NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Zilucoplan for treating antibody-positive generalised myasthenia gravis

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of zilucoplan within its marketing authorisation for treating antibody-positive 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 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 and men over 60.[3] Around 80% of people with 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 is usually treated with anticholinesterases (such as pyridostigmine or, less commonly, neostigmine) which delay the breakdown of acetylcholine, the chemical which stimulates muscle contraction[10]. 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 corticosteroids, with the aim of reducing the corticosteroid 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

Zilucoplan (brand name unknown, UCB Pharma).

Zilucoplan does not currently have a marketing authorisation for treating antibody-positive generalised myasthenia gravis. It has been studied in clinical trials compared with placebo in adults with antibody-positive generalised myasthenia gravis and a Myasthenia Gravis Foundation of America (MGFA) Class between II-IV at screening.

Intervention(s)	Zilucoplan
Population(s)	Adults with antibody-positive generalised myasthenia gravis
Comparators	• standard of care without zilucoplan (including corticosteroids and immunosuppressive therapies, with or without intravenous immunoglobulin or plasma exchange) • efgartigimod (subject to NICE evaluation) • ravulizumab (subject to NICE evaluation)
Outcomes	The outcome measures to be considered include: • improvement in myasthenia gravis • 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.

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	**Related Technology Appraisals:** None **Related appraisals in development:** Efgartigimod for treating generalised myasthenia gravis. NICE technology appraisal guidance [ID4003]. Expected publication date October 2023. Ravulizumab for treating generalised myasthenia gravis. NICE technology appraisal guidance [4019]. Expected publication date July 2023. **Related NICE guidelines:** Suspected neurological conditions: recognition and referral (2019). NICE guideline 127. **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

Questions for consultation

Is the population defined appropriately?

Would zilucoplan be used as an add-on to the current NHS standard care for generalised myasthenia gravis?

Where do you consider zilucoplan will fit into the existing care pathway for antibody-positive generalised myasthenia gravis?

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

Are there any subgroups of people in whom zilucoplan is expected to be more clinically effective and cost effective or other groups that should be examined separately? For example, those based on Myasthenia Gravis Foundation of America (MGFA) Class?

Are the outcomes listed appropriate?

Would zilucoplan be a candidate for managed access?

Do you consider that the use of zilucoplan can result in any potential 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 committee to take account of these benefits.

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 zilucoplan 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic

through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Spillane J, Higham E, Kullmann DM (2012) Myasthenia gravis. *BMJ*; 345:e8497.

2. Patient (2017) Myasthenia Gravis. Accessed February 2023.

3. Meriggioli MN and Sanders DB (2009) Autoimmune myasthenia gravis: emerging clinical and biological heterogeneity. *Lancet Neurology*; 8(5):475-90.

4. Guptill JT and Sanders DB (2010) Update on muscle-specific tyrosine kinase antibody positive myasthenia gravis. *Current Opinion Neurology*; 23(5):530-5.

5. Ruff RL and Lisak RP (2018) Nature and action of antibodies in myasthenia gravis. *Neurologic Clinics*; 36(2):275-91.

6. Maddison P, Ambrose PA, Sadalage G et al. (2019) A Prospective Study of the Incidence of Myasthenia Gravis in the East Midlands of England. *Neuroepidemiology*; 53(1-2):93-99.

7. Leite M, Jacob S, Viegas S et al. (2008) IgG1 antibodies to acetylcholine receptors in 'seronegative' myasthenia gravis. *Brain* 131:1940-52

8. Mantegazza R and Antozzi C (2018) When myasthenia gravis is deemed refractory: clinical signposts and treatment strategies. *Therapeutic Advances in Neurological Disorders*; 11:1756285617749134.

9. Schneider-Gold C, Hagenacker T, Melzer N et al. (2019) Understanding the burden of refractory myasthenia gravis. *Therapeutic Advances in Neurological Disorders*; 12:1756286419832242.

10. BMJ Best Practice (2021) Myasthenia gravis. Accessed February 2023.