

**EVIDENCE BRIEFING  
AUGUST 2018**

**Inebilizumab for Neuromyelitis optica**

<b>NIHRIO ID</b>	12557	<b>NICE ID</b>	9560
<b>Developer/Company</b>	Viela Bio	<b>UKPS ID</b>	Not available

**SUMMARY**

Inebilizumab is a humanised monoclonal antibody that is in clinical development for reducing the risk of an attack in patients with Neuromyelitis Optica Spectrum Disorders (NMOSD). NMOSD, previously known as NMO and as Devic's disease, is a rare, disabling autoimmune disease of the central nervous system. It predominantly affects the optic nerve and spinal cord, however involvement of the brain can occur. Patients with NMOSD present with acute, often severe attacks that lead to blindness, limb weakness or paralysis, difficulty controlling the bladder or bowels, fatigue, pain, and other manifestations.

The main objective of current treatments is to reduce the rate of acute NMOSD attacks. This is the most important goal in treating these patients. There are no approved attack-preventing therapies and different off label immunosuppression medications are being used with low level of evidence for efficacy. Inebilizumab is an experimental therapy that specifically targets B lymphocytes which are the source of the pathogenic auto antibody in this disease, the AQP4-IgG. Depleting B cells by Inebilizumab will potentially reduce risk of NMOSD attack. Inebilizumab binds to and depletes CD19+ B-cells including plasmablasts and plasma cells. These CD19+ plasmablasts are the type of B cells that produce the AQP4-IgG which in turn acts against a key water channel protein expressed on astrocytes in the central nervous system. If licensed, inebilizumab may offer a first line disease-modifying treatment option for patients with NMOSD.

## PROPOSED INDICATION

Neuromyelitis Optica Spectrum Disorders (NMOSD).<sup>1</sup>

## TECHNOLOGY

### DESCRIPTION

Inebilizumab (anti-CD19 MAb, MEDI-551) is a humanised anti-CD19 monoclonal IgG1 antibody, which targets the CD-19 receptor on B lymphocytes and cause lysis of the cell and complete B cell depletion. CD19 is widely expressed on the B-cell lineage including on antibody producing cells (plasmablasts and plasma cells), which are at the end of B cell development and maturation line. Autoantibodies against the AQP4 receptor on the water channel of astrocytes in the central nervous system are believed to be the cause of the neuron damage, so depleting these cells has a potentially significant therapeutic effect in preventing NMOSD attack.<sup>2,3</sup>

In the phase II/III clinical trial (NCT02200770) inebilizumab is administered intravenously at a dose of 300mg on day 1 and day 15, and then every 26 weeks thereafter.

### INNOVATION AND/OR ADVANTAGES

No licenced treatment for NMOSD attack prevention exists, and current treatment are used empirically, off-label, without robust supporting data from randomized, controlled clinical studies. Inebilizumab is one of the first medicinal therapies in development to address the cause of the disease. This presents an advantage over current steroid and immunotherapy treatments, which work by non-specifically dampening the immune system and are associated with a variety of risks, including infection.<sup>4</sup>

### DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Inebilizumab does not currently have Marketing Authorisation in the EU/UK for any indication.

- Inebilizumab is a designated orphan drug in the USA in 2016 for NMOSD
- Inebilizumab is a designated orphan drug in the EU in 2017 for NMOSD<sup>5</sup>

## PATIENT GROUP

### DISEASE BACKGROUND

Neuromyelitis Optica Spectrum Disorders (NMOSD), previously known as NMO and as Devic's disease, is a rare, disabling autoimmune disease of the central nervous system. It most commonly

affects the optic nerve and spinal cord, which can lead to optic neuritis and transverse myelitis.<sup>6</sup> Patients present with acute, often severe, attacks of blindness and paraparesis or quadriparesis, accompanied by sensory and sphincter impairments. Most patients have relapsing attacks (separated by months or years with partial recovery), with usually sequential index episodes of optic neuritis and myelitis. A relapsing course is more frequent in women, and nearly 90% of patients are female (typically late middle-aged). Incomplete recovery from attacks is typical, giving rise to accumulative attack-related disability. More rarely, the disease course is monophasic, with nearly simultaneous index episodes of optic neuritis and myelitis. This form may occur in younger individuals with no sex predilection. Rarely, patients experience other neurological manifestations, including intractable vomiting and nausea due to inflammation in the medulla, endocrine and sleep disorders due to involvement of the hypothalamus, and attacks of cerebral oedema that may cause confusion or coma. Patients with NMOSD frequently have other systemic autoimmune disorders, such as systemic lupus erythematosus (SLE), Sjögren's syndrome or myasthenia gravis.<sup>7</sup> NMOSD used to be considered as a variant of multiple sclerosis, but is now recognized as a standalone disease.

