Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Satralizumab for preventing relapses in neuromyelitis optica spectrum disorders

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of satralizumab (SA-237) within its marketing authorisation for preventing relapses in neuromyelitis optica (NMO) and neuromyelitis optica spectrum disorders (NMOSD).

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. 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[1].

About 1000 people in England have NMO[2]. The median age of onset is 39 years and around 90% of people with NMO are female[3].

Currently there are no approved therapies for treating NMO or NMOSD. Clinical management aims to treat attacks or relapses. Acute episodes are treated with high dose-steroids such as methylprednisolone and plasma exchange (where the plasma containing the antibodies is separated and fresh plasma is returned to the body). Patients may receive immunotherapies such as prednisolone, either alone or in combination with azathioprine or mycophenolate as a maintenance treatment to allow the reduction of steroids and prevent further relapses. If relapse occurs patients may be given rituximab.

The technology

Satralizumab (brand name unknown; Roche pharmaceuticals) is a humanised anti-IL-6 receptor antibody which binds to IL-6 receptors. This prevents the cells involved in the immune system from responding, thereby reducing inflammation and helping to prevent relapse and control the symptoms of neuromyelitis optica and neuromyelitis optica spectrum disorders (people with the aquaporin-4 antibody).

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Satralizumab does not currently have a marketing authorisation in the UK for any indication. It is being studied in phase III trials for the treatment of neuromyelitis optica and neuromyelitis optica spectrum disorders. It is administered by subcutaneous injection (an injection under the skin) and is being developed as both a monotherapy and add-on therapy.

Intervention(s)	Satralizumab
Population(s)	Adults and young people with neuromyelitis optica (NMO) and neuromyelitis optica spectrum disorders (NMOSD).
Comparators	• Established clinical management without satralizumab
Outcomes	The outcome measures to be considered include: • time to first relapse • relapse rate • pain • fatigue • ambulatory function • Vision acuity (the affected eye) • visual acuity (both eyes) • bowel and bladder continence • NMO/NMOSD-related inpatient hospitalisation • 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. The use of satralizumab is conditional on the presence of the AQP4- positive and AQP4- negative antibodies. The economic modelling should include the costs associated with diagnostic testing for the AQP4-positive or AQP-4 negative serologic markers in people with neuromyelitis optica spectrum disorder who would not otherwise have 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	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. Inebilizumab for treating neuromyelitis optica. Proposed NICE technology appraisal [ID 1529]. Publication date to be confirmed. Related Guidelines: None
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) Highly specialised services 2017 (see page 36) NHS England (2018) Manual for prescribed specialised services 2018/19 Chapter 77 (see pages 216-7) NHS England (2013) 2013/14 NHS standard contract for neuromyelitis optica service (adults and adolescents). Service specification no: D04/S(HSS)/b

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	Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2-4 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 neuromyelitis optica and neuromyelitis optica neuromyelitis optica spectrum disorders?

Would satrulizumab be considered as monotherapy or add-on therapy for people with neuromyelitis optica and neuromyelitis optica spectrum disorders?

Where in the treatment pathway do you consider satralizumab will fit?

- Will it be considered as a replacement to maintenance treatment with prednisolone (either alone or in addition to treatment with azathioprine or mycophenolate mofetil)?

Are there any subgroups of people in whom satralizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? Should people with neuromyelitis optica and neuromyelitis optica spectrum disorders (people with the aquaporin-4 antibody) 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 satralizumab 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 satralizumab 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 satralizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

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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 Kessler RA, Mealy MA, Jimenez-Arango JA et al. (2017) Anti-aquaporin-4 titer is not predictive of disease course in neuromyelitis optica spectrum disorder: A multicenter cohort study. Multiple Sclerosic and Related Disorders 17, 198–201.

2 NHS England (2017) https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual.pdf Chapter 77. Accessed July 2019.

3 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). Journal of Neurology 261, 1-16.