Medicines & Healthcare products Regulatory Agency

MHRA

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Information for NHS Medical Directors

Regarding EAMS scientific opinion for efgartigimod alpha
Efgartigimod alfa is indicated for the treatment of adult patients with AChR-antibody seropositive generalised myasthenia gravis (gMG), including patients with refractory gMG who have failed, not tolerated or are ineligible for licensed treatment for refractory gMG.

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising unlicensed medicines to UK patients that have a high unmet clinical need. A positive scientific opinion is only issued by the MHRA if the criteria for the EAMS are fulfilled, which includes demonstrating a positive benefit risk balance (quality, safety and efficacy assessment) and the ability of the pharmaceutical company to supply a medicine according to a consistent quality standard.

EAMS medicines are unlicensed medicines. The term 'unlicensed medicine' is used to describe medicines that are used outside the terms of their UK licence or which have no licence for use in the UK. GMC guidance on prescribing unlicensed medicines can be found below:

https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices/prescribing-unlicensed-medicines

The opinion is based on assessment of the information supplied to the MHRA on the benefits and risks of the medicine. As such this is a scientific opinion and should not be regarded as a licensed indication or a future commitment by the MHRA to licence such a medicine, nor should it be regarded as an authorisation to sell or supply such a medicine. A positive scientific opinion is not a recommendation for use of the medicine and should not be interpreted as such. Under EAMS the risk and legal responsibility for prescribing a 'special' remains with the physician, and the opinion and EAMS documentation published by the MHRA are intended only to inform physicians' decision making and not to recommend use. An EAMS scientific opinion does not affect the civil liability of the manufacturer or any physician in relation to the product.

EAMS procedural assessment at the MHRA

A full assessment of the quality, safety and efficacy of [product INN or code number] has been conducted by the MHRA's assessment teams, including pharmacists, toxicologists, statisticians, pharmacokinetic and medical assessors. This assessment process also includes consideration of the quality, safety and efficacy aspects by the UK independent expert committees including Expert Advisory Groups (EAGs) and the Commission on Human Medicines (CHM):

- The Commission on Human Medicines (CHM) advises ministers on the quality, safety and efficacy of medicinal products. The Chair and Commissioners are appointed in accordance with the Code of Practice for Ministerial Appointments to Public Bodies. The Chair and Commissioners follow a code of practice, in which they are precluded from holding personal interests. The Commission is supported in its work by Expert Advisory Groups (EAGs), covering various areas of medicine.

  https://www.gov.uk/government/organisations/commission-on-human-medicines/about

- Chemistry, Pharmacy and Standards EAG, which advises the CHM on the quality in relation to safety and efficacy of medicinal products

  https://www.gov.uk/government/organisations/commission-on-human-medicines/about/membership#chemistry-pharmacy-and-standards-eag

Pharmacovigilance system

A pharmacovigilance system for the fulfilment of pharmacovigilance tasks has been put in place for this EAMS medicine, including a risk management plan. As the safety profile of the EAMS medicine is not fully established it is particularly important that any harmful or unintended responses to EAMS medicines are reported. Healthcare professionals should be aware of their obligations to report adverse event information upon enrolment of any patients receiving EAMS medicines in the scheme. They will be required to follow the process which the pharmaceutical company which manufactures the EAMS medicine has in place to enable systematic collection of information on adverse events.

For more detailed information on this EAMS medicine, please refer to the Public Assessment Report, EAMS treatment protocol for healthcare professionals, EAMS treatment protocol for patients and EAMS treatment protocol for pharmacovigilance.

https://www.gov.uk/government/collections/early-access-to-medicines-scheme-eams-scientific-opinions

Justification for the fulfilment of the EAMS criteria

There are four EAMS criteria that need to be fulfilled before a medicine can enter the scheme and a positive scientific opinion is issued by the MHRA. The fulfilment of the criteria for this particular medicine is described below.

1	**(a) Life threatening or seriously debilitating condition** gMG is a rare, serious, and debilitating neuromuscular autoimmune condition that causes debilitating and potentially life-threatening muscle weakness. Pathogenic IgG proteins target components of the neuromuscular junctions, resulting in reduced neuromuscular transmission. Despite current treatments, gMG patients often suffer substantial difficulties in mobility, speech, swallowing, and vision, as well as impaired respiratory function and extreme fatigue. Patients have impaired ability to work and to be independent, and experience negative impact on their mental health and quality of life. Up to 20% of patients experience potentially life-threatening myasthenic crisis, with respiratory failure requiring mechanical ventilation. Myasthenic crisis is associated with a mortality rate of just under 5%. In addition to MG crisis, MG is associated with increased mortality. A nationwide population-based study in Denmark, published in 2015, assessed mortality in 702 anti-AChR seropositive MG patients diagnosed between 1985 and 2005, compared to 7020 matched controls. Overall mortality was higher in patients with MG than in controls, with a mortality rate ratio (MRR) of 1.41 (95% CI 1.24–1.60) with highest mortality in the first 5 years after diagnosis (MRR 1.67 [95% CI 1.41–1.98]). **(b) High unmet need: there is no method available/approved medicinal product or existing methods/licensed medicines have serious limitations** In the UK, the only approved treatments for adult gMG include AChE inhibitors, eculizumab (Soliris®, licensed only for anti-AChR seropositive patients with refractory gMG) or an oral suspension of azathioprine (Jayempi®, approved July 2021). Acetylcholinesterase (AChE) inhibitor pyridostigmine is often used as first-line treatment. If pyridostigmine is not effective or only provides short-term relief, corticosteroids may be introduced. If steroids are not sufficiently controlling symptoms or if the patient is suffering from severe side effects, non-steroidal immunosuppressant drugs (NSIDs) might be used. In addition to pharmaceutical treatment options, the NHS may recommend MG patients to undergo a thymectomy which can reduce symptoms particularly in patients with an enlarged thymus gland.

	Corticosteroids (and specially prednisone) are used commonly and so is rituximab which is commissioned by NHS England specialised commissioning for refractory gMG. There is therefore a high unmet need for new therapies to treat gMG.
2	**The medicinal product offers major advantage over existing methods in the UK** Efgartigimod was used in addition to background gMG therapy, but use patients who had received eculizumab in the last 6 months were excluded. A subgroup analysis of anti-AChR seropositive patients who were only receiving concomitant gMG therapy with AChE inhibitor during Study 1704 (actual data to be provided by the applicant), showed that 11/13 (84%) of efgartigimod-treated patients were MG-ADL responders after only one treatment cycle compared to 1/6 (16.7%) in the placebo group. Efficacy has been demonstrated in patients with AChR-Ab seropositive gMG who were who were not fully controlled by current therapy (MG-ADL ≥ 5). Because no data is available to support major advantage over eculizumab, the EAMS indication will exclude patients who are eligible for eculizumab in the first instance.
3	**The potential adverse effects of the medicinal product are outweighed by the benefits, allowing for a conclusion of a positive benefit/risk balance** Efficacy has been demonstrated in patients with seropositive gMG. The safety in this population does not raise major concerns, and the information found in the treatment protocol documents reflects the safety in the agreed indication.
4	**The company is able to supply the product and to manufacture it to a consistent quality standard, including the presence of appropriate GMP certification.** The company has provided all documentation necessary to prove that the EAMS medicine is manufactured/packaged according to GMP.