FDA approves Novartis Leqvio® (inclisiran), first-in-class siRNA to lower cholesterol and keep it low with two doses a year

Dec 22, 2021

- With two maintenance doses a year, Leqvio is the first and only FDA-approved small interfering RNA (siRNA) therapy for LDL-C (bad cholesterol) reduction(1)
- Leqvio provides effective and sustained LDL-C reduction of up to 52% vs. placebo for certain people with atherosclerotic cardiovascular disease (ASCVD) on maximally tolerated statin therapy(2,3)
- Approximately 16 million Americans with ASCVD taking statins to lower cholesterol--including those who have experienced a heart attack or stroke--are not at recommended LDL-C target(4,5)

EAST HANOVER, December 22, 2021 -- Novartis today announced the US Food and Drug Administration (FDA) approval of Leqvio® (inclisiran), the first and only small interfering RNA (siRNA) therapy to lower low-density lipoprotein cholesterol (also known as bad cholesterol or LDL-C) with two doses a year, after an initial dose and one at three months.

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"Leqvio is a revolutionary approach to lower LDL-C, and creates new possibilities for how healthcare systems can impact cardiovascular disease, a defining public health challenge of our time," said Vas Narasimhan, Novartis CEO. "We now have the opportunity, working together with partners, to provide this first-ever approved LDL-C–lowering siRNA-based therapy to tackle ASCVD at scale across the United States."

Leqvio is indicated in the United States as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with clinical atherosclerotic cardiovascular disease (ASCVD) or heterozygous familial hypercholesterolemia (HeFH) who require additional lowering of LDL-C. The effect of Leqvio on cardiovascular morbidity and mortality is being explored in clinical trials currently underway.

"ASCVD is a substantial public health burden affecting 30 million Americans," said Norman Lepor, MD, a Los Angeles based cardiologist and a clinical investigator in the Phase III clinical program for Leqvio. "As a first-of-its-kind siRNA therapy, Leqvio works differently than other cholesterol treatments, with twice-yearly dosing that makes it a compelling option for the millions of people with ASCVD already on cholesterol-lowering medications struggling to reach their LDL-C target."

Leqvio reduces the amount of LDL-C in the bloodstream by improving the liver's natural ability to prevent the production of a protein that plays a role in keeping circulating cholesterol levels high[6,7]. It is a subcutaneous injection given by a healthcare provider with an initial dose, then again at three months, and then every six months[1]. This approach may help those who have trouble sticking to medicines that are self-administered and have greater dosing frequency. Leqvio will be available in early January 2022.

"People with ASCVD have most likely experienced a heart attack or stroke from high cholesterol, causing a burden on the family and having a negative impact on lives," said Andrea Baer, Executive Director of The

Mended Hearts, Inc. "One of the first steps to improving patients' health is to manage high cholesterol and we're encouraged that this new twice-a-year treatment offers a new option."

The FDA approval was based on results from the comprehensive Phase III ORION-9, -10 and -11 clinical trials, in which all 3,457 participants with ASCVD or HeFH had elevated LDL-C while receiving a maximally tolerated dose of statin therapy[2,3]. In the Phase III trials at month 17, Leqvio delivered effective and sustained LDL-C reduction of up to 52% vs. placebo and was reported to be well-tolerated with a safety profile shown to be comparable to placebo[2,3]. The most common side effects were mild to moderate injection site reaction (including pain, redness and rash), joint pain, urinary tract infection, diarrhea, chest cold, pain in legs or arms and shortness of breath[2,3].

Novartis has obtained global rights to develop, manufacture and commercialize Leqvio under a license and collaboration agreement with Alnylam Pharmaceuticals, a leader in RNAi therapeutics.

About Leqvio

Leqvio is an injectable prescription medicine indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with clinical atherosclerotic cardiovascular disease (ASCVD) or heterozygous familial hypercholesterolemia (HeFH) who require additional lowering of low-density lipoprotein cholesterol (LDL-C).

Limitations of Use

The effect of Leqvio on cardiovascular morbidity and mortality has not been determined.

Important Safety Information

The most common side effects of Leqvio were: injection site reaction (including pain, redness, and rash), arthralgia (joint pain), urinary tract infection, diarrhea, bronchitis, pain in legs or arms and dyspnea (shortness of breath).

These are not all the possible side effects of Leqvio. Ask your health care provider for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please click here for Leqvio full Prescribing Information.

About Novartis in cardiovascular renal metabolism

Cardiovascular (CV), renal and metabolic diseases are a global health crisis[8-11].

These chronic, complex and often hereditary diseases are frequently inter-related, and come with healthcare and treatment barriers and a lack of transformative medicines, and almost always lead to the same outcome: death due to CV disease[8-11].

CV disease is the number one killer in the world[8]. Taking more lives than all cancers combined, it contributes to one in every three deaths globally[8,12]. Of all CV events, 80% can be prevented[13]. Patients and their families deserve better, and our society deserves more.

Thanks to a combination of our legacy, global footprint and leading science, Novartis is uniquely positioned to help change this landscape. We are transforming the way we think about the relationship between these diseases and how they are managed throughout life. Our efforts include the use of early interventions and the

development of pioneering treatments that address the spectrum of CV, renal and metabolic diseases, from prevention to management, as well as the creation of innovative access models. By re-writing the way we work with society, we will lead a worldwide effort to improve health outcomes and roll back the crisis of CV death.

Our goal is to bend the curve of life by reducing and stopping premature death from CV disease.

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of Novartis – is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs nearly 15,000 people in the United States. For more information, please visit https://www.novartis.us.

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