Highly Specialised Technologies (HST) criteria checklist

Ravulizumab for treating AQP4 antibody-positive neuromyelitis optica [ID 5105]

**Introduction:** The NICE HST criteria checklist is to highlight where a technology meets/partially meets or does not meet the criteria for routing to the HST programme. Its purpose is to show the details of why a technology may not be appropriate for HST evaluation, but also where it has been identified as suitable.

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| --- | --- | --- | --- |
| **Version no:** | **Revision date** | **Changes made by** | **Summary of change** |
| **1.0** | **7 Sept** | **AS** |  |
| **2.0** | **14 Sept** | **SD** | **Adviser review** |
| **3.0** | **23 Nov** | **AS** | **AD review** |
| **4.0** | **1 Feb** | **AS** | **Following TSOP** |

### Key – does the technology meet the criteria? Please use the colour key to advise if the technology meets the criteria

|  |  |
| --- | --- |
| Met  | There is clear and strong evidence that this criterion is met |
| Unclear | There is some evidence, or the evidence available is unclear. |
| Not met | There is no evidence or limited evidence that the criterion is met.  |

### MA wording: \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*\*\*\*

| **Number** | **Criterion** | **Description of how the technology meets the criteria**  | **Does the technology meet the criteria?** |
| --- | --- | --- | --- |
| 1.
 | The condition is very rare defined by 1:50,000 in England  | * Prevalence estimates for NMOSD vary between studies. This is partly due to variations in prevalence among different geographic areas and ethnicities. Differences in study design, study population, and quality of data may also be a factor.[[1]](#endnote-1)
* Using NHS England data on population size would give a prevalence of 0.88 per 50,000 people.
* Other estimates from England range from 0.36-0.8 per 50,000 adults.[[2]](#endnote-2),[[3]](#endnote-3)
* These estimates include both those with and without aquaporin-4 (AQP4) antibodies. Therefore the prevalence of aquaporin-4-positive NMOSD would be lower than these figures.
* A meta-analysis of worldwide prevalence of NMOSD revealed that the highest prevalence was found in African populations and the lowest was in predominantly White populations.1
 | Met |
|  | Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications  | * NHS England states that about 1,000 people in England have NMOSD.[[4]](#endnote-4) Approximately 73% to 90% of these people have aquaporin-4 (AQP4) antibodies.[[5]](#endnote-5),[[6]](#endnote-6) Therefore the population eligible for the technology in its licensed indication is 730-900 people.
* Clinical expert said there are 672 patients in England with AQP4 NMOSD in England, based on Oxfordshire prevalence study.[[7]](#endnote-7)
* The number of people in England who are eligible for the technology in its full licensed indication (672-900) is therefore >300. While the company and clinical experts have advised that expected UK clinical practice would use ravulizumab as \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* It is the licensed indication which is relevant for HST routing.
* Ravulizumab is also licensed for paroxysmal nocturnal haemoglobinuria (PNH), atypical haemolytic uraemic syndrome (aHUS) and generalized Myasthenia Gravis. The eligible patient populations for these indications in England are as follows:
	+ PNH: ~200-333 (UK figure x 0.84 for England number)
	+ aHUS: ~140-224
	+ Refractory AChR-antibody-positive gMG: ~163-1,222

(MA is for all AChR-antibody-positive gMG. UK clinical use expected to be refractory only).* Therefore, the estimated total population across all indications (inc. NMOSD) ranges from 609-2,451, exceeding the 500 cited in the criterion.
 | Not met |
|  | The very rare condition significantly shortens life or severely impairs its quality  | * The symptoms of NMOSD can range from mild to severe and vary from person to person. The disease attacks the optical nerves, spinal cord, and occasionally the brain.
* In some cases, people may have a good recovery and no further relapses for a long time. However, in severe cases, there can be a number of attacks which lead to irreversible disability.
* The disabilities which can accumulate with each acute attack include vision loss and/or paralysis of limbs.
* Untreated, approximately 50% of people with NMOSD will be wheelchair users and blind, and a third will have died within 5 years of their first attack.[[8]](#endnote-8)
* With prompt diagnosis and treatment, outcomes are improved. When treated, the 5-year survival rate for monophasic (single attack) NMO is 90 percent and for relapsing NMO (more than 1 attack) is 68 percent.[[9]](#endnote-9)
 | Met  |
|  | There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options. | * There is no cure for NMOSD but effective treatment is available.
	+ High dose steroids are used to treat acute NMOSD attacks. Plasma Exchange or Intravenous Immunoglobulins may be given if attacks progress or do not respond to corticosteroid treatment.
	+ Immunosuppressants are then used long-term to prevent relapses.
* However, some people are refractory to current treatments. Clinical expert stated that 50% relapse on 1st line immunosuppressant treatment in 2 yrs, and 48% relapse on rituximab as 2nd/3rd line.
* Clinical experts said ravulizumab would be most valuable for those who relapse despite current treatments (~10-24% of total AQP4 Ab+ NMOSD population).
* Results from the CHAMPION-NMOSD trial (NCT04201262) showed that ravulizumab reduced the risk of relapse in AQP4 Ab+ NMOSD by 98.6% compared to an external placebo. There were zero relapses in the ravulizumab group, with a median treatment duration of 73 weeks. All participants had experienced at least 1 attack or relapse in the 12 months before entering the trial, despite current treatment. ~35% of the participants had been treated with rituximab in the past year.[[10]](#endnote-10)
 | Not met |

Highly specialised technologies vision and routing criteria

The Highly Specialised Technologies Programme is designed to be used in exceptional circumstances. Its purpose is to evaluate technologies for very rare diseases that have:

* small numbers of patients
* limited or no treatment options
* challenges for research and difficulties with collecting evidence, because of the uniqueness of the disease.

