Health Technology Briefing
January 2022

Glatiramer Acetate Depot for treating relapsing forms of multiple sclerosis in adults aged 18 to 55 years

Company/Developer	Viatris – UK licensee (Mapi Pharma developer)

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 28564	NICE ID: 10620	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Glatiramer Acetate (GA) Depot is currently in development for the treatment of relapsing forms of multiple sclerosis (MS). MS is a neurological autoimmune condition that causes problems with vision, arm or leg movement, sensation and/or balance. Relapsing MS (RMS) is the most common type of MS and those living with it will have episodes of new or worsening symptoms i.e., relapses which are generally followed by periods of partial or complete recovery (remissions). There is no cure for MS, but treatments can be used to manage symptoms; to reduce the number of relapses, delay disease progression or disability, and limit new disease activity. Specifically, for RMS, disease modifying therapies are used. Patients currently administer medication daily; additional treatments are required to reduce the number of treatments required whilst also reducing relapses.

GA Depot is an intramuscular injection based on an already licensed drug. It is not fully understood how GA reduces relapses, but it is thought it involves T-cells (a type of immune cell). GA Depot is advantageous compared to the already licensed GA as it is long-lasting with only one injection needed every four weeks as opposed to the current daily or thrice weekly dosing regimen on GA. If licensed, GA Depot will offer an additional treatment option for adults aged between 18 and 55 years with RMS.

Proposed Indication

Treatment of relapsing forms of multiple sclerosis (RMS) in patients aged 18-55.[1]

Technology

Description

Glatiramer acetate (GA) Depot is a long-acting version of GA (Copaxone).[2] The mechanism by which GA exerts therapeutic effects in RMS is not fully elucidated but is presumed to involve modulation of immune processes. Studies in animals and MS patients suggest GA acts on innate immune cells, including monocytes, dendritic cells and B cells, which in turn modulate adaptive functions of B and T cells inducing anti-inflammatory and regulatory cytokine secretion. Whether the therapeutic effect is mediated by the cellular effects described above is not known because the pathophysiology of MS is only partially understood.[3]

In a current phase III trial (NCT04121221), GA Depot or matching placebo is given as an intramuscular injection once every four weeks for a period of 52 weeks. If the first period is completed, participants are offered to continue to the open-label period of the trial for an additional 52 weeks where 40mg of GA Depot will be administered by intramuscular injection once every four weeks.[1]

Key Innovation

As it is only administered once every four weeks, GA Depot would avoid patients having to inject daily or thrice weekly.[1] This intramuscular injection, may be beneficial to patients as opposed to subcutaneous injections but evidence on preferential administration is unclear.[4]

Results from a phase II clinical trial showed that no evidence of disease activity was achieved by 84.6% of the population in the core study, 81.8% for the 2nd year of the study and 90% for years 3, 4 and 5 of the study. Most adverse events were mild.[5]

If licensed, GA Depot will offer a long-lasting treatment option for adults aged between 18 and 55 years with RMS.

Regulatory & Development Status

GA, as a subcutaneous injection, has Marketing Authorisation in the EU/UK for MS (relapsing-remitting).[3,6]

GA Depot is currently in phase II clinical trial for the treatment of primary progressive MS.[7]

Patient Group

Disease Area and Clinical Need

MS is a condition that can affect the brain and spinal cord, causing a wide range of potential symptoms, including problems with vision, arm or leg movement, sensation and/or balance.[8] The clinical course of MS is highly heterogeneous. Approximately 85% of patients present with RMS. A review of risk factors associated with RMS found that exposure to Epstein-Barr virus appear to increase the risk of RMS.[9] RRMS is the most common course of the disease. It is characterised by periods of exacerbation of symptoms (relapses) followed by unpredictable periods of stability (remission). The severity and frequency of relapses varies greatly between patients, but on average occurs once or twice per year.[10] Some of the most common

symptoms in RMS around the time of diagnosis are problems with eyesight, slowed thinking (cognitive symptoms) and unusual feelings in the skin (such as pins and needles or numbness). Fatigue is also very common. This is not normal tiredness, but a mental or physical exhaustion out of all proportion to the activity carried out.[11]

In England, MS estimated prevalence is 190 cases per 100,000 population, with 105,800 individuals in England living with the condition. About 85% of patients are initially diagnosed with RRMS, which means that the prevalence of RRMS is approximately 162 cases per 100,000 which equals to 89,930 people in England living with the condition. It is estimated that between 8 and 11 new cases of MS are diagnosed each year in England per 100,000 population.[12] According to Hospital Episodes Statistics (HES) (ICD-10: G35) data in 2020/21, in England, there were 47,489 finished consultant episodes (FCEs), 45,308 admissions, resulting in 26,417 FCE bed days and 41,440 day cases with primary diagnosis of multiple sclerosis.[13]

Recommended Treatment Options

Current NICE recommended treatment option for RMS are as follows:[14]

- Alemtuzumab (highly active relapsing remitting multiple sclerosis (RRMS))
- Peginterferon beta-1a
- Ozanimod
- Ofatumumab
- Cladribine (highly active RRMS)
- Ocrelizumab
- Dimethyl fumarate
- Teriflunomide
- Fingolimod (highly active RRMS)
- Natalizumab (highly active RRMS)

Clinical Trial Information

Trial	NCT04121221; A Phase III Study in Subjects With Relapsing Forms of Multiple Sclerosis (RMS) to Assess Efficacy, Safety and Tolerability of GA Depot, a Long Acting IM Injection of Glatiramer Acetate, Once Monthly Compared to Placebo **Phase III:** active, not recruiting **Location:** 2 EU countries, USA, Russia, and other countries **Primary Completion Date:** June 2022
Trial Design	Randomised, parallel assignment, quadruple-blinded, placebo-controlled
Population	N = 1,016; 18-55 years old; MS diagnosis fulfilling the 2017 McDonald Criteria; Subjects should be relapse free and neurologically stable from one month before screening visit and from screening visit to baseline visit; subjects must have experienced at least one relapse in the 12 months prior to screening visit or two relapses in the 24 months prior to screening visit, or if one relapse in the 24 months prior to screening visit, subjects should have at least one enhancing lesion in the last MRI scan (within 12 months prior to screening visit)
Intervention(s)	40mg GA Depot (intramuscular injection) once every 4 weeks
Comparator(s)	Matched placebo

Outcome(s)	Annualised Relapse Rate (ARR) [Time frame: 52 weeks]
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of GA Depot in not yet known.

