Novartis receives approval in Singapore for LEQVIO® (inclisiran), an innovative medication that changes the treatment paradigm for patients with high cholesterol

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- Leqvio® (inclisiran) is an innovative medicine that can change how low-density lipoprotein cholesterol (LDL-C) or commonly known as bad cholesterol is treated.[1, 2]
- Cardiovascular disease (CVD) is the leading cause of death worldwide.[3, 4] In Singapore, CVD accounts for 31.7% of all deaths in 2020.[5]At least 50% of high-risk patients do not reach guideline-recommended LDL-C targets despite the widespread use of statinsand other cholesterol-lowering therapies.[6]
- Approval is based on Phase III pivotal trials (ORION-9, ORION-10 and ORION-11), demonstrating effective LDL-C reduction of up to 52% in patients with elevated LDL-C despite maximally tolerated cholesterol-lowering therapy.[1, 2]

Singapore, September 28th, 2021 — Novartis announced the approval of Leqvio®(inclisiran) in Singapore for the treatment of adults with hypercholesterolemia (increased blood cholesterol level) or mixed dyslipidemia (unhealthy levels of one or more kinds of fat in the blood[7]). Leqvio® is an innovative small interfering RNA (siRNA), a type of molecule that aids to lower LDL-C level in the blood, as an add-on to existing cholesterol-lowering therapies and lifestyle modifications. This approval is based on the results of ORION-9, 10 and 11, a comprehensive clinical research program, where Leqvio® provided an effective LDL-reduction of up to 52% in patients with elevated LDL-C, despite maximally tolerated cholesterol-lowering therapy. With two maintenance doses a year (administered as an initial dose, another one at three months and then every six months thereafter) and providing effective LDL-C reduction, Leqvio® works as a complement to cholesterol-lowering medication.[1, 2] As an injection administered by healthcare professionals, it may help with the adherence challenges commonly encountered with self-administered treatments.[1, 2, 8]

CVD, often used interchangeably with the term heart disease, is a broad term that describes a range of diseases of the heart and the blood vessels.[9] CVD is the leading cause of death and disability globally, killing about 18 million people a year.[10] This number is on the rise with nearly 24 million deaths a year globally predicted by 2030.[11] Among others, the main and most modifiable risk factor is elevated LDL-C.[12] If there is too much LDL-C in the blood, it gets deposited in the wall of blood vessels (arteries) together with white blood cells and calcium, among other things. These deposits over time may clog the blood vessel (plaque formation) and can lead to a heart condition called atherosclerotic cardiovascular disease (ASCVD).

“ASCVD is a major driver of heart attacks, strokes and potentially death.[13] Long-term exposure to elevated levels of LDL-C, which builds up plaque in the arteries, can lead to this disease. The most readily modifiable risk factor for ASCVD is reducing LDL-C. Unfortunately, effective and sustained LDL-C reduction remains a challenge, with some Singaporeans with ASCVD not achieving guideline-recommended LDL-C targets on statins alone,” said Prof Tan Huay Cheem, Senior Consultant, Department of Cardiology, National University

Heart Centre, Singapore.

The global cost of CVD such as direct healthcare system costs, indirect cost and premature deaths will be well over one trillion dollars by 2030. In Singapore alone, CVDs contribute to approximately one in three deaths, and it can incur approximately US$8.1 billion in direct and indirect costs on individuals, their households and the public health system.[14] ASCVD will represent the most significant portion of this. Although the true incidence of ASCVD is unknown, Singapore's rapidly aging population and increasingly sedentary lifestyle predispose individuals to chronic health problems which poses an increasing prevalence of risk factors for ASCVD.[15]

Commenting on the cholesterol treatment landscape, Associate Professor Yeo Khung Keong, Senior Consultant, from Department of Cardiology at the National Heart Centre Singapore said, "Cholesterol management requires lifestyle changes inculcating healthy dietary habits and regular exercise. When lifestyle modification does not lower the level of LDL-C, patients are provided treatment options to help control their cholesterol level. Unfortunately, some patients still cannot reach the desired LDL-C goals and this can be due to multiple factors such as side effects, poor adherence to treatment or an underlying genetic disorder. For these patients who have exhausted standard treatment options, this new option may help to close that gap."

"CVD is the largest economic burden the world has today. It is one of the leading causes of death in Singapore and its prevalence will only continue to rise due to our aging population. At Novartis, an essential part of what we do is the development of a growing pipeline of innovative molecules designed to help patients with CVD live longer. Focusing on areas of high unmet medical need, we're bringing forward innovative solutions that will radically improve patient outcomes," said Poh Hwee Tee, Managing Director, Novartis Singapore.