The Highly Specialised Technologies Programme aims to:

* encourage research on, and innovation for, very rare conditions when there are challenges in generating an evidence base that is robust enough to bring the product to market
* secure fairer and more equitable treatment access for very small populations with very rare diseases
* recognise that an approach that maximises health gain for the NHS may not always be acceptable: it could deliver results that are not equitable.

The Highly Specialised Technologies Programme acknowledges that:

* It is important for NICE to apply appropriate limits on the very rare populations that can potentially be routed to the programme. This is because the Highly Specialised Technologies Programme is a deliberate departure from the standard technology appraisal process (valuing the benefits from these technologies more highly by having a much higher [incremental cost-effectiveness ratio [ICER]](https://www.nice.org.uk/Glossary/incremental-cost-effectiveness-ratio) threshold) for the reasons outlined above.
* Each time NICE routes a topic to the Highly Specialised Technologies Programme it is deciding that, if the technology is recommended, the NHS must commit to allocate resources that would have otherwise been used on activities that would be expected to generate greater health benefits.
* NICE has sought to strike a balance between the desirability of supporting access to treatments for very rare diseases against the inevitable reduction in overall health gain across the NHS that this will cause. Both considerations are valid and important, and neither can be given absolute priority over the other. Therefore, the Highly Specialised Technologies Programme criteria and their anticipated application intentionally do not seek to capture every case when there are challenges in generating an evidence base or when there is a small population with a rare disease.
* This approach ensures that technologies routed to the Highly Specialised Technologies Programme fulfil the vision of the programme and manages the displacement in the wider NHS.

However, it can be difficult to identify the exceptional circumstances when the highly specialised technologies methods and processes should be used because of the difficulty in getting the information needed. Proxy information is often relied on and used to make subjective judgements. The routing criteria identify which technologies should be routed for highly specialised technologies guidance. These criteria help make subjective judgements as informed, justifiable, consistent and predictable as possible. NICE’s capacity to develop highly specialised technologies guidance can react to need and there is no limit on the number of technologies that can be routed.

The final routing criteria for the Highly Specialised Technologies Programme are:

* The disease is very rare – defined as 1:50,000 population in England.
* Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications.
* The very rare disease for which the technology is indicated significantly shortens life or severely impairs quality of life.
* There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options.
1. Papp, V. et al. Z. (2021). Worldwide incidence and prevalence of neuromyelitis optica: a systematic review. Neurology, 96(2), 59-77. [↑](#endnote-ref-1)
2. O'Connell, K., et al. (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), 1126-1128. [↑](#endnote-ref-2)
3. Jacob, A., et al. (2013). The epidemiology of neuromyelitis optica amongst adults in the Merseyside county of United Kingdom. Journal of neurology, 260(8), 2134-2137. [↑](#endnote-ref-3)
4. 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 [↑](#endnote-ref-4)
5. Hamid, S. H. et al. (2017). The impact of 2015 neuromyelitis optica spectrum disorders criteria on diagnostic rates. Multiple Sclerosis Journal, 23(2), 228-233. [↑](#endnote-ref-5)
6. Hyun, J. W. et al. (2016). Evaluation of the 2015 diagnostic criteria for neuromyelitis optica spectrum disorder. Neurology, 86(19), 1772-1779. [↑](#endnote-ref-6)
7. Prevalence and incidence of neuromyelitis optica spectrum disorder, aquaporin-4 antibody-positive NMOSD and MOG antibody-positive disease in Oxfordshire, UK [↑](#endnote-ref-7)
8. Huda, S. et al. (2019). Neuromyelitis optica spectrum disorders. Clinical Medicine, 19(2), 169. [↑](#endnote-ref-8)
9. Jasiak-Zatonska, M. et al. (2016). The immunology of neuromyelitis optica—current knowledge, clinical implications, controversies and future perspectives. International journal of molecular sciences, 17(3), 273. [↑](#endnote-ref-9)
10. Alexion. (27th October 2022). Ultomiris showed zero relapses in adults with neuromyelitis optica spectrum disorder (NMOSD) with median treatment duration of 73 weeks [press release]. <https://www.astrazeneca.com/media-centre/press-releases/2022/ultomiris-showed-zero-relapses-in-adults-with-neuromyelitis-optica-spectrum-disorder-nmosd-with-median-treatment-duration-of-73-weeks.html> Accessed November 2022. [↑](#endnote-ref-10)