Relevant Guidance

NICE Guidance

- 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. 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.
- NICE technology appraisal. Ocrelizumab for treating relapsing–remitting multiple sclerosis (TA533). July 2018.
- NICE technology appraisal guidance. 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 clinical guideline. Multiple sclerosis in adults: management (CG186). October 2014.
- 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). London: NHS England; 2019.

Other Guidance

- NICE pathway. Multiple Sclerosis. June 2021.[15]
- Ghezzi. A. European and American Guidelines for Multiple Sclerosis Treatment. 2018.[16]

Additional Information

Viatris/Mapi Pharma 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

1 ClinicalTrials.gov. *A Study to Asses Efficacy, Safety and Tolerability of Monthly Long-acting IM Injection of GA Depot in Subjects With RMS*. *Trial ID: NCT04121221*. Status: Active, not recruiting. Available from: https://clinicaltrials.gov/ct2/show/NCT04121221 [Accessed 17 December 2021].

2 Mapi Pharma. *Glatiramer Acetate Depot.* 2021. Available from: https://mapi-pharma.com/products/glatiramer-acetate-depot-gad/ [Accessed 17 December 2021].

3 Electronic Medicines Compendium. *Copaxone 40 mg/ml solution for injection in pre-filled syringe.* Available from: https://www.medicines.org.uk/emc/product/7046/smpc#gref [Accessed 17 December 2021].

4 Ridyard CH, Dawoud DMM, Tuersley LV, Hughes DA. A Systematic Review of Patients' Perspectives on the Subcutaneous Route of Medication Administration. *The Patient - Patient-Centered Outcomes Research*. 2016;9(4):281-92. Available from: https://doi.org/10.1007/s40271-015-0160-x.

5 Mapi Pharma. *Mapi Pharma Presents Glatiramer Acetate Depot (GA Depot) Results at the 8th Joint ACTRIMS-ECTRIMS Meeting MSVirtual2020.* 2021. Available from: https://www.globenewswire.com/news-release/2020/09/10/2091682/0/en/Mapi-Pharma-Presents-Glatiramer-Acetate-Depot-GA-Depot-Results-at-the-8th-Joint-ACTRIMS-ECTRIMS-Meeting-MSVirtual2020.html [Accessed 17 December 2021].

6 British National Formulary (BNF). *GLATIRAMER ACETATE.* Available from: https://bnf.nice.org.uk/drug/glatiramer-acetate.html [Accessed 17 December 2021].

7 ClinicalTrials.gov. *3 Studies found for: GA depot.* 2021. Available from: https://clinicaltrials.gov/ct2/results?cond=&term=GA+depot&cntry=&state=&city=&dist= [Accessed 17 December 2021].

8 National Health Service. *Overview - Multiple sclerosis.* 2018. Available from: https://www.nhs.uk/conditions/multiple-sclerosis/ [Accessed 17 December 2021].

9 McKay KA, Kwan V, Duggan T, Tremlett H. Risk factors associated with the onset of relapsing-remitting and primary progressive multiple sclerosis: a systematic review. *BioMed research international*. 2015. Available from: https://doi.org/10.1155/2015/817238.

10 National Institute for Health and Care Excellence. *Multiple sclerosis.* Available from: https://bnf.nice.org.uk/treatment-summary/multiple-sclerosis.html [Accessed 17 December 2021].

11 Multiple Sclerosis Trust. *Relapsing remitting MS.* Available from: https://mstrust.org.uk/a-z/relapsing-remitting-ms-0#am-i-having-a-relapse [Accessed 17 December 2021].

12 GOV.UK. *Multiple sclerosis: prevalence, incidence and smoking status - data briefing.* 2020. Available from: https://www.gov.uk/government/publications/multiple-sclerosis-prevalence-incidence-and-smoking-status/multiple-sclerosis-prevalence-incidence-and-smoking-status-data-briefing [Accessed 17 December 2021].

13 NHS Digital. *Hospital Admitted Patient Care Activity, 2020-21: Diagnosis*. Available from: https://files.digital.nhs.uk/D9/DD187B/hosp-epis-stat-admi-diag-2020-21-tab.xlsx [Downloaded 08 October 2021].

14 National Institute for Health and Care Excellence. *Disease-modifying therapies for multiple sclerosis.* Available from: https://pathways.nice.org.uk/pathways/multiple-

sclerosis#path=view%3A/pathways/multiple-sclerosis/disease-modifying-therapies-for-multiple-sclerosis.xml&content=view-index [Accessed 17 December 2021].

15 National Institute for Health and Care Excellence. *Multiple sclerosis overview.* 2021. Available from: https://pathways.nice.org.uk/pathways/multiple-sclerosis [Accessed 17 December 2021].

16 Ghezzi A. European and American Guidelines for Multiple Sclerosis Treatment. *Neurology and Therapy*. 2018;7(2):189-94. Available from: https://doi.org/10.1007/s40120-018-0112-1.

NB: This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.