NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Eculizumab for treating refractory myasthenia gravis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of eculizumab within its marketing authorisation for treating refractory myasthenia gravis.

Background

Myasthenia gravis is a long-term condition which causes certain muscles to become weak and tire easily. It is caused by a problem with the immune system, which mistakenly produces antibodies that block the chemical signals between nerves and muscles, meaning that muscles are unable to tighten (contract). The thymus gland is the main source of the abnormal antibodies. The muscles around the eyes are commonly affected first, which causes drooping of the eyelid and double vision. Muscles controlling facial expression, chewing, swallowing, speaking and, less commonly, breathing and neck and limb movements can also be affected. When several different muscle groups are affected, the condition is known as generalised myasthenia gravis. In very severe cases, muscle weakness causes life-threatening difficulties with breathing and swallowing. This is known as myasthenic crisis.

Myasthenia gravis affects about 15 in every 100,000 people in the UK[1,2]. It can develop at any age, but most commonly affects women under 40 years of age and men over 60 years of age[1-3]. In approximately 10–15% of people with myasthenia gravis, the disease does not respond to any currently available treatment[4].

Mild myasthenia gravis is usually treated with anticholinesterases (such as pyridostigmine or, less commonly, neostigmine) which delay the breakdown of acetylcholine, the chemical which stimulates muscle contraction. If treatment with anticholinesterases is not effective, or they are not suitable for long term use, then corticosteroid tablets such as prednisolone are used. Immunosuppressive therapies such as azathioprine may be offered in addition to steroids, with the aim of reducing the steroid dose over time. Surgery to remove the thymus gland may be an option for some people. Myasthenic crisis is treated in hospital with intravenous injections of antibodies (immunoglobulins) from healthy donor blood, or by removing plasma from the blood to reduce the number of abnormal antibodies (known as plasmapheresis or plasma exchange).

The technology

Eculizumab (Soliris, Alexion) is a monoclonal antibody which suppresses immune responses by inhibiting part of the complement cascade. It is administered intravenously.

Eculizumab does not currently have a marketing authorisation in the UK for treating myasthenia gravis. It has been studied in clinical trials in adults with generalised myasthenia gravis whose disease has not responded to, or has relapsed following, treatment with immunosuppressive therapies. To be included in the clinical trials of eculizumab, people must have received treatment with at least 2 immunosuppressive therapies, or received at least 1 immunosuppressive therapy and also require chronic plasma exchange or intravenous immunoglobulin therapy.

Intervention(s)	Eculizumab
Population(s)	People with refractory generalised myasthenia gravis
Comparators	Standard of care without eculizumab
Outcomes	The outcome measures to be considered include: • activities of daily living • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	None

Related National Policy	Department of Health, NHS Outcomes Framework 2016-2017, Apr 2016. Domains 2 and 4. NHS England, Manual for prescribed specialised services 2016-2017, May 2016. Chapters 11 and 12 (adult specialist neurosciences and ophthalmology services).

Questions for consultation

How is refractory myasthenia gravis defined?

Would eculizumab be offered to people:

- whose myasthenia gravis has not responded to immunosuppressive therapy(ies), such as azathioprine?
- whose myasthenia gravis has relapsed following treatment with immunosuppressive therapy(ies)?
- who are unable to tolerate immunosuppressive therapy(ies)?

Have all relevant comparators for eculizumab been included in the scope?

How is standard of care for refractory myasthenia gravis defined? That is, what treatments are offered to people whose disease has not responded to treatment with immunosuppressive therapy?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom eculizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 eculizumab 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.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider eculizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of eculizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

References

1 NHS Choices website Myasthenia Gravis overview [accessed September 2016]

2 Medscape. Myasthenia gravis [accessed September 2016]

3 Patient.co.uk (2014) Myasthenia Gravis [accessed September 2016]

4 Alexion Pharmaceuticals. Eculizumab in other diseases [accessed September 2016]