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DAMIAN RASCH, D.O.

ENCINITAS · LA JOLLA, CALIFORNIA



# PCSK9 Inhibitors

*Cholesterol drugs that help your liver clear LDL from your blood. How they work, how much they do and who they're for.*

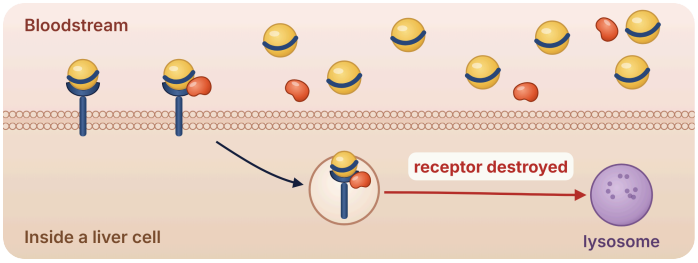
**15%**
fewer major heart and stroke events in the two large outcome trials

**27%**
fewer heart attacks with Repatha in the FOURIER trial

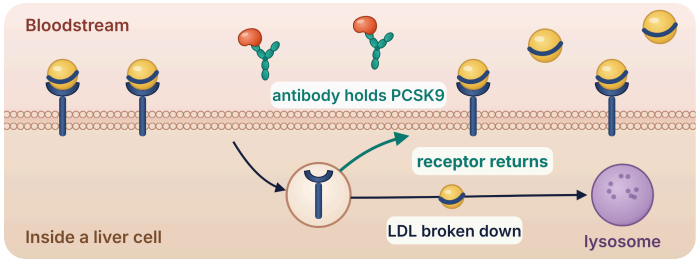
**4–8 weeks**
after you start, your LDL is checked again

HOW THEY WORK

## They save the receptors that clear LDL




Untreated: PCSK9 sends receptors off to be destroyed




Treated: receptors return and keep clearing LDL

Your liver carries **LDL receptors** that grab LDL from your blood and clear it. It also makes **PCSK9**, which latches onto those receptors and marks them for destruction. Repatha (evolocumab) and Praluent (alirocumab) are antibodies that grab PCSK9 before it reaches a receptor. Leqvio (inclisiran) makes your liver build less PCSK9. Lipfendra (enlicitide), approved in July 2026, is a daily pill that blocks it.

HOW MUCH THEY LOWER

## A large drop in LDL and apoB




LDL falls by roughly half or a bit more, depending on the drug. Lp(a) drops most with Repatha, least with Leqvio and less in real-world use. For every 39 mg/dL of LDL reduction, the risk of heart attack, stroke and cardiovascular death falls about 20 percent (one fifth). The cholesterol change happens in weeks, and protection builds over years.

**Invisible, and working**

You won't feel different on a PCSK9 inhibitor, so the shots and copays can be hard to stick with. Treat each one as a deposit against an emergency room visit you'd rather not have.



WHO THEY'RE FOR AND WHAT TO EXPECT ARE ON THE BACK

LIVING WITH A PCSK9 INHIBITOR

# Who they're for and what to expect

## WHO THEY'RE FOR

| | |
|---|---|
| **Established heart or artery disease** | A heart attack, stroke, leg artery disease that needed a procedure, or coronary disease seen on angiography, with LDL still above 70 mg/dL on the most statin you tolerate. A heart attack in the past year moves you up the list. |
| **Familial hypercholesterolemia** | An inherited condition in which untreated LDL can sit at 200 to 400 mg/dL, a gap statins rarely close. |
| **Statin intolerance** | About 10 to 15 percent of patients get muscle aches or weakness that keep them off an effective dose. A PCSK9 inhibitor alone is approved for them. |

## TAKING IT

| | |
|---|---|
| **The schedule** | Repatha and Praluent are self-injected at home every two weeks with a hidden needle. Leqvio is given in the office, again three months later, then every six months. Lipfendra is one tablet each morning on an empty stomach. |
| **Your targets** | Under 55 mg/dL for very high risk, which includes most people with heart disease, and under 70 mg/dL for heart disease that is not at very high risk (2026 ACC/AHA guideline). |
| **If LDL barely moves** | A drop of only 20 or 30 percent means something is off, such as missed shots, a drug left out of the refrigerator too long, or an undiagnosed thyroid problem. |
| **A missed dose** | LDL drifts up slowly. Take the next one when you remember and get back on schedule. |
| **Your other pills** | You usually stay on at least a moderate statin dose unless you can't tolerate one, and usually on ezetimibe too. Together the three hit production, absorption and clearance. |

## COMMON WORRIES

| | |
|---|---|
| **Too low, or memory** | Trial patients reached LDL below 25 mg/dL with no rise in memory or mood problems. Your brain makes its own cholesterol. |
| **Diabetes** | No worsening of blood sugar in studies. |
| **Long-term safety** | More than a decade of study, with no cancer or infection signal. The common side effect is redness, mild pain or itching where you inject. |
| **When to hold off** | Pregnancy rules it out, and the drug is stopped well before a planned pregnancy. |

## CALL THE OFFICE

Call Dr. Rasch's office right away for a hard lump under the skin, or increasing pain, warmth or red streaking where you inject. Plan to stay on the drug, since LDL climbs back within weeks to months of stopping. If the shots or cost wear you down, talk with him before you quit.

## READ THE FULL ARTICLE

damianrasch.com/pcsk9-inhibitors

For education only, and not a substitute for advice from your own physician. Sources include Bergeron et al., Circulation 2015, Rosenson et al., JACC 2018, Imran et al., PLoS One 2023, AlTurki et al., Am J Cardiol 2019 and Jia et al., Vasc Health Risk Manag 2022.

DR. DAMIAN RASCH, D.O. · BOARD-CERTIFIED INVASIVE CARDIOLOGIST · ENCINITAS AND LA JOLLA, CA

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