

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Ravulizumab for treating AQP4 antibody-positive neuromyelitis optica spectrum disorder

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of ravulizumab within its marketing authorisation for treating AQP4 antibody-positive neuromyelitis optica spectrum disorder.

Background

Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease where the immune system attacks the nerves in the eyes and central nervous system (CNS). This 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. The symptoms vary from person to person. 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. Each relapse can result in cumulative disability and can lead to permanent neurologic impairment if not treated effectively. NMOSD is associated with high mortality and morbidity when not diagnosed early and treated.

About 1,000 people in England have NMOSD¹ and approximately 73% to 90% of these people have aquaporin-4 (AQP4) antibodies.^{2,3} AQP4 antibody-positive NMOSD incidence is higher in females with a ratio of 9 females to 1 male affected.⁴

There is no cure for NMOSD so management focuses on treating acute attacks, preventing relapses and treating the residual symptoms of the condition. Acute episodes are treated with steroids. If symptoms do not respond to steroids, plasma exchange or immunoglobulins can be used. Maintenance treatment to prevent further episodes of NMOSD includes azathioprine or mycophenolate mofetil. A low dose of steroids may also be required for maintenance. If relapse occurs, rituximab may be given.⁵

The technology

Ravulizumab (Ultomiris, Alexion) is administered intravenously. It does not currently have marketing authorisation in the UK for NMOSD. It is being studied in adults and children with anti-AQP4 Ab-positive NMOSD.

Intervention(s)	Ravulizumab
Population(s)	People with aquaporin-4 antibody positive (AQP4-Ab [+]) neuromyelitis optica spectrum disorder (NMOSD)
Comparators	Established clinical management without ravulizumab
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • time to first relapse • relapse rate • visual acuity (the affected eye) • visual acuity (both eyes) • bowel and bladder continence • NMO/NMOSD-related inpatient hospitalisations • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p> <p>The use of ravulizumab is conditional on the presence of aquaporin-4 antibodies. The economic modelling should include the costs associated with diagnostic testing for aquaporin-4 antibodies 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 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).</p> <p>Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.</p>

Other considerations	<p>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.</p>
Related NICE recommendations	<p>Related Technology Appraisals:</p> <p>In development Inebilizumab for treating neuromyelitis optica spectrum disorders [ID1529] NICE Technology appraisal guidance. Publication date to be confirmed</p> <p>Suspended/discontinued Eculizumab for treating relapsing neuromyelitis optica (terminated appraisal) (TA647) (2020) NICE Technology appraisal guidance.</p> <p>Satralizumab for preventing relapses in neuromyelitis optica spectrum disorders [ID1319] NICE Technology appraisal guidance. Publication date to be confirmed</p>
Related National Policy	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019). Chapter 77. Neuromyelitis optica service (adults and adolescents). NHS manual for prescribed specialist services (2018/2019)</p>

Questions for consultation

Does the NMO UK [Treatment Algorithm](#) reflect established clinical management for NMOSD in England? How would established clinical management without ravulizumab be defined?

Where do you consider ravulizumab will fit into the existing care pathway for NMOSD? Would it only be used to prevent relapse?

Are there any relevant comparators which have not been included in the scope?

How many patients are likely to be eligible for treatment in England? Would all people with aquaporin-4 antibody positive neuromyelitis optica spectrum disorder (NMOSD) be eligible?

Would ravulizumab be a candidate for managed access?

Do you consider that the use of ravulizumab 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 ravulizumab 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 NHS England (2018). Neuromyelitis optica service (adults and adolescents) Manual for Prescribed Specialised Services 2018/19. <https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual.pdf> Accessed August 2022
- 2 Hamid SH, Elson L, Mutch K, Solomon T, Jacob A. The impact of 2015 neuromyelitis optica spectrum disorders criteria on diagnostic rates. *Mult Scler.* 2017;23(2):228–233.
- 3 Hyun JW, Jeong IH, Jung A, Kim SH, Kim HJ. Evaluation of the 2015 diagnostic criteria for neuromyelitis optica spectrum disorder. *Neurology.* 2016;86(19):1772–1779.
- 4 Gold SM, Willing A, Leypoldt F, Paul F, Friese MA. Sex differences in autoimmune disorders of the central nervous system. *Semin Immunopathol.* (2019) 41:177–88. doi: 10.1007/s00281-018-0723-8
- 5 NMO UK, NMO treatment algorithm. <http://www.nmouk.nhs.uk/wp-content/uploads/2011/06/NMO-Treatment-Algorithm5.pdf> Accessed August 2022.