Report AUBAGIO® Teriflunomide

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: teriflunomide **Brand Name:** Aubagio **Originator/licensee:** Sanofi-Aventis Groupe **Classification:** NI **ATC code:**L04AA31 **Orphan Status:** **Eu:** No **Us:** - **Mechanism of action:** Teriflunomide is an immunomodulatory and inflammatory agent that inhibits the mitochondrial enzyme DHO-DH, which connects with the respiratory chain. As a consequence, teriflunomide reduces the proliferation of rapidly dividing cells that depend on *de novo* synthesis of pyrimidine to expand. The mechanism exerted in MS seems due to a reduced number of T-lymphocytes [1].	**Authorized Indication:** **EMA:** teriflunomide is indicated for the treatment of adult and paediatric pts aged 10 years and older with RRMS [2]. **Route of administration:** OS **Licensing status** **EU CHMP P.O. date:** 22/04/2021 **FDA M.A. date:**- **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:**- --- **ABBREVIATIONS:** **AE**: Adverse Events **BW:** Body Weight **CHMP:** Committee for Medicinal Products for Human Use **C.I.:** Confidence Interval **DHO-DH:** Dihydroorotate Dehydrogenase **M.A**: Marketing Authorization **MS:** Multiple Sclerosis **O.S.:** Oral Administration **PK:** Pharmacokinetic **P.O.:** Positive Opinion **pts:** patients **QD:** Once Daily **RRMS:** Relapsing-Remitting Multiple Sclerosis **SAE**: Serious Adverse Events **tabs:** tablets **URTI:** Upper Respiratory Tract Infection **vs**: versus	**Summary of clinical EFFICACY:** **Study TERIKIDS (NCT02201108):** a two year, multicentre, randomized, double blind, placebo-controlled, parallel group trial to evaluate efficacy, safety, tolerability, and PK of teriflunomide administered orally QD in paediatric pts with relapsing forms of MS followed by an open label extension. A total of 185 pts aged 10-17 were screened (166 enrolled and randomized; 109 received teriflunomide and 57 placebo). The study duration included: - a double-blind treatment period of up to 96 weeks (of these, eight weeks were intended to provide individual PK parameters to allow the dose adjustment to the 14 mg adult-equivalent dose for the rest of the study). Pts received teriflunomide 3.5 mg (BW< 40 kg) or 7 mg (BW ≥ 40 kg) orally QD. - a 96-week open label extension, i.e., up to a maximum of 192 weeks after randomization. The primary endpoint was the assessment of time to first clinical relapse after randomization, assessed over 96 weeks. The median time to first clinical relapse was 39.14 weeks (95% C.I.,0.1 to 98.0) for the placebo group and 75.29 weeks (95% C.I., 0.1 to 98.7) for the teriflunomide group. Teriflunomide reduced risk of relapse (-34%); however, the difference was not statistically significant vs placebo (P = 0.29) [3-4]. **Summary of clinical SAFETY:** During the 96 weeks double-blind period, incidence of SAE in teriflunomide and placebo groups were 11.01% and 10.53%,respectively. Incidence of non-serious AE in teriflunomide and placebo groups were77.98% and 70.18%,respectively. In teriflunomide group mainly abdominal pain (11.01%), non-cardiac chest pain (3.57%), pyrexia (5.50%), nasopharyngitis (25.59%), URTI (21.10%), paraesthesia (11.01%) and alopecia (21.12%) were reported. No deaths were observed [3-4]. **Ongoing studies:** • ***For the same indication:*** Yes[5] • ***For other indications:*** Yes[6] [Phase III, but if it is an O/OE drug, also Phase II] **Discontinued studies (for the same indication):** Yes **References:** 1. https://www.ema.europa.eu/en/documents/product-information/aubagio-epar-product-information_en.pdf 2. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/aubagio 3. https://clinicaltrials.gov/ct2/show/results/NCT02201108?term=NCT02201108&draw=2&rank=1 4. https://adisinsight.springer.com/trials/700245861 5. https://clinicaltrials.gov/ct2/results?cond=Sclerosis%2C+Multiple&intr=Teriflunomide&Search=Apply&recrs=b&recrs=a&recrs=d&age_v=&gndr=&type=Intr&rslt= 6. https://clinicaltrials.gov/ 7. https://gallery.farmadati.it/ 8. https://www.drugs.com/price-guide/aubagio 9. https://www.epicentro.iss.it/sclerosi-multipla/epidemiologia 10. https://www.aism.it/la_gardenia_di_aism_sostiene_la_ricerca_sulla_sclerosi_multipla_pediatrica_un_problema_0 11. https://bmcneurol.biomedcentral.com/articles/10.1186/s12883-018-1026-3 12. https://www.clinicaltrials.gov/ct2/show/NCT04806737?recrs=abdf&type=Intr&intr=Teriflunomide&phase=012&draw=2&rank=2 13. https://www.clinicaltrials.gov/ct2/results?cond=Relapsing+Remitting+Multiple+Sclerosis&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&age=0&gndr=&type=Intr&rslt=&phase=0&phase=1&phase=2&Search=Apply	**Cost of therapy:** In Italy, the price for teriflunomide (28 coated tabs, 14 mg) is 1.530,82 € (retail price including VAT) [7]. **Epidemiology:** In Italy, people affected by SM are over 110,000 and it is estimated that in almost 10% of cases the onset occurred before reaching 18 years of age. It means that at least 11,000 pts (<18 years) are affected with MS [10]. **POSSIBLE PLACE IN THERAPY** The current first-line treatment of MS in children consists of either interferon beta or glatiramer acetate. In children with breakthrough disease (defined as relapses while on first-line therapies), escalation to higher efficacious second-line therapies, such as natalizumab, fingolimod, mitoxantrone, cyclophosphamide, rituximab, and daclizumab may be considered based on the extrapolated data from adult cohorts [11]. **OTHER INDICATIONS IN DEVELOPMENT:** HTLV-1 Associated Myelopathy/Tropical Spastic Paraparesis; Celiac Disease [12]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: -** **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** No [13]. *Service reorganization Y/N: No *Possible off label use Y/N: Yes

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