About Leqvio®(inclisiran)

Leqvio® (inclisiran, KJX839) is an innovative small interfering RNA (siRNA) therapy to reduce low-density lipoprotein cholesterol (LDL-C) levels via an RNA interference (RNAi) mechanism of action for patients with atherosclerotic cardiovascular disease (ASCVD), a deadly form of cardiovascular disease if left untreated. With two maintenance doses a year and effective LDL-C reduction, Leqvio® works as a complement to maximally tolerated cholesterol-lowering medication and lifestyle modification.[1, 2] Leqvio® works differently from other therapies by preventing the production of the target protein in the liver, increasing liver uptake of LDL-C and clearing it from the blood.[1] Leqvio® is dosed initially, again at 3 months and then once every 6 months for maintenance.[1,2] In three clinical trials conducted in patients with ASCVD, ASCVD risk equivalent or heterozygous familial hypercholesterolemia, patients taking Leqvio® maintained LDL-C reduction throughout each 6-month dosing interval.[1,2] Administered in-clinic as a subcutaneous injection, Leqvio® may integrate seamlessly into a patient's healthcare routine.[1,2]

In Phase III trials, the common frequently occurring adverse events were injection site reaction, injection site pain, injection site redness, and injection site rash. Those were generally mild and none were severe or persistent.[17]

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 Novartis in Cardiovascular-Renal-Metabolism

Bending the curve of life requires addressing some of society's biggest public health concerns. Novartis has an established and expanding presence in diseases covering the heart, kidney and metabolic system. In addition to treatment for heart failure, hypertension and diabetes, Novartis has a growing pipeline of innovative

molecules addressing cardiovascular, metabolic and renal diseases.

About Novartis

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 products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 109,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.sg.

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References

1. Ray K, Wright R, Kallend D, et al. Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol. N Engl J Med. 2020;382(16):1507–1519.
2. Raal, F, Kallend D, Ray K, et al. Inclisiran for Heterozygous Familial Hypercholesterolemia. N Engl J Med. 2020;382(16):1520–1530.
3. World Health Organization. Cardiovascular diseases (CVDs). Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) [Last accessed: September 2020].
4. American Cancer Society. Global Cancer Facts & Figures 4th Edition. Available from: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and… [Last accessed: August 2020].
5. My Heart (Singapore Heart Foundation), Singapore Statistics, Source: https://www.myheart.org.sg/my-heart/heart-statistics/singapore-statistics/
6. Singapore Medical Journal, Cholesterol goal achievement and lipid-lowering therapy in patients with stable or acute coronary heart disease in Singapore: results from the Dyslipidemia International Study II, Source: https://doi.org/10.11622/smedj.2019021 [Accessed on 8 September 2021]
7. Dyslipidemia: Symptoms, Treatment, and More (healthline.com). [Last accessed on 9 September, 2021]
8. Eva Martin-Ruiz et al. Systematic Review of the Effect of Adherence to Statin Treatment on Critical Cardiovascular Events and Mortality in Primary Prevention. Journal of Cardiovascular Pharmacologu and Therapeutics. January 17, 2018
9. Health Hub, Screening for Heart Disease, Source: https://www.healthhub.sg/live-healthy/16/screening_heart_disease [Last accessed 9 September 2021].
10. World Health Organization. Cardiovascular diseases (CVDs). Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular - diseases-(cvds) [Last accessed: September 2020].

11. McClellan M, Brown N, Califf RM, Warner JJ. Call to Action: Urgent Challenges in Cardiovascular Disease: A Presidential Advisory from the American Heart Association. Circulation. 2019;139(9):E44–E54.
12. Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the Management of Dyslipidaemias: Lipid Modification to Reduce Cardiovascular Risk. Eur Heart J. 2020;1(41):111–188.
13. World Health Organization. WHO Cardiovascular diseases –Programme. Available from: https://www.who.int/health-topics/cardiovascular-diseases/#tab=tab_1 [Last accessed: September 2020]
14. https://sph.nus.edu.sg/2018/12/cost-of-silent-risk-factors-for-cardiovascular-disease-in-asia/. [Last accessed September 2020]
15. Peter Yan et al. Statin-centric versus low-density lipoprotein-centric statin-centric versus low-density lipoprotein-centric approach for atherosclerotic cardiovascular disease prevention: a Singapore perspective. Singapore Med J 2016; 57(7): 360-367 doi: 10.11622/smedj.2016118
16. Stoekenbroek RM, Kallend D, Wijngaard PL, et al. Inclisiran for the treatment of cardiovascular disease: the ORION clinical development program. Future Cardiol. 2018;14(6):433–442.
17. Singapore Leqvio® PI. LEQVIO April 2020, corr Dec 2020.SIN

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- https://www.novartis.com/sg-en/sg-en/news/media-releases/novartis-receives-approval-singapore-leqvio-inclisiran-innovative-medication-changes-treatment-paradigm-patients-high-cholesterol
- https://www.novartis.com/news/media-releases/new-novartis-analyses-investigational-inclisiran-demonstrate-consistently-effective-and-sustained-ldl-c-reduction-month-17-regardless-age-and-gender
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- https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)
- https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/global-cancer-facts-and-figures/global-cancer-facts-and-figures-4th-edition.pdf
- https://www.myheart.org.sg/my-heart/heart-statistics/singapore-statistics/
- https://doi.org/10.11622/smedj.2019021
- https://www.healthline.com/health/dyslipidemia
- https://www.healthhub.sg/live-healthy/16/screening_heart_disease
- https://www.who.int/news-room/fact-sheets/detail/cardiovascular
- https://www.who.int/health-topics/cardiovascular-diseases/#tab=tab_1
- https://sph.nus.edu.sg/2018/12/cost-of-silent-risk-factors-for-cardiovascular-disease-in-asia/