

Category

Best Biotechnology Product

Drug / Device Name

EVKEEZA®

Compound/ Tech Name

evinacumab-dgnb

Trade Name

EVKEEZA

Date of Approval

2021-02-11

Indications

EVKEEZA is an ANGPTL3 (angiopoietin-like 3) inhibitor indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies to treat patients aged 5 years and older with homozygous familial hypercholesterolemia (HoFH)

Therapeutic Categories

Homozygous familial hypercholesterolemia (HoFH), an ultra-rare, inherited genetic disorder of lipid metabolism

Attached Files:

- evkeeza_pi.pdf
- evkeeza_ppi.pdf

Background information and need for drug/device

Familial Hypercholesterolemia (FH) is a common, life-threatening genetic condition that causes high cholesterol. Due to a mutation in one of the genes that helps clear cholesterol from the body, people with FH have a high amount of low-density lipoprotein-cholesterol (LDL-C). Untreated, FH leads to early heart attacks and heart disease. Those that have one mutation have Heterozygous Familial Hypercholesterolemia (HeFH) and those that have two have Homozygous Familial Hypercholesterolemia (HoFH).

HoFH is the much rarer and more severe form of FH. It's an ultra-rare disease that affects approximately 1 in 250,000 people (~1,300) in the U.S., many of whom are undiagnosed. Given the progressive nature of the disease, early and accurate diagnosis is key as HoFH can progress quickly, often presenting with LDL-C levels at least four times the normal level, putting people at high risk for heart attacks even younger than age 10. Even further, people living with HoFH desperately needed a new treatment option because their mutations resulted in the loss of LDL receptor (LDLR) function making many existing cholesterol-lowering medications that work through the LDLR pathway less effective for them. The vast majority of HoFH patients could not even get close to their target LDL-C

level prior to the introduction of EVKEEZA.

EVKEEZA, through its unique mechanism of action, was shown to reduce LDL-C levels in people with HoFH, even those with nearly no LDL receptor activity, and is a transformational treatment for those living with this devastating disease.

Attached Files:

- HoFHInfographic_20211215.pdf
- PCNA FH ENGLISH PRINT FINAL Dec 2021 003 002.pdf
- hofhinfographic.pdf

History of the development of the drug/device

The discovery of EVKEEZA traces back to unexpected origins – Campodimele, a small Italian village whose residents had very low cholesterol levels and lived long lives. Researchers initially credited their longevity to their diet, the fresh air and simple lifestyle but it was later found to be the result of a genetic mutation.

Regeneron scientists discovered the ANGPTL group of proteins and the ANGPTL3 gene, which was found to be responsible for the very low cholesterol levels in the residents of Campodimele. By inhibiting ANGPTL3, Regeneron scientists hypothesized that they could help treat people with HoFH by reducing their LDL-C levels independent of the LDLR.

Between 2008 and 2010, Regeneron utilized its Velocimmune® technology to develop REGN1500, a fully human monoclonal antibody designed to block ANGPTL3. By 2011, administration of REGN1500 was shown to lower plasma triglycerides and cholesterol in mice and monkeys. Over the next five years, Regeneron submitted an Investigational New Drug Application (IND) and embarked on trials in humans. In several studies, EVKEEZA lowered circulating triglycerides and cholesterol in patients with dangerously high levels of cholesterol and reduced LDL-C in patients with HoFH. In 2017 the U.S. Food and Drug Administration (FDA) granted breakthrough therapy designation for the treatment of hypercholesterolemia in patients with HoFH. In February 2021, it was approved for patients 12 years and older, marking the first FDA-approved treatment that binds to and blocks the function of ANGPTL3. Most recently, in March 2023, the approved indication was expanded to patients as young as 5 years old.

Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition

EVKEEZA exemplifies the potential of genetics-based research to revolutionize patient treatment, which was made possible due to Regeneron's decades long investment in genetic research and monoclonal antibody technologies that helped to identify completely new ways of targeting diseases, especially in areas of high unmet need.

Following the science to address patient needs no matter what: Regeneron's approach to following the science wherever it leads drives unexpected breakthroughs across therapeutic areas. In this case, the company's efforts ultimately helped this ultra-rare disease community, a population only a little larger than that of the Italian village. Rare diseases sometimes have a connotation of being "untreatable" but the company's efforts to understand the diseases' underlying biology, ushered in a first-in-class FDA-approved medicine that renews hope for HoFH by addressing the disease through its

unique mechanism of action and delivering markedly improved LDL-C control amongst this toughest-to-treat patient population.

Pioneers in antibody research: Antibody medicines are an established class of treatment that are only getting better with the help of cutting-edge science. Regeneron is leading the way, with their proprietary VelociSuite® technologies, which has created a substantial proportion of all original, FDA-approved or authorized fully human monoclonal antibodies currently available. EVKEEZA was invented using this platform, which allows Regeneron scientists to determine which genes in the genome are the best targets for therapeutic intervention and then rapidly generate high-quality, fully human antibodies as drug candidates addressing these targets. Through its VelociSuite technologies, Regeneron has raised the bar for R&D excellence and productivity in biotech, improving and accelerating discovery and development.

Attached Files:

- FDA Approves Firstinclass Evkeeza evinacumabdgmb for Patients with Ultrarare Inherited Form of High Cholesterol.pdf
- FDA Approves Firstinclass Evkeeza evinacumabdgmb for Young Children with Ultrarare Form of High Cholesterol.pdf

Please provide appropriate references (ie Pubmed links)

- Isolation of Angiopoietin-1, a Ligand for the TIE2 Receptor, by Secretion-Trap Expression Cloning (Cell 1996); [https://www.cell.com/fulltext/S0092-8674\(00\)81812-7](https://www.cell.com/fulltext/S0092-8674(00)81812-7)
- Identification of a mammalian angiopoietin-related protein expressed specifically in liver (Genomics 1999); <https://pubmed.ncbi.nlm.nih.gov/10644446/>
- ANGPTL3 blockade with a human monoclonal antibody reduces plasma lipids in dyslipidemic mice and monkeys (Journal of Lipid Research 2015); <https://pubmed.ncbi.nlm.nih.gov/25964512/>
- Genetic and Pharmacologic Inactivation of ANGPTL3 and Cardiovascular Disease (New England Journal of Medicine 2017); <https://www.nejm.org/doi/full/10.1056/NEJMoa1612790>
- A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics (New England Journal of Medicine 2018); <https://pubmed.ncbi.nlm.nih.gov/31774950/>
- Evinacumab for Homozygous Familial Hypercholesterolemia (New England Journal of Medicine 2020); <https://www.nejm.org/doi/full/10.1056/NEJMoa2004215>