NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Inebilizumab for treating neuromyelitis optica spectrum disorders

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of inebilizumab within its marketing authorisation for treating 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 relapsing condition are female[4].

Acute episodes are treated with steroids. 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. If relapse occurs, rituximab may be given[5].

The technology

Inebilizumab (brand name unknown, Viela Bio) is a humanised anti-CD19 monoclonal IgG1 antibody. It specifically targets the CD-19 receptor on B lymphocytes and causes lysis of the cell and complete B-cell depletion. CD-19+ B-cells are the source of the pathogenic auto antibody, AQP4-IgG. AQP4-IgGs cause neuron damage as they act against an important water channel protein expressed on cells in the central nervous system. Inebilizumab is administered intravenously.

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Inebilizumab does not currently have a marketing authorisation in the UK for treating neuromyelitis optica spectrum disorders. It has been studied in a clinical trial compared with placebo in adults who had at least 1 attack requiring rescue therapy in the previous 12 months, or 2 attacks requiring rescue therapy in the past 24 months. The trial included people with AQP4-IgG sero-positive NMO/NMOSD and AQP4-IgG sero-negative NMO.

Intervention(s)	Inebilizumab
Population(s)	People with neuromyelitis optica spectrum disorders
Comparators	• Established clinical management without inebilizumab • Eculizumab (subject to ongoing NICE appraisal)
Outcomes	The outcome measures to be considered include: • time to onset of an NMO/NMOSD attack • relapse rate • ambulatory function • visual acuity (the affected eye) • visual acuity (both eyes) • pain • bowel and bladder continence • NMO/NMOSD-related inpatient hospitalisations • adverse effects of treatment • health-related quality of life.

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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. If the use of inebilizumab is conditional on the presence of AQP4-Ab, the economic modelling should include the cost associated with diagnostic testing for AQP4-Ab who would not have otherwise been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals'. Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.
Other considerations	If the evidence allows, the following subgroups will be considered: • AQP4-IgG sero-positive NMO/NMOSD • AQP4-IgG sero-negative NMO. 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	Proposed Technology Appraisals: Eculizumab for treating relapsing neuromyelitis optica Proposed NICE technology appraisal [ID 1271]. Publication date to be confirmed.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019): Chapter 77. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2.

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Questions for consultation

Are azathioprine, mycophenolate mofetil and methotrexate relevant comparators for inebilizumab for treating neuromyelitis optica spectrum disorders? Is eculizumab a relevant comparator (subject to ongoing NICE appraisal)? Are there any other comparators for inebilizumab?

Would inebilizumab be used as monotherapy or as part of maintenance therapy for treating neuromyelitis optica spectrum disorders?

How would inebilizumab fit into the clinical pathway for treating neuromyelitis optica spectrum disorders?

- Is it expected to be used after the acute episode has been treated with prednisolone-based treatment?
- How many people 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 the visual acuity outcomes appropriate to capture visual loss or decline?

Are there any subgroups of people in whom inebilizumab 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 inebilizumab 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 inebilizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might

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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 inebilizumab 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Tenembaum S, Chitnis T, Nakashima I et al. (2016) Neuromyelitis optica spectrum disorders in children and adolescents. Neurology. 87(9 Suppl 2):S59-66
2. NMO UK. Aquaporin 4-antibodies. Accessed May 2019.

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3. NHS England (2018). Neuromyelitis optica service (adults and adolescents) Manual for Prescribed Specialised Services 2018/19. Accessed May 2019.
4. Borisow N, Mori M, Kuwabara S et al. (2018) Diagnosis and Treatment of NMO Spectrum Disorder and MOG-Encephalomyelitis. Front. Neurol. 9:888.
5. NMO UK, NMO treatment algorithm. Accessed May 2019.

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