NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Ravulizumab for treating AQP4 antibody-positive neuromyelitis optica spectrum disorder

Final 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, central nervous system (CNS) and sometimes also the brain. 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 muscle weakness can range from a mild 'heavy' feeling in one limb, to complete paralysis in all four limbs. 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, permanent neurological impairment and disability. Without treatment, within 5 years of their first attack approximately 50% of people with NMOSD will be wheelchair users and blind, and a third will have died. While early diagnosis and treatment can improve outcomes, some people are refractory to current treatments and experience severe long-term disability.

Data from NHS England suggests that about 1,000 people in England have NMOSD[1] and approximately 73% to 90% of these people have aquaporin-4 (AQP4) antibodies.[2,3] This is supported by a prevalence study which suggests that there are 672 people in England with AQP4 antibody-positive NMOSD.[4] Incidence is higher in females with a ratio of 9 females to 1 male affected.[5] It is also disproportionately affects people of Black and Asian ethnicity.

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.[6]

The technology

Ravulizumab (Ultomiris, Alexion) is administered intravenously. It does not currently have marking 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	The outcome measures to be considered include: • 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	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 and cost of biosimilar and generic products should be taken into account. 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). 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	**Related Technology Appraisals:** **In development** Inebilizumab for treating neuromyelitis optica spectrum disorders [ID1529] NICE Technology appraisal guidance. Publication date to be confirmed **Suspended/discontinued** Eculizumab for treating relapsing neuromyelitis optica (terminated appraisal) (TA647) (2020) NICE Technology appraisal guidance. Satralizumab for preventing relapses in neuromyelitis optica spectrum disorders [ID1319] NICE Technology appraisal guidance. Publication date to be confirmed
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019). Chapter 77. Neuromyelitis optica service (adults and adolescents). NHS manual for prescribed specialist services (2018/2019)

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, Elsone 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, Joung A, Kim SH, Kim HJ. Evaluation of the 2015 diagnostic criteria for neuromyelitis optica spectrum disorder. Neurology. 2016;86(19):1772–1779.

4 O'Connell, K., Hamilton-Shield, A., Woodhall, M., Messina, S., Mariano, R., Waters, P., Ramdas, S., Leite, M.I. and Palace, J., 2020. Prevalence and incidence of neuromyelitis optica spectrum disorder, aquaporin-4 antibody-positive NMOSD and MOG antibody-positive disease in Oxfordshire, UK. Journal of Neurology, Neurosurgery & Psychiatry, 91(10), pp.1126-1128.

5 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

6 NMO UK, NMO treatment algorithm. http://www.nmouk.nhs.uk/wp-content/uploads/2011/06/NMO-Treatment-Algorithm5.pdf Accessed August 2022.