Report REPATHA® evolocumab

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: evolocumab **Brand Name:** Repatha **Originator/licensee:** Amgen Europe B.V. **Classification:** NI **ATC code:** C10AX13 **Orphan Status**: Eu: No Us: Yes **Mechanism of action**: Evolocumab is a monoclonal antibody that selectively binds to PCSK9, a protein that attaches to LDLR on the surface of hepatocytes and causes the degradation of these receptors. By blocking PCSK9, evolocumab prevents the PCSK9-mediated degradation of LDLR. The increase in hepatic levels of LDLR determines the reduction of serum LDL-C levels [1].	**Authorized Indication:** **EMA:** Evolocumab is indicated in paediatric pts aged 10 years and over with HoFH in combination with other lipid-lowering therapies [2]. **FDA**: Evolocumab is indicated as an adjunct to diet and other LDL-C-lowering therapies in pediatric pts aged 10 years and older with HoFH, to reduce LDL-C [3]. **Route of administration:** SC **Licensing status** **EU CHMP P.O. date:** 14/10/2021 **FDA M.A. date:** 24/09/2021 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** No **ABBREVIATIONS:** **AEs:** Adverse events **CHMP:** Commettee for Medicinal Products for Human Use **HeFH:** Heterozigous Familial Hypercholesterolemia **HoFH**: Homozigous Familial Hypercholesterolemia **LDL-C:** Low Density Lipoprotein-Cholesterol **LDLR:** Low Density Lipoprotein Receptor **LSM**: least-squares mean **MA:** Marketing Authorization **PCSK9**: Proprotein Convertase Subtilisin/Kexin type 9 **PO**: Positive Opinion **pts**: patients **sc**: subcutaneous	**Summary of clinical EFFICACY:** **NCT01588496** is a phase 3, randomised, double-blind, placebo-controlled trial on pts (aged ≥12 years) with HoFH. Pts were randomized to receive either SC evolocumab 420mg every four weeks (n=33) or placebo (n=16) for 12 weeks. All pts received stable background statin therapy and 92% (45/49) were receiving ezetimibe too. The primary endpoint was the percentage change in LDL-C from baseline to week 12. At week 12, the LSM percentage change in ultracentrifugation LDL-C was -23.1% in the evolocumab group and 7.9% in the placebo group, corresponding to a reduction vs placebo of 30.9% (p<0.0001) [4]. **Summary of clinical SAFETY:** During the **NCT01588496** trial, AEs occurred in 36% of the pts treated with evolocumab vs 63% of those in the placebo group. In particular, frequent AEs were upper respiratory tract infection (9% vs 6%), influenza (9% vs 0), gastroenteritis (6% vs 0) and nasopharyngitis (6% vs 0). No serious AEs occurred and no patient discontinued study drug because of an AE [4]. **Ongoing studies:** ● ***For the same indication: Yes**** ● ***For other indications: Yes*** **Discontinued studies (for the same indication):** ***Yes***** ***Note***: *1. *Open-label extension of pivotal trial NCT02392559 for HeFH. Completed in June 2021, results not yet available.* 2. Study to evaluate Lerodalcibep with Evolocumab as active comparator [5] ***Discontinued trial: NCT03331666, trial to assess the impact of evolocumab on platelet function of FH patients. Actual enrollment: 4 participants. Terminated prematurely due to COVID-19.* [5] **References:** 1.https://www.ema.europa.eu/en/documents/overview/repatha-epar-summary-public_en.pdf 2.https://www.ema.europa.eu/en/medicines/human/summaries-opinion/repatha-0 3.https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2021/125522Orig1s031ltr.pdf 4. https://pubmed.ncbi.nlm.nih.gov/25282520/ 5. https://clinicaltrials.gov/ 6. https://gallery.farmadati.it/ 7.https://www.ema.europa.eu/en/documents/product-information/repatha-epar-product-information_en.pdf 8.https://www.osservatoriomalattierare.it/malattie-rare/ipercolesterolemia-familiare/15435-ipercolesterolemia-familiare-in-italia-migliora-la-capacita-di-diagnosi 9. https://pubmed.ncbi.nlm.nih.gov/30317987/ 10. https://www.ema.europa.eu/en/medicines	**Cost of therapy:** In Italy, the ex-factory price of a 140mg pre-filled pen is 196,15€ [6]. The dosage of 420mg, administered using three 140mg pens consecutively [7], corresponds to a monthly cost of 588,45€. **Epidemiology:** HoFH is a rare disease, with a prevalence of approximately one in 200,000-300,000 people, which means about 300 cases in Italy. [8] **POSSIBLE PLACE IN THERAPY** The first-line therapy in children and adolescents with HoFH is represented by statins. A second drug used to reduce LDL-C plasma levels is ezetimibe, whereas bile acid sequestrants are normally not used in children. Evolocumab is currently indicated in adolescents over 12 years old with HoFH as an additional therapy to other lipid-lowering agents [9]. **OTHER INDICATIONS IN DEVELOPMENT:** Prevention of cardiac allograft vasculopathy, COVID-19. [5] **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** No **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION (HoFH):** •Recent EU M.A., not yet available on the Italian market: Evinacumab (approved for adult and adolescent pts aged ≥12 with HoFH) [10]. •Ongoing phase III trials: Lerodalcibep (Eligibility Criteria: ≥10 years) [5].

Issued on: