scoping process sets the framework for the appraisal, for example defines the population and the relevant comparators in this

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			population. It is not normal to review the clinical data for the technology during scoping. Not action required.
Wording	Alexion	As previously noted to NICE, regulatory submission to the European Medicines Agency (EMA) for eculizumab in this indication [redacted] However [redacted] the wording of the draft remit should be revised to read "To appraise the clinical and cost effectiveness of eculizumab within its marketing authorisation for treating anti-AChR antibody positive refractory generalised myasthenia gravis", which is a significantly more limited target patient population than that described in the draft remit. To more accurately describe the background of the disease of the target patient population, generalised myasthenia gravis is defined as muscle weakness or symptoms that progress to bulbar muscles (facial, chewing, swallowing, respiratory and neck) or limb muscles. Generalised MG is not defined by the number of muscle groups. In other words, when muscle groups other than ocular muscles are affected, the condition is known as generalised myasthenia gravis (gMG). Also, as noted above, evaluation of eculizumab is appropriate under the HST programme, not the STA programme.	Comments noted. The remit is broad (that is, does not specify 'anti-AChR antibody positive' disease) because the marketing authorisation (MA) is unknown at this time. The appraisal committee will appraise the technology within its MA only. If the MA specifies anti-AChR antibody positive disease, the committee can make recommendations for only this group. No changes to the remit have been made. The definition of generalised myasthenia gravis in the background section of the scope has been amended. Please refer

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			to the response to your earlier comment about HST.
	Association of British Neurologists	The wording is appropriate	Comments noted. No action required.
Timing Issues	Alexion	Evaluation for eculizumab in this indication is appropriate under the HST pathway and not the STA pathway. [redacted] initiating the scoping and appraisal process at this time is premature.	Please refer to the response to your earlier comment about HST.
	Association of British Neurologists	non-urgent. Full consideration is required [see below].	Comments noted. No action required.
Additional comments on the draft remit	Alexion	Alexion has completed the Consultee and Commentator comment form and provided other information to NICE as requested. This should not, however, be construed as any acceptance on the part of Alexion that a technology appraisal of eculizumab for refractory gMG is fair or reasonable in the context of NICE's defined procedures. We strongly believe that eculizumab, in this proposed ultra-orphan indication, should only be considered in accordance with the HST procedure; it is our firm view that eculizumab is wholly unsuitable for the standard technology appraisal. Our reasons for this view are set out below.	Please refer to the response to your earlier comment about HST.

Comment 2: the draft scope

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Background information	Alexion	The draft remit and background information misconstrues the target patient population for eculizumab in this indication, which is in fact the very small portion of generalised myasthenia gravis (gMG) patients who are anti-AChR antibody positive and refractory to standard treatment for MG.	The background section is intended to provide a brief summary of the disease, on a broad level, to provide context for the positioning of the technology in the pathway. The epidemiology data are not intended to reflect the population for whom eculizumab will be considered. The population in which eculizumab will be appraised is specified in the population section of the scope and will ultimately be determined by the final marketing authorisation for eculizumab. Please also refer to the response to your earlier comment about the remit wording. No action required.

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	Association of British Neurologists	superficial; doesn't address the patient group that Eculizumab is intended to help- ie the treatment resistant population- clinical characteristics	The background section is intended to provide a brief summary of the disease, on a broad level, to provide context for the positioning of the technology in the pathway. The epidemiology data are not intended to reflect the population for whom eculizumab will be considered. The population in which eculizumab will be appraised is specified in the population section of the scope and will ultimately be determined by the final marketing authorisation for eculizumab.
The technology/ intervention	Alexion	If approved by the European Commission (EC), eculizumab is expected to be indicated for patients with gMG who are anti-AChR antibody positive and refractory to standard treatment.	Comments noted. No action required.
	Association of British Neurologists	Yes	Comments noted. No action required.

