Report PONVORY® Ponesimod

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: ponesimod **Brand Name:** Ponvory® **Originator/licensee:** Janssen-Cilag International N.V. **Classification:** NCE **ATC code:**L04AA50 [1] **Orphan Status:** **Eu:**No **Us:**No **Mechanism of action:** ponesimod is a selective immunosuppressant. It binds with high affinity toS1P receptor located on lymphocytes, blocking the capacity of lymphocytes to egress from lymph nodes and reducing the number of lymphocytes in peripheral blood. [2]	**Authorized Indication:** **EMA:.**ponesimod is indicated for the treatment of adult pts with RMS with active disease defined by clinical or imaging features. [2] **FDA:** ponesimod isindicated for the treatment of RMS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. [3] **Route of administration:**OS **Licensing status** **EU CHMP P.O. date:**25/03/2021 **FDA M.A. date:**18/03/2021 **EU Speed Approval Pathway:**No **FDA Speed Approval Pathway:**No --- **ABBREVIATIONS:** **AESI:** adverse event of special interest **AISM:** associazione italiana sclerosi multipla **ALT:** alanine aminotransferase **ARR:** annualized relapse rate **AST:** aspartate aminotransferase **CHMP:** Committee for Medicinal Products for Human Use **M.A.:** Marketing Authorization **MS:** multiple sclerosis **OS:** oral administration **P.O.:** Positive Opinion **Pts:** patients **RMS:** relapsing multiple sclerosis **RR:** relapsing-remitting **RRMS:** relapsing-remitting multiple sclerosis **SAE:** serious adverse event **S1P:** sphingosine 1-phosphate **TEAE:** treatment-emergent adverse event **URTI:** upper respiratory tract infection	**Summary of clinical EFFICACY:** OPTIMUM(NCT02425644)isa phase 3, multicenter, double-blind,active-comparator, superiority randomized clinical trial designed to compare ponesimod vs. teriflunomide in ptswith RMS. 1,133 pts were randomized (1:1) to 20 mg ponesimod or 14 mg teriflunomide once daily for 108 weeks.The primary efficacy endpoint was the ARR based on the number of confirmed relapses per patient-year from randomization to the end of the study. Ponesimod reduced ARR by 30.5% compared with teriflunomide(mean ARR, 0.202 vs 0.290; rate ratio, 0.695 [99% confidence limits, 0.536-0.902]; p<0.001).[4] **Summary of clinical SAFETY:** The proportion of pts who had at least one TEAE was similar between the two groups (ponesimod 88.8% vs. teriflunomide 88.2%).The most common TEAEs reported in at least 5% of pts treated with ponesimod, occurring with higher frequency compared to the teriflunomide group, are the following:anincreased ALTlevel (19.5%vs 9.4%), nasopharyngitis (19.3%vs 16.8%), URTI(10.6% vs 10.4%), hypertension (8.0% vs 7.8%), an increased AST level (6.4% vs 3.5%), urinary tract infection (5.7% vs 5.1%), dyspnea (5.3% vs 1.2%) and dizziness (5.0% vs 2.7%) [5]. The proportion of pts who had at least one treatment-emergent SAEwas similar in both treatment arms (8.7% vs 8.1%).Overall, TEAEs leading to treatment discontinuation were more frequent in the ponesimod group (8.7% vs. 6.0%).Two patients in the teriflunomidegroup died; both deaths wereconsidered not associated withthe study drug.[4] **Ongoing studies:** • ***For the same indication:***Yes • ***For other indications:***No **Discontinued studies (for the same indication):**Yes --- **References:** 1.https://www.whocc.no/ddd/lists_of_temporary_atc_ddds_and_alterations/atc_codes/ 2.https://www.ema.europa.eu/en/medicines/human/summaries-opinion/ponvory 3.https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/213498s000lbl.pdf 4.Kappos L, Fox RJ, et al.: Ponesimod Compared With Teriflunomide in Patients With Relapsing Multiple Sclerosis in the Active-Comparator Phase 3 OPTIMUM Study: A Randomized Clinical Trial. JAMA Neurol., 2021. 5. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/213498Orig1s000MedR.pdf 6. https://www.epicentro.iss.it/sclerosi-multipla/epidemiologia 7.https://www.salute.gov.it/portale/salute/p1_5.jsp?lingua=italiano&id=177&area=Malattie_del_sistema_nervoso 8. https://journals.sagepub.com/doi/pdf/10.1177/1352458517751049 9.https://clinicaltrials.gov/ct2/results?cond=&term=&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&intr=Ponesimod&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= 10. https://adisinsight.springer.com/drugs/800024855 11. https://adisinsight.springer.com/search 12.https://clinicaltrials.gov/ct2/results?cond=Relapsing+Multiple+Sclerosis&term=&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= 13.https://clinicaltrials.gov/ct2/show/NCT03232073?recrs=abdef&intr=Ponesimod&phase=12&draw=2&rank=2	**Cost of therapy:**Not available. **Epidemiology:** In Italy, MS has a prevalence of 113/100,000 and it is estimated that 68,000-75,000 people are affected by MS, with 1,800-2,000 new cases every year. Based on a recent study conducted by AISM, the total number of people with MS in Italy is over 118˙000. [6] RRMS is the most common form of the disease: about 85% of pts with MS have a RR disease onset; in about 65% of cases this form evolves towards the secondary progressive form. [7] --- **POSSIBLE PLACE IN THERAPY** There are several available drugs for the treatment of RRMS: beta interferons, peginterferon beta-1a, glatiramer acetate, teriflunomide, dimethylfumarate, cladribine, fingolimod, daclizumab, natalizumab, ocrelizumab and alemtuzumab. The choice of the treatment depends on some factors, such as patient characteristics and comorbidities, disease severity/activity, drug safety profile and accessibility of the drug. [8] **OTHER INDICATIONS IN DEVELOPMENT:**No. [9][10] **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: No. [9] **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Ozanimod, fenebrutinib, tolebrutinib, ublituximab, evobrutinib, masitinib, daclizumab. [11][12] *Service reorganization: No *Possible off label use: No **Notes:** Theongoing long-term extension studyinvestigates safety, tolerability and disease control of ponesimod 20 mg in ptswith RMS (OPTIMUM-LT; NCT03232073). [13]