NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Efgartigimod for treating generalised myasthenia gravis

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of efgartigimod 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 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. In around 10% of people these antibodies are not detected.[1] 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.[2,3] It can develop at any age, but most commonly affects women under 40 and men over 60.[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 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). Eculizumab is also indicated for people whose disease does not respond to treatment and are anti-acetylcholine receptor antibody-positive. 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

Efgartigimod (brand name unknown, argenx) is a human antibody fragment with increased affinity to the protein, FcRn. It binds to FcRn, allowing circulating immunoglobulin antibodies to be broken down and removed from the body much more quickly. Efgartigimod is administered intravenously.

Efgartigimod does not currently have a marketing authorisation in the UK for treating generalised myasthenia gravis. It has been studied in clinical trials compared with placebo in adults with generalised myasthenia gravis.

Intervention(s)	Efgartigimod
Population(s)	Adults with generalised myasthenia gravis
Comparators	Established clinical management without efgartigimod (including corticosteroids and immunosuppressive therapies, with or without intravenous immunoglobulin or plasma exchange)
Outcomes	The outcome measures to be considered include: • Change in Myasthenia Gravis-Activities of Daily Living (MG-ADL) Score • 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.
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	Terminated appraisals: Eculizumab for treating refractory myasthenia gravis (terminated appraisal) (2020). NICE Technology Appraisal 636. 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 NICE pathways: Neurological conditions (updated 2021) NICE Pathway
Related National Policy	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 (2013/14) NHS Standard Contract for Diagnostic Service for Rare Neuromuscular Disorders (All ages). D04/S(HSS)/a. NHS England (2018) Updated Commissioning Guidance for the use of therapeutic immunoglobulin (Ig) in immunology, haematology, neurology and infectious diseases in England The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) 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

Which treatments are considered to be established clinical practice in the NHS for generalised myasthenia gravis?

Have all relevant comparators for efgartigimod been included in the scope? Is eculizumab a relevant comparator?

Where do you consider efgartigimod would fit into the existing treatment pathway for generalised myasthenia gravis?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom efgartigimod is expected to be more clinically effective and cost effective or other groups that should be examined separately? For example, those based on anti-acetylcholine receptor (AChR) antibody status?

Is the Myasthenia Gravis Foundation of America (MGFA) classification system used in the NHS? Would efgartigimod be used in people with myasthenic crisis (MGFA class 5)?

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 efgartigimod 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 efgartigimod 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 efgartigimod 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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

2. Patient, Myasthenia gravis. 2017. Accessed November 2021.

3. Muscular Dystrophy UK. Myasthenia gravis Overview. 2011. Accessed November 2021.

4. National Health Service (NHS). Myasthenia gravis overview. 2020. Accessed November 2021.