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Population	Alexion	No; the population is not defined appropriately. As described above, if approved by the EC, eculizumab is expected to be indicated for patients with gMG who are anti-AChR antibody positive and refractory to standard treatment; it is not expected to be indicated for all patients with MG, gMG, or even all patients with refractory gMG. The anticipated target patient population will number fewer than 500 patients in England.	Comments noted. The population in the draft scope is people with refractory generalised myasthenia gravis. The population is broad because the marketing authorisation is unknown at this time. The appraisal committee will appraise the technology within its marketing authorisation.
	Association of British Neurologists	Population for which Eculizumab intended is not defined at all.	
Comparators	Alexion	Eculizumab is expected to be indicated for only those anti-AChR antibody positive gMG patients who are refractory to treatment with standard of care used in the NHS. We note that anticholinesterase inhibitors are only symptomatic treatments, and immunosuppressants are a non-specific approach to managing patients. However, eculizumab specifically targets the complement mediated damage in patients who are anti-AChR antibody positive, the dominant mechanism that leads to the severity and unpredictability of gMG symptoms and risks for crisis.	Comments noted. Workshop attendees agreed that the appropriate comparator for eculizumab is the continuation of immunosuppressive therapies (with or without intravenous immunoglobulin or plasma exchange). Workshop attendees agreed that eculizumab would be given in addition to these treatments. Anticholinesterase

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			inhibitors are not listed as comparators. The intervention and comparator sections of the scope have been amended accordingly.
	Association of British Neurologists	This is the most important factor. It The role of Eculizumab cannot be determined without much more analysis of the alternative treatments.	Comments noted. No action required.
Outcomes	Alexion	The outcome measure of rate hospitalisations is appropriate to include.	Workshop attendees agreed to include hospitalisations as an outcome. The scope has been amended accordingly.
	Association of British Neurologists	Outcome measures will capture in part the health related benefits. The Regain 3 study has been assessed critically by the clinicians who ran the study, who concluded that the failed primary outcome is of greater significance the secondary outcomes which were positive. The findings of the study are therefore not clear cut and the role of Eculizumab needs more consideration.	Comments noted. No action required.
Economic analysis	Alexion	The standard assessment of cost effectiveness envisaged as part of NICE's technology appraisal process is not suitable for ultra-orphan medicinal products, such as eculizumab for refractory gMG, because it fails to take into account all of the benefits of treatment within the QALY measure or the high costs of development of a treatment for these very rare diseases.	Please refer to the response to your earlier comment about HST.

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		Eculizumab should therefore be evaluated under the HST procedure which evaluates value for money rather than cost effectiveness.	
	Association of British Neurologists	Economic analysis is entirely dependant on other treatment options, given the cost of this drug.	Comments noted. No action required.
Equality and Diversity	Alexion	gMG patients who are refractory to standard treatment are significantly more likely than non-refractory gMG patients to be non-employed, and among the non-employed, they are significantly more likely to report being disabled. (Source: Boscoe AN, Cutter GR, Xin H. Determinants of Non-Employment in Refractory Myasthenia Gravis. Poster presentation at the 14th International Congress on Neuromuscular Diseases (ICNMD), Toronto, Ontario, July 5-9, 2016.)	Thank you for your comments. The committee will consider whether its recommendations could have a different impact on people protected by the equality legislation than on the wider population (such as older people). In line with the NICE reference case for single technology appraisals, the perspective of the analysis on costs should be that of the NHS and Personal Social Services perspective. This does not include indirect costs such as lost work productivity. The

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			committee, at its discretion, may consider non-reference case analyses if appropriate.
	Association of British Neurologists	I have no concerns here.	Comments noted. No action required.
Other considerations	Alexion	Please see comments below as to why eculizumab for treating anti-AChR antibody positive refractory generalised myasthenia gravis should be considered under the HST pathway, not the STA pathway.	Please refer to the response to your earlier comment about HST.
	Association of British Neurologists	Given the enormous costs of this drug, it is impossible to assess this drug in the absence of discussion ofother cheaper off-patent drugs that may be of similar efficacy	Comments noted. Workshop attendees agreed that the appropriate comparator for eculizumab is the continuation of immunosuppressive therapies (with or without intravenous immunoglobulin or plasma exchange). The comparator section of the scope has been amended accordingly.
Innovation	Alexion	If approved by the EC, eculizumab will be the only medicine specifically approved for gMG patients who are anti-AChR antibody positive and	Comments noted. The company and other

