Health Technology Briefing
June 2023

Ocrelizumab (subcutaneous) for the treatment of primary progressive or relapsing multiple sclerosis

Company/Developer	Roche Products Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 34693	NICE ID: Not available	UKPS ID: 670050

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Ocrelizumab (subcutaneous) is in clinical development for the treatment of relapsing multiple sclerosis (MS) and primary progressive MS. MS is a condition where the body's immune system mistakenly attacks the nerves in the central nervous system which consists of the brain and spinal cord. This damage prevents messages travelling from the central nervous system (CNS) to other parts of the body. It causes a range of potential symptoms from pins and needles to difficulties with balance and walking. The symptoms of MS can restrict the individual's physical activity and income-earning ability, resulting in a major financial burden on the patient and a substantial economic burden because of indirect and informal care costs, with most patients needing additional assistance in conducting daily activities, which is mostly provided by informal caregivers, such as partners or other relatives.

Ocrelizumab is a disease-modifying therapy, which is a type of medicinal product that treats the underlying symptoms of MS. It is a second-generation recombinant humanized monoclonal antibody that targets white blood cells in the body's immune system. It sticks to a type of these cells called B cells and stops them from attacking the CNS. This prevents inflammation and nerve damage, reducing the number and severity of relapses and slowing the worsening of symptoms. Ocrelizumab given as intravenous infusion is already approved for the treatment of relapsing MS and early primary progressive MS, however ocrelizumab administered as a subcutaneous (under the skin) injection may have some advantages over IV including at home administration that may appeal to some patients and slower absorption rates that may abrogate side effects. If licensed, ocrelizumab subcutaneous will offer an additional therapeutic option for patients with MS.

Proposed Indication

Treatment of adult patients with relapsing or primary progressive multiple sclerosis (MS).[1]

Technology

Description

Ocrelizumab (Ocrevus) is a recombinant humanised monoclonal antibody that selectively targets CD20-expressing B cells (types of white blood cells).[2] These white blood cells play a role in MS by attacking the sheaths around the nerves in the brain and spinal cord, causing inflammation and damage. By targeting the B cells, ocrelizumab helps to reduce their activity and thereby relieves symptoms or slows down the worsening of the disease.[3] Following cell surface binding, ocrelizumab selectively depletes CD20-expressing B cells through antibody-dependent cellular phagocytosis (ADCP), antibody-dependent cellular cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC), and apoptosis. The capacity of B-cell reconstitution and pre-existing humoral immunity are preserved. In addition, innate immunity and total T-cell numbers are not affected.[2]

Ocrelizumab administered as SC is currently in phase III clinical development for the treatment of MS. In the clinical trial (NCT05232825, OCARINA II), patients are administered one subcutaneous (SC) injection at a dose which is expected to result in non-inferior exposure to ocrelizumab intravenous (IV). The subsequent doses of study drug will be administered as SC injections. A minimum of 22 weeks should be kept between the first and second SC doses, and between subsequent SC doses. Participants will undergo 48 weeks of study treatment.[1]

Key Innovation

Multiple sclerosis (MS) is the most common cause of serious physical disability in adults of working age. it has a significant detrimental effect on quality of life for people living with it and their families/carers.[4]
Ocrelizumab administered as an intravenous infusion (IV) is the first CD20 + B-cell-selective monoclonal antibody approved for treatment of relapsing multiple sclerosis (RMS) and primary progressive multiple sclerosis (PPMS).[2,5]
However, there is a common interest among patients, clinicians and pharmaceutical industry in moving from IV to SC administration of monoclonal antibodies due to benefits of improved patient compliance and reduced costs to the healthcare system.[6] Ocrelizumab administered as SC may have some advantages over IV including at home administration that may appeal to some patients and slower absorption rates that may abrogate side effects.[7]
If licensed, ocrelizumab SC will provide an additional treatment option for patients with primary progressive MS and relapsing MS.

Regulatory & Development Status

Ocrevus IV infusion has marketing authorisation in the EU/UK for treatment of relapsing and progressive MS.[2,3]

Patient Group

Disease Area and Clinical Need

MS is an acquired, chronic, immune-mediated, inflammatory condition of the central nervous system (CNS) that can affect the brain, brainstem, and spinal cord. The inflammatory process causes areas of demyelination (damage to white matter), gliosis (scarring), and neuronal damage throughout the CNS.[8] It is a lifelong condition that can sometimes cause serious disability, although it can occasionally be mild. In many cases, it is possible to treat symptoms. Average life expectancy is slightly reduced for people with MS. It is most diagnosed in people in their 20s, 30s and 40s although it can develop at any age. It is about 2 to 3 times more common in women than men.[9] MS can have a wide range of symptoms including muscle spasms, stiffness and weakness, vision problems, abnormal sensations, mobility problems and pain.[10] The symptoms are unpredictable. Some people's symptoms develop and worsen over time while for others, they come and go. The periods when these symptoms get worse are known as relapses, while the periods when the symptoms improve or disappear are known as remissions.[10] In primary progressive MS, symptoms gradually worsen and accumulate over several years, and there are no periods of remission, though people often have periods where their condition appears to stabilise.[9] The cause of MS is unknown — it is thought that acute then chronic immune-mediated inflammation is precipitated by an abnormal response to environmental triggers in people who are genetically predisposed.[11]

