Health Technology Briefing
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Inebilizumab for neuromyelitis optica spectrum disorders

Company/Developer	Amgen Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 38376	NICE ID: Not available	UKPS ID: Not available

Licensing and Market Availability Plans

Inebilizumab is currently in phase II/III clinical development.

Summary

Inebilizumab is in clinical development for the treatment of adults with neuromyelitis optica spectrum disorder (NMOSD). NMOSD is a rare autoimmune condition in which the immune system attacks and damages one's own spinal cord and optic nerves (nerves in the eyes). Autoantibodies (proteins that attacks own cells) against a cell surface protein found in neural cells called aquaporin-4 (AQP4) bind to AQP4 channels on astrocytes (cells in the brain and spinal cord), resulting in damage to astrocytes and other neural cells, causing nervous system damage. This causes symptoms such as numbness, weakness, bowel and bladder difficulties and vision loss. There is no cure for NMOSD and currently treatment focus on treatment of sudden attacks and symptoms of them, as well as treating relapses (return or worsening of attacks) and preventing them.

Inebilizumab is a monoclonal antibody (type of protein) that attaches to immune cells called B cells and destroys them. In most people with NMOSD, B cells produce antibodies that attack AQP4, a protein involved in nerve cell function. By reducing the numbers of B cells, the medicine is expected to prevent damage to nerve cells and reduce the symptoms of the condition. Inebilizumab will be administered intravenously. Patients receiving current treatment options still experience relapses and treatment-related side effects. Therefore, there remains unmet need in in the treatment of NMOSD. If approved inebilizumab will offer a treatment option for patients with NMOSD.

Proposed Indication

For the treatment of adult patients with neuromyelitis optica spectrum disorders (NMOSD).[1]

Technology

Description

Inebilizumab (Uplizna, anti-CD19 MAb, MEDI-551) is a humanised anti-CD19 monoclonal IgG1 antibody, which targets the CD-19 receptor on B lymphocytes, including the AQP4-Ig producing plasmablasts, and mediates the antibody-dependent and cell-mediated toxicity of B cells, which results in B-cell depletion and suppression of disease activity.[2,3] CD19 is widely expressed on the B-cell lineage including on antibody producing cells (plasmablasts and plasma cells).[2,3] In NMOSD, the presence of AQP4-Ig is highly specific. Autoantibodies against the AQP4 (AQP4-Ig) binds to AQP4 channels on astrocytes, triggering activation of the classical complement cascade, leading to granulocyte, eosinophil, and lymphocyte infiltration. This culminates in injury first to astrocyte, then oligodendrocytes followed by demyelination and neuronal loss.[4] Therefore, depleting the AQP4-Ig producing cells has a potentially therapeutic effect in preventing or reducing NMOSD attacks.

Inebilizumab is in development for the treatment of NMOSD patients, aged 18 years and older.[1,5] In the phase II/III trial (NCT02200770), inebilizumab will be administered intravenously (IV) at a dose of 300mg.[1]

Key Innovation

There is currently no cure for NMOSD.[6] In the phase III clinical trial N-Momentum (NCT02200770), inebilizumab treatment significantly reduced the risk of clinical relapses, disability worsening, MRI lesion activity, and requirement of hospitalisations compared with placebo, and in a long-term analysis of this trial, inebilizumab was associated with a continuous reduced risk of NMOSD attacks and reduced odds of worsening disability versus placebo.[3,7] Immunomodulatory and immunosuppressive therapies are currently used to manage NMOSD. However, patients treated with these current treatment options still experience relapses and treatment-related side effects limit their use.[8] Consequently, significant unmet need remains for more effective treatment options in NMOSD. Inebilizumab is currently approved in the EU, and it may potentially substitute conventional treatment such as rituximab and classical immunosuppressive therapies, which were as yet the mainstay of treatment for both, AQP4-IgG-positive and -negative NMOSD.[9,10] If licensed, inebilizumab will offer an additional treatment option for NMOSD patients.