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		refractory to standard treatment. In other words, only eculizumab will be indicated for treatment of a very rare and extremely devastating disease. The level of unmet clinical need is very high for these few patients and the eculizumab clinical trial program shows the transformational clinical possibility for this small number of very ill patients.	consultees will be able to fully describe why they consider eculizumab to be innovative in their evidence submissions, which will then be considered by the appraisal committee. No action required.
	Association of British Neurologists	The technology is innovative. It addresses one of the key immunological mechanisms that drive myasthenia gravis.I don't think the technology itself is critical to the health-related benefit. The immunological cascade that creates myasthenia can be 'attacked' at other points along the cascade.	
Questions for consultation	Alexion	As noted above, NICE should evaluate eculizumab for anti-AChR antibody positive refractory gMG under the HST process. See below Alexion responses demonstrating how eculizumab for anti-AChR antibody positive refractory gMG meets each of the seven HST prioritisation criteria.	Please refer to the response to your earlier comment about HST.
	Association of British Neurologists	1. How is refractory myasthenia defined? This is a critical question. There is no publication in the public domain to enable me to determine how the company defined refractory for the Regain 3 trial. In normal clinical practice, most refractory patients haven't been properly managed. I have therefore only managed one tryly refractory patient in 15 years running a myasthenia clinic, because conventional treatment used correctly was able to treat the majority patients succesfully. The NIH clinical trials database doesn't define this. There are of course a number of refractory patients but there is no agreement of which drugs need to fail before a patient would be considered refractory. 2. Would Eculizumab be offerred to Azathioprine failures?	Thank you for your informative comments. Based on this information, and the discussion at the scoping workshop, the scope has been updated.

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		In my opinion it depends why the patient has failed Azathioprine. The drug is often used for too short a time period and in a dose that might be too low. So a failure to respond to Azathioprine is usually a consequence of poor clinical practice. If a patient has failed to respond to Azathioprine when used correctly, most clinicians would use another immunosuppressive drug such as Mycophenolate. I have unpublished data to show that some patients respond to Mycophenolate who fail Azathioprine, despite an immunological response to Azathioprine. 3. Would Eculizumab be offerred to patient who have relapsed following treatment with immunosuppressive agents. Good question. A patient shouldn't relapse if treated succesfully with immunosuppression unless there is a confounding event, such as infection, or a side effect resulting in a reduced dose of an immunosuppressive agent [eg Ciclosporin with drawal following renal failure]. Any patient who has responded to an immunosuppressive agent and who then relapses probably wasn't on a sufficient dose of the immunosuppressive agent. 4. Would Eculizumab be offered to patients who are unable to tolearte immunosupppressive agents? There is quite a choice of immunosuyppressive agents; Azathioprine, Methotrexate, Ciclosporin, Mycophenolate, Tacrolimus etc. It would be odd to be unable to toleate all of them. If this really was the case, then most clinicians would consider the use of Rituximab. It has been hard to get commissioners to pay for Rituximab though it is now off-license and would be the nedxt treatment of choice under these circumstances. I strongly feel that to assess Eculizumab without a consideration of the the role of other drugs with efficacy which haven't been assessed in this way, such as Rituximab would be an error fromn the cost-benefit analysis perspective. I think that you	

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		have insifficient evidence to make the Eculizumab assessment- the drug failed it's phase 3 trial primary outcome, so I believe that further work is required. I don't know if you have the power to request drug comparison studies. From the perspective of the NHS budget, the cost of one patient's Eculizumab would fund many trials to fully assess the comparative benefits of Eculizumab and Rituximab 5. Have all the relevant comparators for Eculizumab been included? Not absolutely sure since the Regain 3 study is unpublished. The inclusion criteria included failure of 2 immunosuppressive drugs, or failure of one, plus chronic plasma exchange or IV immunoglobulin use. I have been asked to treat half a dozen IV immunoglobulin -dependant patients in recent years. All responded to conventional immunosuppressive treatment when used correctly and came off their immunoglobulin. I therefore question the definition of refractory. There is no mention of the use of Rituximab. This is a vital and much cheaper comparator, with apparently excellent outcomes in the literature. 6. The standard of care for refractory MG is not defined. I lead the group who prepared the Association of British Neurologists Myasthenia guidelines. We did not define this group because most patients in the group require higher quality myasthenia care rather than different treatments. We therefore suggested that patients not responding should be sent for a ssessment by a myasthenia expert. 7. Are there subgroups of people in whom Eculizumab is expected to be more clinically effective?	

