LOJUXTA® ▼/JUXTAPID (LOMITAPIDE) CAPSULES

BACKGROUNDER

At Amryt Pharma, we strive to transform the lives of people with rare, debilitating conditions, such as homozygous familial hypercholesterolaemia (HoFH). Lomitapide is currently approved in the US, EEA, Canada, Argentina, Colombia, Israel and Japan.

What is Lojuxta®/Juxtapid (lomitapide) capsules?

- Lojuxta/Juxtapid is a powerful cholesterol-lowering prescription medicine taken alongside a low-fat diet and other lipid-lowering therapies in adult patients with HoFH.
- Lojuxta/Juxtapid is a 'first in class' medicine – a drug that uses a unique mechanism of action.
- The European Commission (EC) approved Lojuxta in July 2013.
- The U.S. Food & Drug Administration (FDA) granted authorisation for lomitapide under the trade name 'Juxtapid' in December 2012.

Current standard therapy

- Current standard of care for HoFH includes lifestyle management (diet, exercise), lipid-lowering treatments including statins, ezetimibe and new drugs like PCSK9 inhibitors.
- Many lipid-lowering treatments work through the Low-Density Lipoprotein (LDL) receptor to try to clear the blood stream of the high levels of cholesterol.
    - However as these receptors do not work properly in people with HoFH, due to the underlying genetic mutations, they have limited effect in lowering cholesterol levels in HoFH patients.
- Another therapy is available, which involves the mechanical removal of cholesterol from the blood stream through a process similar to dialysis called Lipoprotein Apheresis (LA).[1]
    - While LA can be effective in lowering cholesterol in the acute setting, cholesterol levels rebound rapidly returning to 50 percent of their original levels by day three and to 90% by day seven.

- Apheresis is typically needed multiple times per week to be sufficient to control the disease.

- The combination of statins, ezetimibe, PCSK9 inhibitors and LA may lower cholesterol levels to an extent, but these treatments will not result in consistent and maintained lowering to recommended target levels.
    - As such patients with HoFH still have high cholesterol levels and are at a continued risk of progressive atherosclerotic disease and life-threatening cardiac events, for example, heart attack, stroke, major cardiac surgery and premature cardiac death.

How Lojuxta®/Juxtapid (lomitapide) works

- Lojuxta/Juxtapid works differently to other lipid-lowering therapies.
- It works by reducing the production and release of cholesterol from the liver and by reducing the absorption of cholesterol from the intestines following a meal.
- It does not work by trying to clear the high levels of cholesterol in the bloodstream such as apheresis, and it works independently of the LDL receptor in the liver.
- As such Lojuxta/Juxtapid offers patients an opportunity to lower their cholesterol towards target levels when others lipid-lowering therapies such as statins, ezetimibe and PCSK9 inhibitors have failed to achieve target levels.
- The effects of Lojuxta/Juxtapid on cardiovascular morbidity and mortality has not been determined.

How it's taken

Lojuxta/Juxtapid is a hard capsule, taken once a day and if required, the dose can be escalated slowly to achieve optimal lipid lowering balanced with tolerability.[2]

Clinical data

- The approval for Lojuxta/Juxtapid is based on a multi-national, single arm, open-label Phase 3 study which evaluated the safety and efficacy of lomitapide in reducing cholesterol levels in 29 adult patients with HoFH. The study confirmed

that Lojuxta/Juxtapid was an efficacious drug in the management of HoFH and was published in the Lancet in 2013.[2]

- There are several publications that report data following treatment of Lojuxta/Juxtapid in the 'real world' – the largest of these studies in Europe confirms it to be a powerful cholesterol-lowering agent.[3]
- There is also data from the global Lomitapide Observational Worldwide Evaluation Registry (LOWER), the largest dataset of patients receiving treatment with lomitapide globally which confirms that lomitapide is effective in achieving control of cholesterol levels in HoFH.

Safety profile

- Lojuxta/Juxtapid has an acceptable safety profile for the approved indication and is acceptably tolerated.
- Through its mechanism of action, Lojuxta/Juxtapid blocks the absorption of fats in the intestine. As such it may cause gastrointestinal adverse effects. The most common side effects reported across clinical studies were gastrointestinal effects, including diarrhoea, nausea, indigestion and vomiting.
    - Patients taking Lojuxta/Juxtapid need to follow a low fat diet with less than 20 percent energy from fat. They also need to take essential fatty acids and vitamin E supplements as due to Lojuxta/Juxtapid's mechanism of action, the absorption of these are also blocked.
    - By reducing the production and release of cholesterol in the liver, Lojuxta/Juxtapid may cause an increase in fat in the liver (fatty liver / steatosis) and may cause an increase in liver enzymes.
    - Patients need to have their liver closely and regularly monitored whilst taking Lojuxta/Juxtapid and to avoid drugs that interact with it in the liver or that cause fatty liver such as alcohol.

Please note that in any written communication based on this document a black triangle must be added when referring to Lojuxta®▼ (lomitapide).

References

[1] Graesdal A et al. Apheresis in homozygous familial hypercholesterolemia: the results of a follow-up of all Norwegian patients with homozygous familial hypercholesterolemia. Journal of Clinical Lipidology (2012) 6, 331-229.
[2] Cuchel M et al. Efficacy and safety of a microsomal triglyceride transfer protein inhibitor in patients with homozygous familial hypercholesterolaemia: a single-arm, open-label, phase 3 study. *The Lancet*. 2013:381(9860); 40-46
[3] D'Erasmo et al. Efficacy of Lomitapide in the Treatment of Familial Homozygous Hypercholesterolemia: Results of a Real-World Clinical Experience in Italy. Advances in Therapeutics. 2017: 34(5);1200-1210