NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Ravulizumab for treating generalised myasthenia gravis

Final scope

Pre-invite remit/appraisal objective

To appraise the clinical and cost effectiveness of ravulizumab within its marketing authorisation for treating generalised 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 against the nicotinic acetylcholine receptor (AChR) “or muscle-specific tyrosine kinase (MuSK). The antibodies 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 (ocular myasthenia gravis). 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] It can develop at any age, but most commonly affects women under 40 years of age and men over 60 years of age.[2,3] Around 80% of people with ocular myasthenia gravis will progress to generalised myasthenia gravis within 2 years.[2] About 80% to 90% of people with myasthenia gravis have detectable antibodies against AChR, while 3% to 7% have antibodies against MuSK.[4-6] In around 10% of people antibodies are not detected.[7] It is difficult to estimate the number of people with myasthenia gravis whose disease does not respond to currently available treatments; estimates range from about 10% to 20%.[8,9]

Mild myasthenia gravis and some cases of moderate disease are usually treated with cholinesterase inhibitors such as pyridostigmine which delay the breakdown of acetylcholine, the chemical which stimulates muscle contraction.[10] If treatment with cholinesterase inhibitors 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 (thymectomy) is an option for people with mild disease and antibodies against AChR, and people with moderate disease. Myasthenic crisis is treated in hospital with mechanical ventilation, 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) and supportive care.[10]

The technology

Ravulizumab (Ultomiris, Alexion Pharma)

Ravulizumab does not currently have a marketing authorisation in the UK for treating generalised myasthenia gravis. It has been studied in a clinical trial, as monotherapy, compared with placebo in adults with generalised myasthenia gravis.

Intervention	Ravulizumab
Population	Adults with generalised myasthenia gravis
Comparators	Established clinical management without ravulizumab including corticosteroids and immunosuppressive therapies, with or without intravenous immunoglobulin or plasma exchange
Outcomes	The outcome measures to be considered include: • improvement in myasthenia gravis • hospitalisations • 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
Other considerations	The availability and cost of biosimilar and generic products should be taken into account. 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	**Related Guidelines:**

	Suspected neurological conditions: recognition and referral (2019). NICE guideline 127. Review date: TBC **Related Quality Standards:** Suspected neurological conditions: recognition and referral (2021). NICE quality standard 198
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) Clinical Commissioning Policy: Rituximab bio-similar for the treatment of myasthenia gravis (adults). 170084P. NHS England (2014/15) NHS Standard Contract for Neuromuscular Operational Delivery Network Specification. D04/ODN/a. NHS England (2013/14) NHS Standard Contract for Neurosciences: Specialised Neurology (Adult). D04/S/a NHS England (2018) Updated Commissioning Guidance for the use of therapeutic immunoglobulin (Ig) in immunology, haematology, neurology and infectious diseases in England NHS England (2021) Highly specialised services 2019 Diagnostic service for rare neuromuscular disorders (adults and children) p.38 NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 11: Adult specialist neurosciences services, Chapter 12: Adult specialist ophthalmology services Chapter 48: Diagnostic service for rare neuromuscular disorders (adults and children) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

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