NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Eculizumab for treating refractory myasthenia gravis

Final scope

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 muscle groups other than the eye muscles 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]. It is difficult to estimate the number of people with myasthenia gravis whose disease does not respond to currently available treatments; estimates range from approximately 1% to 15%[4,5].

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 are offered in addition to steroids, with the aim of reducing the steroid dose over time. If the disease does not respond to the first immunosuppressive treatment, alternative immunosuppressants may be offered (including mycophenolate mofetil, methotrexate, ciclosporin and rituximab). 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 compared with placebo in clinical trials in adults with generalised myasthenia gravis whose disease has not responded to, or has relapsed following, treatment with immunosuppressive therapies. Only people with anti-acetylcholine receptor antibody-positive disease were studied. 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. People in both arms of the trial were able to continue receiving immunosuppressive therapy. Intravenous immunoglobulins and plasma exchange were also permitted during the trial.

Intervention(s)	Eculizumab in addition to standard of care (including immunosuppressive therapies with or without intravenous immunoglobulin or plasma exchange)
Population(s)	People with refractory generalised myasthenia gravis
Comparators	Standard of care without eculizumab (including immunosuppressive therapies with or without intravenous immunoglobulin or plasma exchange)
Outcomes	The outcome measures to be considered include: • activities of daily living • mortality • number of hospitalisations • 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).

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]

5 National Institute for Health Research, March 2016 Briefing; NIHR HSRIC ID: 6090