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		The answer to this question is unknown. 8. Equality/unlawful descrimination etc. Spending inequitably large sums of money on certain patient groups may disadvantage other patient groups given resource limits. Whether this falls under the legislation isn't clear to me. As such, looking at Eculizumab in isolation from other patient treatment factors may be unlawful. I think this assessment needs to be carried out as part of a holistic assessment of approaches to treating refractory patients in general. This might include provision of regional specialist clinics, consideration of funding arrangements for competitor drugs, such as Rituximab. I am uncertain therefore whether the STA Process is appropriate for this assessment. Is Eculizumab innovative with the potential to make a significant impact on health-related benefits? QUALY calculation It certainly is a new and interesting drug. It failed its primary end point, but may or may not have a role. It is hard to determine from a single study. The treatment is impractical to administer as it requires regular intravenous infusions, which would limit any patient reciving it. From the QUALY perspective, a patient receiving the drug would not be able to return to normal economic activities because of the frequent hospital admissions needed to adminsister the drug.	
Additional comments on the draft scope	Alexion	**Alexion Comments on HST Prioritisation Criteria & Applicability to Eculizumab for Refractory gMG** ***NICE HST Criteria 1*: The target patient group for the technology in its licensed indication is so small that treatment will usually be concentrated in very few centres in the NHS**	Please refer to the response to your earlier comment about HST.

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Alexion Response: If approved by the European Commission (EC), eculizumab is anticipated to be indicated for myasthenia gravis (MG) patients who 1) progress to generalised MG (gMG), 2) are refractory to currently available therapies, and 3) are anti-acetylcholine receptor (AChR) antibody-positive.

In an epidemiological study specific to the UK, it was estimated that the prevalence of MG was approximately 150 per million population. These findings are similar to that found in other published studies.[1] The same UK study found that approximately 75% of MG patients progressed to gMG. Studies also indicate that of those patients with gMG, between 10 to 15% will be refractory to treatment with currently available treatments.[2] However, in the UK, as cited in the March 2016 NIHR HSRIC briefing, an expert communicated that the percentage of gMG patients who are truly refractory may be even lower at around 5%.[3] Narrowing the target patient group even further is the fact that not all refractory gMG patients are anti AChR antibody positive. Published studies suggest that only 53% of refractory gMG patients are anti-AChR antibody-positive.[4] While not UK specific, there is no reason to believe the percentage of patients who are anti-AChR antibody-positive in the UK would differ.
<table>
<tr><th>Patient Population</th><th>Estimated Patient Numbers</th></tr>
<tr><td>England Population</td><td>54.5 million</td></tr>
<tr><td>England MG prevalent population</td><td>8,175 patients</td></tr>
<tr><td>England gMG prevalent population</td><td>6,131 patients</td></tr>
<tr><td>England Refractory gMG prevalent population</td><td>307-920 patients</td></tr>
<tr><td>England Anti-AChR antibody-positive refractory gMG prevalent population (TARGET POPULATION)</td><td>163-487 patients</td></tr>
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		In summary, as shown in the table above, the anti-AChR antibody positive refractory gMG target patient group is expected to be small, with fewer than 500 patients throughout England (range of 163 to 487 patients), when applying the 5% to 15% refractory gMG estimates noted above. In particular, when applying the UK expert's estimate of 5%, we think the target population for use of eculizumab to treat anti-aChR antibody-positive refractory gMG will be at the lower end of the range, around 163 patients. Moreover, given the rarity of AChR antibody-positive refractory gMG and in accordance with the recently published International Consensus Guidance for management of MG, which includes authors from the Department of Clinical Neurology at John Radcliffe Hospital, Oxford University Hospitals Trust, eculizumab should be available for target patients only through a select number of expert centres in the NHS.[5] There are currently four designated expert centres that provide diagnostic services for rare neurological conditions, which could be updated to include anti-AChR antibody-positive refractory gMG: Great Ormond Street Hospital for Children NHS Foundation Trust, Oxford University Hospitals NHS Trust, The Newcastle Upon Tyne Hospitals NHS Foundation Trust, and University College London Hospital. A service framework for Rare Neuromuscular Disorders with congenital myasthenia syndromes diagnosed and managed in Oxford also currently exists that could be adapted to include refractory generalized MG. In short, existing pathways are in place that could be updated to include the diagnosis and management of patients with anti-AChR antibody positive refractory gMG in a select number of centres as required under the HST pathway. ***NICE HST Criteria 2: The target patient group is distinct for clinical reasons*** Alexion Response: In anti-AChR antibody positive gMG patients, complement-mediated failure of neuromuscular transmission is driven by membrane attack complex-dependent lysis and C5a-dependent inflammation at the	

