NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Eculizumab for treating relapsing neuromyelitis optica spectrum disorders

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of eculizumab within its marketing authorisation for treating relapsing neuromyelitis optica spectrum disorders.

Background

Neuromyelitis optica spectrum disorder (NMOSD) is a demyelinating autoimmune disease that can lead to optic neuritis, where the optic nerve becomes inflamed, and transverse myelitis, where the spinal cord becomes inflamed. Optic neuritis can affect one or both eyes with symptoms including pain on moving the eye and acute loss of vision. Symptoms of transverse myelitis depend on the area of the spine where swelling occurs and include, muscle spasms and weakness leading to back pain, leg pain and bladder or bowel dysfunction. NMOSD can be a single event but is relapsing in most cases. Relapsing attacks are separated by months or years, but in rare cases they can be almost continuous. Relapses usually lead to permanent neurologic impairment if not treated effectively. NMOSD is associated with high mortality and morbidity when not diagnosed early and treated.

NMOSD is a disorder that can affect adults, and in rare cases, also children[1]. It is diagnosed when someone experiences either optic neuritis or transverse myelitis and is associated with the aquaporin-4 antibody in approximately 80% of cases[2].

About 1,000 people in England have neuromyelitis optica spectrum disorder[3] and around 90% of people with the condition are female[2].

Acute episodes are treated with steroids[4]. If symptoms do not respond to steroids, plasma replacement can be used. Maintenance treatment to prevent further episodes of NMOSD include first line prednisolone with either azathioprine, mycophenolate mofetil, or methotrexate[5]. If relapse occurs, rituximab may be given. If rituximab is not effective, treatment with mitoxantrone or cyclophosphamide may be considered[6].

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 relapsing neuromyelitis optica spectrum disorder. It has been studied in a clinical trial compared with placebo in people with relapsing neuromyelitis optica spectrum disorders who had at least 2 relapses in the previous 12 months, or 3 relapses in the previous 24 months.

Intervention(s)	Eculizumab
Population(s)	People with relapsing neuromyelitis optica spectrum disorders
Comparators	Established clinical management without eculizumab
Outcomes	The outcome measures to be considered include: • time to first relapse • relapse rate • 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	Related Technology Appraisals: Eculizumab for treating atypical haemolytic uraemic syndrome (2015). NICE highly specialised technologies guidance 1. Review date January 2018. Appraisals in development (including suspended appraisals) Eculizumab for treating refractory myasthenia gravis [ID1064]. Suspended.

	Related Guidelines: None
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Chapter 77. Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domain 2.

Questions for consultation

Are rituximab, mitoxantrone and cyclophosphamide relevant comparators for eculizumab for treating neuromyelitis optica spectrum disorders? Are there any other comparators for eculizumab?

How would eculizumab fit into the clinical pathway for relapsing neuromyelitis optica spectrum disorders?

- Is it expected to be used after prednisolone-based treatment?
- How many patients are likely to be eligible for treatment in England?
- If recommended would treatment be administered at highly specialised centres?

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.

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 compared with the Highly Specialised Technology (HST) process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction). Further information about the HST eligibility criteria are available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf

References

1. Tenembaum S, Chitnis T, Nakashima I, et al. Neuromyelitis optica spectrum disorders in children and adolescents. Neurology. 2016 Aug 30;87(9 Suppl 2):S59-66
2. NMO UK, http://www.nmouk.nhs.uk/healthcare-professionals/aqp4-antibodies (accessed February 6 2019
3. NHS England (2017) https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual.pdf Chapter 77. Accessed January 2019.
4. Trebst C, Jarius S, Berthele A et al (2014) Update on the diagnosis and treatment of neuromyelitis optica: Recommendations of the Neuromyelitis Optica Study Group (NEMOS). J Neurol 261: 1-16
5. Kessler R, Mealy M and Levy M (2016). Treatment of Neuromyelitis Optica Spectrum Disorder: Acute, Preventive, and Symptomatic. Curr Treat Options Neurol. 2016 Jan; 18(1): 2.
6. NMO UK, NMO treatment algorithm [online; accessed February 6 2019]

