Report KESIMPTA® ofatumumab

Product Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Ofatumumab **Brand Name:** Kesimpta® **Originator/licensee:** Novartis Ireland Ltd **Classification:** NCE **ATC code:** L01XC10 **Orphan Status:** **ES:** No **USA:** No **Mechanism of action:** a fully human monoclonal antibody that targets a receptor called CD20 expressed on the B-cells, that provides rapid B-cell depletion.	**Authorized Indication:** **EMA:** Ofatumumab is indicated for the treatment of adult pts with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features **FDA:** Ofatumumab is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. **Route of administration:** SC **Licensing status** **CHMP positive opinion:** 28/01/2021 **FDA M.A. date:** 20/08/2020 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** No --- **ABBREVIATIONS:** **AISM:** Associazione Italiana Sclerosi Multipla **ARR**: Annualized Relapse Rate **CDP**: Confirmed Disability Progression **DH**: Day Hospital **EDSS**: Expanded Disability Status Scale **IV**: intravenously **MS**: Multiple Sclerosis **Pts:** patients **RRR:** Relative risk reduction **SC:** subcutaneous	**Summary of clinical EFFICACY:** The **ASCLEPIOS I (NCT02792218)** and **ASCLEPIOS II (NCT02792231)** studies are twin, identical design, flexible duration (up to 30 months), double-blind, randomized, multi-center Phase III studies The ASCLEPIOS I and II studies enrolled 1,882 pts with MS, 18-55 years of age, EDSS score between 0 and 5.51. Ofatumumab demonstrated a significant reduction in ARR (primary endpoint) by 51% (0.11 vs 0.22) and 59% (0.10 vs 0.25) compared with teriflunomide (p<.001 in both studies) in ASCLEPIOS I and II, respectively. Ofatumumab also showed a RRR of 34.4% (p=.002) in 3-month CDP compared with teriflunomide in a pre-specified meta-analysis, as defined in ASCLEPIOS I. Ofatumumab significantly reduced the mean number of both Gd+ T1 lesions (98% and 94% RRR in ASCLEPIOS I and II, respectively, both p<.001) and new or enlarging T2 lesions (82% and 85% RRR in ASCLEPIOS I and II, respectively, both P<.001) vs. teriflunomide. [1] **Summary of clinical SAFETY:** Ofatumumab had a similar safety profile to teriflunomide, with the frequency of serious infections and malignancies also being similar across both treatment groups. Upper respiratory tract infection, headache, injection-related reactions, and local injection site reactions were the most commonly observed adverse reactions with Ofatumumab (incidence >10%). Injection-related reactions occurred in 20.2% in the ofatumumab group and in 15.0% in the teriflunomide group (placebo injections). Serious infections occurred in 2.5% and 1.8% of the pts, respectively. [1] **Ongoing studies:** ● **For the same indication:** Yes, NCT03650114 ● **For other indications:** Yes *[Fase III, but if it is an O/OE drug, also Fase II]* **Discontinued studies (for the same indication):** No ***References*** 1. *Hauser SL, Bar-Or A, Cohen JA, et al. ASCLEPIOS I and ASCLEPIOS II Trial Groups. Ofatumumab versus Teriflunomide in Multiple Sclerosis. N Engl J Med. 2020 Aug 6;383(6):546-557. doi: 10.1056/NEJMoa1917246.* 2. *https://www.express-scripts.com/corporate/articles/fda-approved-drugs-september-2020* 3. *https://ww.epicentro.iss.it/sclerosi-multipla/epidemiologia* 4. *https://ww.ema.europa.eu/en/medicines/human/summaries-opinion/kesimpta* 5. *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6281141/* 6. *https://www.micromedexsolutions.com/home/dispatch* 7. *https://mymsaa.org/news/fda-approves-ofatumumab-the-first-self-administered-b-cell-therapy-for-relapsing-forms-of-ms/*	**Cost of therapy** In USA estimated wholesale acquisition cost (WAC) per dose is roughly $6,900 (a single dose is a prefilled syringes and pen devices containing 20mg of Ofatumumab for SC injection). **Posology:** 20 mg every 4 weeks after 20-mg loading doses at days 1, 7, and 14. [2] **Epidemiology** In Italy MS has a prevalence of 113/100.000 and it is estimated that 68.000-75.000 people are affected with MS with 1800-2000 new cases every year. [3] Based on a recent study conducted by AISM, the total number of people with MS in Italy is over 118.000. [3] Relapsing-remitting MS is the most common form of the disease: about 85% of pts with MS have a relapsing-remitting disease onset; in about 65% of cases this form evolves towards the secondary progressive form. [4] --- **POSSIBLE PLACE IN THERAPY** Currently, most disease-modifying agents (immunomodulating or immunosuppressives) have been approved for use only in relapsing forms of MS. For pts with RMS who have failed previous therapies the use of natalizumab (second-line treatment) is recommended [5] [6] **OTHER INDICATIONS IN DEVELOPMENT** B-Cell Lymphomas, Small Lymphocytic Lymphoma, Chronic Lymphocytic Leukemia **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT** NO **OTHER DRUGS IN DEVELOPMENT FOR THE SAME INDICATION** Yes --- *Service reorganization Y/N **Yes** (no more DH IV injection) [7] *Possible off label use Y/N **Yes** --- **NOTES** Unlike the previously approved B-cell therapy Ocrevus (ocrelizumab), Kesimpta will be available as a subcutaneous injection that is auto-administered once monthly directly by the patient. This constitute a great advantage, allowing patients to receive the treatment at home. [4] [7]