January 18, 2024
Ultragenyx Japan K.K.

Media-related information

Ultragenyx obtains marketing authorization for Evkeeza® Intravenous Drip Infusion 345mg for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) in Japan

Ultragenyx Japan K.K. (Head Office: Koto-ku, Tokyo, President: Tadashi Kiriya) announced today that it has been approved to manufacture and sell Evkeeza Intravenous Drip Infusion 345mg (generic name: Evinacumab (genetical recombination, hereinafter "Evkeeza") in Japan with homozygous familial hypercholesterolemia (HoFH). The drug was designated as an orphan drug by the Ministry of Health, Labor and Welfare (MHLW) in March 2019.

HoFH is an extremely rare genetic disorder in which severe hypercholesterolemia (>450mg/dL is caused, which can lead to premature cardiovascular disease and young deaths in untreated individuals.
In Japan, HoFH is regarded as one of the designated intractable diseases, and it has been reported that there were 371 patients who retained the recipient's certificate of medical treatment for specified diseases in fiscal 2021. *1

Evkeeza is the first recombinant human monoclonal antibody that binds to and blocks the function of angiopoietin-like3(ANGPTL3) *2, a protein that plays a key role in lipid metabolism. The blocking of ANGPTL3 by Evkeeza reduces LDL-C levels independent of LDL receptor function.

This approval is based on the results of a global phase III study (R1500-CL-1629 study) involving Japanese subjects aged 12 years or older with HoFH. R1500-CL-1629 trial was a randomized, double-blind, parallel-group study in subjects with HoFH receiving maximally tolerated doses of lipid-lowering therapy. The primary endpoint, percent change from baseline in LDL-C at 24 weeks post-dose, was statistically superior and clinically meaningful in subjects treated with Evkeeza compared with placebo. [Percent change from baseline in LDL-C at 24 weeks after treatment: -47.1 ± 4.6 in the Evkeeza-treated group and 1.9 ± 6.5 in the placebo-treated group; differences between groups: -49.0 ($p<0.0001$)]. During the double-blind treatment period, the incidence of adverse events was 65.9% (29/44 patients) in the evinacumab group and 81.0% (17/21 patients) in the placebo group. Adverse events reported in more than 5% of subjects in the evinacumab group that occurred more frequently than in the placebo group: influenza like illness in 11.4% (5/44 patients) and rhinorrhea in 6.8% (3/44 patients).

When approving drug, Professor Mariko Shiba, Center for Cardiovascular Diseases, Osaka Medical and Pharmaceutical University, said as follows:
"Patients with HoFH have limited benefit from cholesterol-lowering drugs such as statins, and even with LDL apheresis therapy (plasmapheresis therapy), arterial stiffness often progressed because it was difficult to control LDL-C levels sufficiently. We are very happy that evinacumab is now able to obtain marketing approval and be able to deliver it to patients with HoFH, with the appropriate goal of reducing LDL-C."

Note that Evkeeza was approved in February 2021 in the U.S., and June 2021 in the EU. As of January, this year, it has been approved in four countries and regions, including the U.S., EU, the UK and Canada.

Regeneron Pharmaceuticals, Inc. developed Evkeeza, and commercializes the product in HoFH in the U.S. under the generic name evinacumab-dgnb. Ultragenyx is responsible for commercialization efforts for Evkeeza in countries outside of the U.S.

Evkeeza® Intravenous Drip Infusion 345mg Product Summary

Brand name	Evkeeza Intravenous Drip Infusion 345mg
Generic name	Evinacumab (Genetical Recombination)
Efficacy or efficacy	Homozygous familial hypercholesterolemia
Dosing schedule	Usually, 15mg/kg is administered as evinacumab (genetical recombination) by intravenous drip infusion once every 4 weeks over a period of 60 minutes or longer.
Adverse Reactions	Infusion reactions (4.8%) were observed as the Important adverse events. Anaphylactic reaction and Infusion reactions including infusion site pruritus may occur. If any abnormal findings are observed, appropriate measures such as slowing down the infusion rate and interrupting or discontinuing administration should be taken depending on the seriousness of the reaction. Take appropriate measures and monitor until signs and symptoms resolve.

About Ultragenyx

Ultragenyx Pharmaceutical Inc. is a biopharmaceutical company dedicated to providing patients with new therapies for the treatment of serious rare genetic diseases and ultra-rare genetic diseases. We have constructed a diverse portfolio of approved drugs and therapeutic drug candidates with the aim of dealing with diseases with high unmet medical needs, clear mechanisms of disease, and for which there are still no approved treatments for the primary disease.
The Company is led by management with experience in the development and commercialization of rare disease

treatments. Its strategy is aimed at providing safe and effective treatments to urgently requiring patients, with the premise of time-efficient and cost-efficient drug development. See the company's website for more information. https://www.ultragenyx.com/

References

*1: WEB website https://www.nanbyou.or.jp/entry/5354 of Intractable Diseases Center https://www.nanbyou.or.jp/entry/5354

Footnote

*2: ANGPTL3 (angiopoietin-like protein 3) is a blood protein synthesized in the liver that plays critical roles in regulating lipid metabolism by inhibiting lipoprotein lipase (LPL) and vascular endothelial lipase (EL).

For further information, contact:
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