In 2018, the estimated prevalence of MS was 190 cases per 100,000 population, with 105,800 individuals in England. MS is more than twice as common in females than males, 272 versus 106 per 100,000 population.[12] In England (2021-22), there were 60,069 finished consultant episodes (FCEs) and 57,462 admissions for multiple sclerosis (ICD-10 code G35) which resulted in 34,534 FCE bed days and 52,150 day cases.[13]

Recommended Treatment Options

The following treatments are currently recommended by the National Institute for Health and Care Excellence (NICE) for the treatment of adults with relapsing MS.[14]

- Diroximel fumarate
- Ponesimod
- Ozanimod
- Ofatumumab
- Alemtuzumab
- Peginterferon beta-1a
- Cladribine
- Ocrelizumab
- Dimethyl fumarate
- Teriflunomide
- Fingolimod
- Natalizumab

Ocrelizumab is recommended as an option for treating early primary progressive MS with imaging features characteristic of inflammatory activity in adults.

Clinical Trial Information

Trial	**OCARINA II;** NCT05232825**.** A Study to Investigate the Pharmacokinetics, Pharmacodynamics, Safety and Radiological and Clinical Effects Of Subcutaneous Ocrelizumab Versus Intravenous Ocrelizumab In Patients With Multiple Sclerosis **Phase III** - Recruiting **Location(s):** 5 EU countries, USA, Canada, and other countries

	Primary completion date: March 2023
Trial Design	Randomised, open label, parallel assignment
Population	N=234 (estimated); subjects diagnosed of primary progressive MS (PPMS) or relapsing MS (RMS); aged 18 to 65years
Intervention(s)	Ocrelizumab SC injection
Comparator(s)	Ocrelizumab IV infusion
Outcome(s)	Serum ocrelizumab area under the concentration-time curve (AUCW1-12) [Time Frame: Day 1 to Week 12] See trial records for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

NHS indicative price of Ocrevus 300mg/10ml concentrate for solution for infusion is £4,790 per vial.[15]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Tolebrutinib for treating relapsing multiple sclerosis (TS ID 11845). Expected publication date to be confirmed.
- NICE technology appraisal in development. Cladribine for treating relapsing multiple sclerosis (TS ID 11834). Expected publication date to be confirmed.
- NICE technology appraisal in development. Ublituximab for treating relapsing-remitting multiple sclerosis (TS ID 11795). Expected publication date to be confirmed
- NICE technology appraisal. Diroximel fumarate for treating relapsing–remitting multiple sclerosis (TA794). June 2022.
- NICE technology appraisal. Ponesimod for treating relapsing–remitting multiple sclerosis (TA767). February 2022.
- NICE technology appraisal. Ozanimod for treating relapsing–remitting multiple sclerosis (TA706). June 2021.
- NICE technology appraisal. Ofatumumab for treating relapsing multiple sclerosis (TA699). May 2021.
- NICE technology appraisal. Alemtuzumab for treating highly active relapsing remitting multiple sclerosis (TA312). March 2020.
- NICE technology appraisal. Peginterferon beta-1a for treating relapsing–remitting multiple sclerosis (TA624). February 2020.
- NICE technology appraisal. Cladribine for treating relapsing–remitting multiple sclerosis (TA616). December 2019
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- NICE technology appraisal. Beta interferons and glatiramer acetate for treating multiple sclerosis (TA527). June 2018.
- NICE technology appraisal. Dimethyl fumarate for treating relapsing-remitting multiple sclerosis (TA320). August 2014.
- NICE technology appraisal. Teriflunomide for treating relapsing–remitting multiple sclerosis (TA303). June 2014.
- NICE technology appraisal. Fingolimod for the treatment of highly active relapsing–remitting multiple sclerosis (TA254). April 2012.
- NICE technology appraisal. Natalizumab for the treatment of adults with highly active relapsing–remitting multiple sclerosis (TA127). August 2007.
- NICE guideline. Multiple sclerosis in adults: management (NG220). June 2022.
- NICE quality standard. Multiple sclerosis (QS108). January 2016

NHS England (Policy/Commissioning) Guidance

- NHS England. Treatment Algorithm for Multiple Sclerosis Disease-Modifying Therapies (NHS England Reference: 170079ALG). 2019

Other Guidance

- Ghezzi A. European and American Guidelines for Multiple Sclerosis Treatment. 2018.[16]
- Association of British Neurologists. Revised (2015) guidelines for prescribing disease-modifying treatments in multiple sclerosis. 2015.[17]

Additional Information

References

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