The prognosis of NMOSD is variable: patients may recover completely from individual attacks, but residual neurological deficits are common and sometimes severe. Unrecognised or untreated, up to 30% of patients may die in the first 5 years of their illness of an attack of severe myelitis leading to respiratory failure. A high proportion of patients will become legally blind in one or both eyes and/or have substantial residual paraparesis. The impact of early treatment with an effective long term agent is unknown, but current evidence suggests that the attack rate may be reduced by over 50% with effective immunosuppressive therapy.<sup>7</sup>

## CLINICAL NEED AND BURDEN OF DISEASE

The prevalence of NMO in the UK is 0.7 per 100,000.<sup>8</sup>

According to HES data for England, there were 418 admissions in 2016-17 for neuromyelitis optica (ICD-10 G36.0), and 513 finished consultant episodes.<sup>9</sup>

## PATIENT TREATMENT PATHWAY

### PATIENT PATHWAY

There is no cure at present for NMOSD, and treatments focus on preventing acute attacks and minimizing the damage when attack occur. For treating an acute attack patients usually receive steroids in the first instance, followed by therapeutic plasma exchange if further treatment is required. As NMO takes a relapsing course in most cases, with often incomplete recovery and rapid accumulation of neurological deficits, long-term off label maintenance immunosuppressive treatments are used.<sup>10</sup>

### CURRENT TREATMENT OPTIONS

- Acute: High-dose corticosteroids, in particular intravenous methylprednisolone (IVMP), are used as first-line therapy to reduce inflammation around the site of the nerve damage.

- When steroids are ineffective, plasma exchange or plasmapheresis is used as escalation therapy.<sup>4</sup>
- Long-term immunosuppressants such as azathioprine, methotrexate or mycophenolate are used off-label with the goal of reducing risk of relapse, but have not been proven effective in randomized controlled studies. These agents appear to have similar efficacy based on case series and uncontrolled studies.<sup>10</sup>
- Similarly, off-label Rituximab therapy appears to reduce the frequency of NMOSD relapses and neurological disability in patients with NMOSD based on uncontrolled studies and case series, although the safety profile suggests that caution should be used in prescribing it as first-line therapy.<sup>11</sup>

## PLACE OF TECHNOLOGY

If licensed, inebilizumab would offer a first line treatment option for patients with NMOSD who currently have no curative treatments available.

## CLINICAL TRIAL INFORMATION

<b>Trial</b>	N-Momentum, <a href="#">NCT02200770</a> , CD-IA-MEDI-551-1155, 2014-000253-36; inebilizumab vs placebo; phase II/III.
<b>Sponsor</b>	MedImmune
<b>Status</b>	Ongoing
<b>Source of Information</b>	Publication, <sup>6</sup> trial registry <sup>1</sup>
<b>Location</b>	EU (not incl UK), USA, Canada and other countries.
<b>Design</b>	Randomised, placebo-controlled.
<b>Participants</b>	n=252 (planned); aged 18 years and older; NMO/NMOSD.
<b>Schedule</b>	Randomised to inebilizumab 300 mg IV on day 1 and day 15, then every 26 weeks thereafter; or placebo on day 1 and day 15.
<b>Follow-up</b>	Active treatment for maximum 197 days, followed by an open label period of minimum one and maximum three yrs.
<b>Primary Outcomes</b>	Time to onset of an adjudicated NMO/NMOSD attack.
<b>Secondary Outcomes</b>	Annualised attack rate; adverse events; TMAX and CMAX; incidence of anti-drug antibodies directed against MEDI-551; worsening in EDSS (Expanded Disability Status Scale); change in low-contrast visual acuity binocular score; cumulative total active MRI lesions; number of NMO/NMOSD-related in-patient hospitalisations.
<b>Key Results</b>	-
<b>Adverse effects (AEs)</b>	-
<b>Expected reporting date</b>	Study completion date reported as Aug 2019.

## ESTIMATED COST

The cost of inebilizumab is not yet known.

## ADDITIONAL INFORMATION

## RELEVANT GUIDANCE

### NICE GUIDANCE

None identified.

### NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Neuromyelitis Optica Service (Adults and Adolescents). D04/S(HSS)/b.
- NHS England. 2013/14 NHS Standard Contract for Neurosciences: Specialised Neurology (Adult). D04/S/a.
- NHS England. 2013/14 NHS Standard Contract for Specialised Ophthalmology. D12/S/a.

### OTHER GUIDANCE

- Trebst et al. Update on the diagnosis and treatment of neuromyelitis optica: recommendations of the Neuromyelitis Optica Study Group (NEMOS). 2014.<sup>10</sup>

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