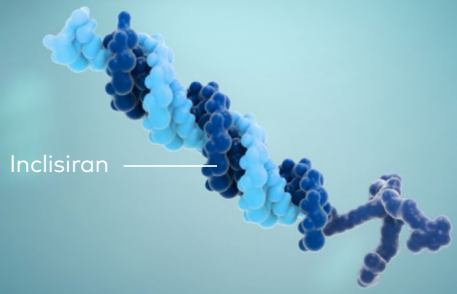
Pr LEQVIO™
inclisiran injection

**A mechanism of action unique to LEQVIO™†‡**

# A mechanism of action that includes the cellular mechanism of RNA interference†‡




## The first and only siRNA PCSK9 inhibitor indicated in non-familial hypercholesterolemia with ASCVD and HeFH†‡

LEQVIO™ (inclisiran injection) is indicated as an adjunct to lifestyle changes, including diet, to further reduce low-density lipoprotein cholesterol (LDL-C) level in adults with the following conditions who are on a maximally tolerated dose of a statin, with or without other LDL-C lowering therapies:

- Heterozygous familial hypercholesterolemia (HeFH), or
- Non-familial hypercholesterolemia with atherosclerotic cardiovascular disease (ASCVD)

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

ASCVD = atherosclerotic cardiovascular disease; HeFH = heterozygous familial hypercholesterolemia; PCSK9 = proprotein convertase subtilisin/kexin 9; RNA = ribonucleic acid; siRNA = small interfering ribonucleic acid.
†Clinical significance has not been established.
‡Comparative clinical significance is unknown.

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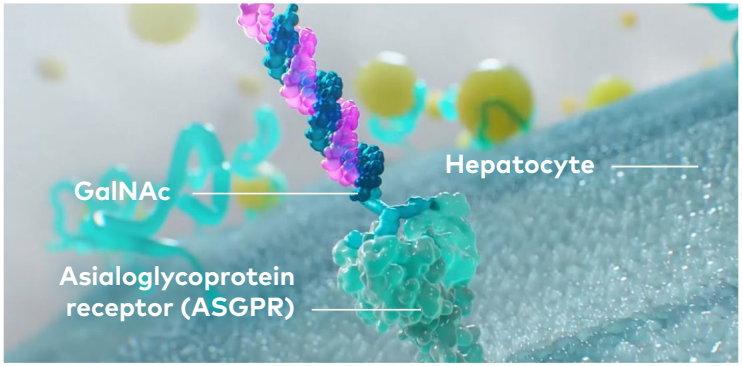
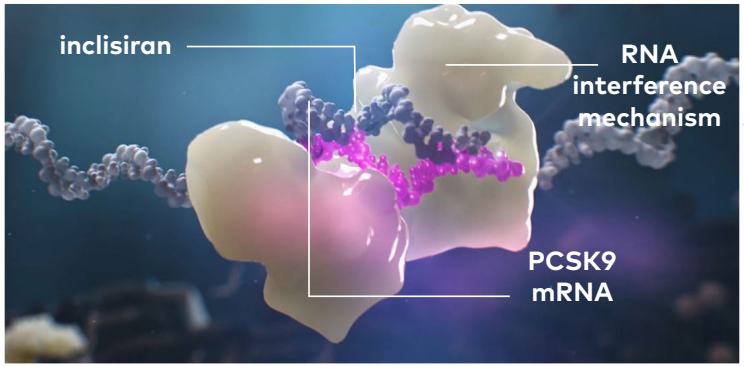
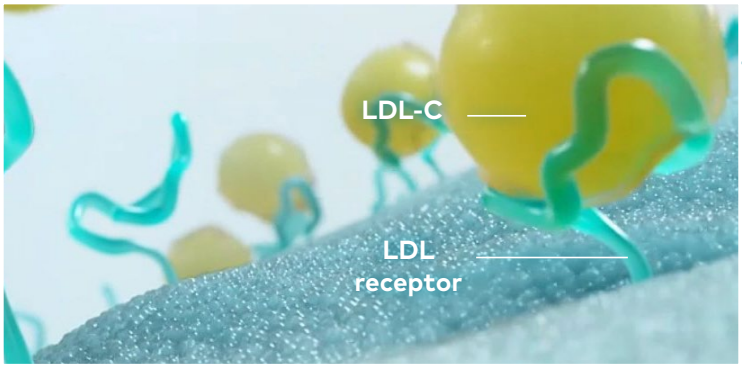
# LEQVIO™ (inclisiran injection) Mechanism of Action†‡




## A double-stranded siRNA that causes the degradation of PCSK9 mRNA to increase hepatocyte LDL-C receptor recycling and expression.

The **N-acetylgalactosamine** (GalNAc) conjugated on the sense strand of LEQVIO™ **facilitates uptake at the liver** and selectively targets hepatic ASGPR.

LEQVIO™ works with the **RNA interference mechanism** to **direct the catalytic breakdown of mRNA for PCSK9.**

The degradation of PCSK9 mRNA **increases LDL receptor recycling and expression** on the hepatocyte cell surface, which generally **increases LDL-C uptake and lowers LDL-C levels** in the circulation.

**After inclisiran is cleared from the plasma, its mechanism of action also includes long-term intracellular presence (>42 days in monkeys and >98 days in rats after a single administration), which contributes to its long duration of effect in lowering LDL-C.**

ASGPR = asialoglycoprotein receptor; GalNAc = N-acetylgalactosamine; LDL-C = low-density lipoprotein-cholesterol; mRNA = messenger ribonucleic acid; PCSK9 = proprotein convertase subtilisin/kexin-9; RNA = ribonucleic acid; siRNA = small interfering ribonucleic acid.
†Comparative clinical significance is unknown.
‡Clinical significance has not been established.

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# The first siRNA PCSK9i that can have a twice annual dosing regimen†‡§


The recommended dose of LEQVIO™ is 284 mg administered as a single subcutaneous injection: initially, again at 3 months, and then once every 6 months.§

Please see the LEQVIO™ Product Monograph for complete recommended dosing regimen and administration information.

## Consider LEQVIO™

**Scan the QR code**
**to access the LEQVIO™ Product Monograph.**

**For more information:**

Consult the Product Monograph at https://www.ask.novartispharma.ca/download.htm?res=leqvio_scrip_e.pdf&resTitleId=1816 for important information about:

- Contraindications regarding the concomitant use with other lipid-lowering therapies.
- Relevant warnings and precautions regarding disturbances in glucose metabolism, homeostasis, patients with severe hepatic impairment, transaminase elevations, injection-site reactions, severe renal impairment, pregnant or breast-feeding women, and fertility.
- Conditions of clinical use, adverse reactions, drug interactions and dosing instructions.

The Product Monograph is also available by calling 1-800-363-8883 or by email at medinfo.canada@novartis.com.

HCP = healthcare professional; PCSK9i = proprotein convertase subtilisin/kexin-9 inhibitor; siRNA=small interfering ribonucleic acid.
†Comparative clinical significance is unknown.
‡Clinical significance has not been established.
§LEQVIO™ is intended for administration by healthcare professional (doctor, nurse, or pharmacist).

**References: 1.** PrLEQVIO™ (inclisiran injection) Product Monograph. Novartis Pharmaceuticals Canada Inc. July 23, 2021. Available at: https://www.ask.novartispharma.ca/download.htm?res=leqvio_scrip_e.pdf&resTitleId=1816. **2.** Data on File. Novartis Pharmaceuticals, 2021.

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Printed in Canada. 226091E

September 2022.

MEMBER OF INNOVATIVE MEDICINES CANADA

REVIEWED BY PAAB