Report EVKEEZA® Evinacumab

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: evinacumab **Brand Name:** Evkeeza® **Originator/licensee:** Regeneron Ireland Designated Activity Company (DAC) **Classification:** NCE **ATC code:** C10AX17 [1] **Orphan Status:** **Eu:** No **Us:** Yes **Mechanism of action:** evinacumab binds and inhibits ANGPTL3 that plays a role in the regulation of lipid metabolism by inhibiting LPL and EL. This inhibition leads to reduction in HDL-C, TG and LDL-C by promoting VLDL processing and clearance upstream of LDL formation [2].	**Authorized Indication:** **EMA:** evinacumab is indicated as an adjunct to diet and other LDL-C lowering therapies for the treatment of adults and adolescents with HoFH aged ≥12 years [3]. **FDA:** EVKEEZA is an ANGPTL3 inhibitor indicated as an adjunct to other LDL-C lowering therapies for the treatment of adult and pediatric pts with HoFH aged ≥12 years [2]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 22/04/2021 **FDA M.A. date:** 11/02/2021 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** No --- **ABBREVIATIONS:** **AEs:** Adverse Events **ANGPTL3:** Angiopoietin-like 3 **CHMP:** Committee for Medicinal Products for Human Use **CI**: Confidence Interval **EL:** Endothelial Lipase **HDL-C:** High-density Lipoprotein-Cholesterol **HoFH:** Homozygous Familial Hypercholesterolaemia **IV**: intravenous **LDL:** Low-density Lipoprotein **LDL-C:** Low-density Lipoprotein-Cholesterol **LPL:** Lipoprotein Lipase **M.A.:** Marketing Authorization **P.O.:** Positive Opinion **Pts:** patients **SAEs**: Serious Adverse Events **TG:** Triglycerides **VLDL:** Very Low-density Lipoprotein	**Summary of clinical EFFICACY:** **ELIPSE HoFH (NCT03399786)** is a double-blind, placebo-controlled, phase 3 trial that enrolled pts ≥12 years of age with HoFH. 65 pts, who were receiving stable lipid-lowering therapy, were randomized 2:1 to receive evinacumab IV (15 mg/kg every four weeks) or placebo. After completion of the double-blind period, pts had the option of entering a 24-week open-label study. The primary endpoint was the percent change in the calculated LDL-C level from baseline to week 24 during the double-blind treatment period. At week 24, pts in the evinacumab group had a 47.1% reduction from baseline in the LDL-C level, as compared with a 1.9% increase in the placebo group, for a between-group least-squares mean difference of -49.0 percentage points (95% CI, -65.0 to -33.1; p<0.001) [4] [5]. **Summary of clinical SAFETY:** AEs during the treatment period occurred in 29/44 pts (66%) in the evinacumab group and in 17/21 (81%) of those in the placebo group. SAEs during the treatment period occurred in 2/44 pts (5%) in the evinacumab group and were reported as urosepsis and a suicide attempt. An influenza-like illness was reported in 5/44 pts (11%) in the evinacumab group and in no pts in the placebo group. No pts discontinued either evinacumab or placebo because of an AE; there were no deaths [4] [6]. **Ongoing studies:** ● ***For the same indication:*** Yes ● ***For other indications:*** Yes [Phase III, but if it is an O/OE drug, also Phase II] **Discontinued studies (for the same indication):** No --- **References:** 1. https://www.whocc.no/ddd/lists_of_temporary_atc_ddds_and_alterations/atc_codes/?order_by=1 2. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761181s000lbl.pdf 3. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/evkeeza 4. Raal F.J., Rosenson R.S. et al.: Evinacumab for Homozygous Familial Hypercholesterolemia; N Engl J Med 2020; 383:711-20. 5. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761181Orig1s000MedR.pdf 6. https://clinicaltrials.gov/ct2/show/NCT03399786?term=NCT03399786&draw=2&rank=1 7. https://www.drugs.com/price-guide/evkeeza 8. https://www.osservatoriomalattierare.it/malattie-rare/ipercolesterolemia-familiare 9. https://bur.regione.veneto.it/BurvServices/pubblica/Download.aspx?name=98_Allegato_A_DDR_98_06-10-2016_332625.pdf&type=4&storico=False 10. https://clinicaltrials.gov/ct2/results?cond=&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&intr=Evinacumab&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= 11. https://clinicaltrials.gov/ct2/results?cond=Homozygous+Familial+Hypercholesterolemia&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&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=	**Cost of Therapy:** The US price for evinacumab (150 mg/mL) is 11,265.13 $ for a 2.3 mL vial. *The cost for an infusional therapy calculated for a 74 kg patient (15 mg/kg, four-weeks infusion) is 45,060.52 $* [7]. **Epidemiology:** HoFH is a rare disease, with an incidence of approximately 1 in 300,000 to 1 in 1,000,000 people worldwide [6][8]. --- **POSSIBLE PLACE IN THERAPY** Statins are first-line therapy for treating HoFH. The combination with ezetimibe is recommended as second-line of treatment. Combination therapies with bile acid sequestrants, niacin or fibrates could represent an option as third line therapy. Lomitapide or evolocumab could be used as last option of treatment, in addition to a basal hypolipidemic therapy [9]. **OTHER INDICATIONS IN DEVELOPMENT:** Hypertriglyceridemia [10]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: -** **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Inclisiran, lerodalcibep, IBI306 [11]. *Service reorganization: Yes *Possible off label use: Yes

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