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		neuromuscular junction (NMJ). Currently-approved therapies only target reducing production or altering binding properties of these auto-antibodies in order to limit complement activity at the NMJ.[6] Refractory anti-AChR antibody positive gMG patients do not respond to therapy that targets only the auto-antibody mechanism. This clinically distinct group of patients suffers a higher frequency of hospitalisation visits and is at much higher risk of myasthenic crisis and chronic disability.[7] Upon a positive EC decision, eculizumab is expected to be the only therapy indicated for this clinically distinct patient population. ***NICE HST Criteria 3: The condition is chronic and severely disabling*** Alexion Response: Refractory gMG is an incurable disease that burdens patients with severe morbidities and high levels of disability despite currently available therapies. Anti-AChR antibody positive refractory gMG patients have uncontrolled terminal complement activation at the surface of voluntary muscle that causes destruction of the neuromuscular junction and profound muscle weakness despite intensive immunotherapy, which may result in impaired respiratory function with shortness of breath, and/or episodes of pulmonary failure requiring mechanical ventilation; impaired swallowing, choking and/or episodes requiring the need of a gastric tube; upper and lower extremity weakness leading to markedly impaired mobility, extreme fatigue, and need for assistance on daily tasks: slurred speech and visual impairment. Patients with refractory gMG are significantly more likely than patients with non-refractory MG to have exacerbations and myasthenic crises, more likely to require acute admission or assessment through accident and emergency departments , and more likely to require hospitalisation, often involving intensive care unit stays.[8]	

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		NICE HST Criteria 4: The technology is expected to be used exclusively in the context of a highly specialised service Alexion Response: As noted above, upon a positive EC decision eculizumab is expected to be the only therapy indicated for anti-AChR antibody positive refractory gMG patients, the prevalent population of which is estimated to number fewer than 500 patients in England. In addition, as noted above, there are currently four designated expert centres that provide diagnostic services for rare neurological conditions, which could be updated to include anti-AChR antibody-positive refractory gMG: Great Ormond Street Hospital for Children NHS Foundation Trust, Oxford University Hospitals NHS Trust, The Newcastle Upon Tyne Hospitals NHS Foundation Trust, and University College London Hospital. A service framework for Rare Neuromuscular Disorders with congenital myasthenia syndromes diagnosed and managed in Oxford also currently exists that could be adapted to include refractory generalized MG. Again, existing pathways are in place that could be updated to include the diagnosis and management of patients with anti-AChR antibody positive refractory gMG in a select number of highly specialised centres as required under the HST pathway. ***NICE HST Criteria 5: The technology is likely to have a very high acquisition cost*** Alexion Response: The anticipated maintenance dosing regimen for eculizumab for refractory MG is 1200mg every 2 weeks. The acquisition cost of one 300mg vial of eculizumab is currently £3,150 (excluding VAT). ***NICE HST Criteria 6: The technology has the potential for life long use***	

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		Alexion Response: Eculizumab for refractory MG is intended for life-long, chronic administration. Per Alexion's proposed Statement of Product Characteristics (SmPC), the clinical studies show that stopping treatment with eculizumab, in a disease characterised by uncontrolled terminal complement activation, exposes patients to the risk of substantial disease worsening, as demonstrated by reappearance and/or clinically significant deterioration of MG symptoms. ***NICE HST Criteria 7: The need for national commissioning of the technology is significant*** Alexion Response: A significant unmet medical need exists amongst the small group of patients who are significantly disabled by their refractory gMG, as well as their on-going risk for myasthenic crisis and need for intensive care and prolonged hospitalisation as a result. The infrastructure already exists in terms of a national service framework for the care and management of patients with complex neurological conditions. The NHS has previously recognized the need for national commissioning of eculizumab for treatment of patients with paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic uremic syndrome (aHUS). Existing arrangements with NHS England for treatment of patients with PNH and aHUS with eculizumab support the need for a similar national agreement with regard to eculizumab for the treatment of patients with national commissioning is essential to ensure accurate diagnosis of anti-AChR antibody positive refractory gMG in the small subset of MG patients with this condition, equity of access and appropriate prescribing of eculizumab and to ensure proper adherence to treatment protocols as they are developed. **References** [1] Robertson et al., J Neurol Neurosurg Psychiatry 1998; 65: 492–496. Heldal et al., Neurology 2009;73;150-151	

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		[2] Silvestri et al., J Clin Neuromuscul Dis. 2014; 15(4):167-178. Buzzard et al., Muscle Nerve 2015; 52: 204–210. Suh et al., Yale J Biol Med. 2013; 86(2):255-260. [3] National Institute for Health Research, March 2016 Briefing; NIHR HSRIC ID: 6090. [4] Suh et al., Yale J Biol Med. 2013; 86(2):255-260. [5] Sanders et al., Neurology 2016;87:1–7 [6] Gilhus et al., Nature Reviews Neurology 2016; 12:259-268. [7] Howard et al., Muscle Nerve. 2013; 48(1):76-84. [8] Howard et al., Muscle Nerve. 2013; 48(1):76-84. Engel-Nitz N, Boscoe AN, Wolbeck R, Johnson J, Silvestri N. Clinical Burden of Refractory Generalized Myasthenia Gravis in the United States. Poster presentation at the 14th International Congress on Neuromuscular Diseases (ICNMD), Toronto, Ontario, July 5-9, 2016.	
	Association of British Neurologists	The Phase 3 REGAIN Study Study failed primary goal of MG-ADL, however the secondary outcomes were achieved- QMG improvement at week 26 of -4.6 vs. -1.6 for placebo is regarded as clinically significant. It's very important to consider that the QMG score is non-linear, so even though the outcome is positive, raw data is required to fully assess its significance. The clinicians who I believe lead the Regain study have just published a paper which is important to this assessment. They suggest that the failured outcome measure,MG-ADL may be more sensitive for assessing treatment response than point-in-time disease status as assessed by QMG. This observation undermines to some degree the outcomes of the study. Reference: QMG and MG-ADL Correlations: Study of Eculizumab Treatment of Myathenia Gravis. Muscle Nerve 2016 Dec 23, doi: 10.1002/mus.25529. [Epub ahead of print] I realise that my comments may appear to be negative on Eculizumab. I am aware of the massive lobbying on behalf of this drug. I have been approached multiple times from companies around the world collecting clinicians thoughts on Eculizumab. There has been hard lobbying on its behalf. I do believe that it is a very interesting drug. The trial data is not 100% convincing because of the negative primary end point. There is an argument for saying that the efficacy of Eculizumab is only partially proven, the patients who might benefit	Thank you for your comments. The committee will consider both the clinical effectiveness and the cost effectiveness of eculizumab when appraising it. No action required.

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		from it are undefined, and given the cost, to examine it in isolation from a wider consideration of the treatment of myasthenia gravis would be inappropriate	