Regulatory & Development Status

Inebilizumab currently has Marketing Authorisation in the EU for treatment of adults with NMOSD who are AQP4 antibody positive.[10]

Inebilizumab is also currently in phase II/III clinical development for myasthenia gravis, autoimmune encephalitis, IgG4 related disease and systemic sclerosis.[11]

Inebilizumab was granted orphan drug designation in the USA in 2016 for the treatment of neuromyelitis optica and NMOSD.[12]

Patient Group

Disease Area and Clinical Need

NMOSD is a relapsing autoimmune demyelinating disease of the central nervous system (CNS) that primarily affects the spinal cord and the optic nerves. Antibodies to the AQP4-IgG have been identified as pathologic and are part of the diagnostic criteria for NMOSD. Symptoms of NMOSD can include numbness and weakness of the extremities, and bowel and bladder difficulties secondary to transverse myelitis, or vision loss secondary to optic neuritis.[13] Over 95% of patients with NMOSD have no relatives with the disease, but there is a strong association with a family history of autoimmune diseases (50% of cases). NMOSD is seen in all races, genders and ages with incidence rates differing between groups but NMOSD cases seropositive for AQP4-IgG is most common in late middle-aged women.[14]

NMSOD has a high mortality rate if not diagnosed and treated appropriately, with 23% of patients having a median survival of three years from enrolling in studies and at five years from onset 50% of untreated patients require a wheelchair or have significant visual loss.[15] In Europe there is an estimated 1 case of NMOSD per 100,000 people, potentially affecting less than 1,000 people in the UK.[16] In England, 2022-23, there were 944 finished consultant episodes (FCE) and 739 admissions for neuromyelitis optica (ICD-10 code G36.0) which resulted in 4,416 FCE bed days and 490 day cases.[17]

Recommended Treatment Options

There are currently no NICE recommended treatment options for NMOSD. However, current treatments focus on the treatment of acute attacks and relapses, prevention of relapses and treatment of residual symptoms of an attack. 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.[6,18]

Clinical Trial Information

Trial	**N-Momentum**, NCT02200770; A Double-masked, Placebo-controlled Study With Open-label Period to Evaluate the Efficacy and Safety of MEDI-551 in Adult Subjects With Neuromyelitis Optica and Neuromyelitis Optica Spectrum Disorders. **Phase II/III:** Completed **Location(s):** 7 countries in EU, USA, Canada and other countries **Study completion date:** November 2020
Trial Design	Randomised, parallel assignment, quadruple masked
Population	N=231; subjects with recently active neuromyelitis optica /NMOSD who are seropositive or seronegative for autoantibodies against AQP4-IgG; aged 18 years and older.
Intervention(s)	Participants in the randomised-control period (RCP) received inebilizumab 300mg on Day 1 and Day 15. Participants in the open label period (OLP) received inebilizumab 300 mg on Day 1 and matching placebo on Day 15, followed by a single IV dose of inebilizumab 300 mg every 6 months until maximum of 3 years after the last participant entered the OLP.
Comparator(s)	Matched placebo.
Outcome(s)	Primary outcome:

	Time to adjudication committee (AC)-determined NMOSD attack during RCP [time frame: day 1 (baseline) through day 197] See trial record for full list of other outcomes.
Results (efficacy)	See trial record.
Results (safety)	See trial record.

Trial	**N-MOmentum LT**, NCT06180278; A Long-term, Open-label, Low-interventional Safety Study of Inebilizumab in the Treatment of NMOSD **Phase IV:** Not yet recruiting **Primary completion date:** June 2028
Trial Design	Single group assignment, open label
Population	N=30 (expected); subjects who have completed at least 2 years in the open-label period of the N-MOmentum study or are newly initiating inebilizumab treatment at a participating site
Intervention(s)	Participants with NMOSD who previously enrolled in N-MOmentum study, who participated for at least 2 years in the open label phase (OLP) of the study, and participants newly initiating will have haematology, chemistry, B-cell count, serum immunoglobulin (Ig) levels, adverse events, concomitant medications list, NMOSD attacks information, antidrug antibody (ADA) status and titres collected.
Comparator(s)	No comparator
Outcome(s)	Primary outcomes: - Change from baseline in serum Ig levels (total Ig, IgG, IgM, IgA, IgE) over time [time frame: up to 42 months] - Change from baseline in peripheral CD20+ B-cell counts over time [time frame: up to 42 months] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of inebilizumab is not yet known.

Relevant Guidance

NICE Guidance

No guidance 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

- Wingerchuk et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. 2015.[19]
- Trebst et al. Update on the diagnosis and treatment of neuromyelitis optica: recommendations of the Neuromyelitis Optica Study Group (NEMOS). 2014.[20]

Additional Information

Amgen Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

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