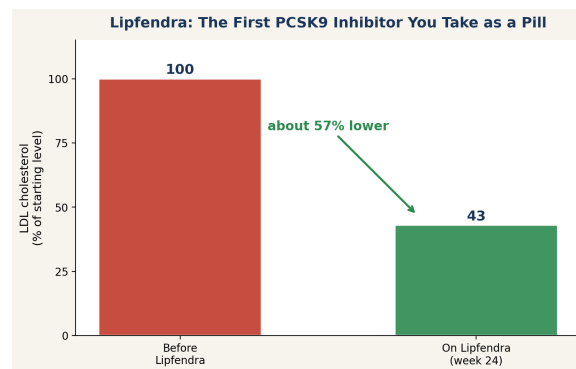


Understanding Lipfendra (Enlicitide)

The first cholesterol-lowering PCSK9 inhibitor you take as a pill

A once-a-day pill that lowers LDL by about 57% on top of a statin -- no shots.



Online: <https://go.riasalimd.com/lipfendra-guide>

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Names & Terms You Will Hear

Term	Meaning
Lipfendra	The brand name of enlicitide, made by Merck. The FDA approved it in July 2026.
Enlicitide (enlicitide decanoate)	The generic drug name. During testing it was called MK-0616.
PCSK9 inhibitor	A medicine that blocks a liver protein called PCSK9 so the liver can clear more LDL from the blood.
Oral PCSK9 inhibitor	A PCSK9 inhibitor you swallow as a pill. Lipfendra is the first one. All the others are shots.
Macrocyclic peptide	The type of molecule Lipfendra is -- a small ring-shaped, protein-like drug that can be taken by mouth.
LDL-C (LDL cholesterol)	The 'bad' cholesterol that builds up in artery walls. Lowering it lowers heart risk.
HeFH (heterozygous familial hypercholesterolemia)	A common inherited condition that keeps LDL high from a young age. Lipfendra is approved to help here too.
Non-HDL-C, ApoB, Lp(a)	Other blood markers of heart risk. Lipfendra lowered all three in studies.



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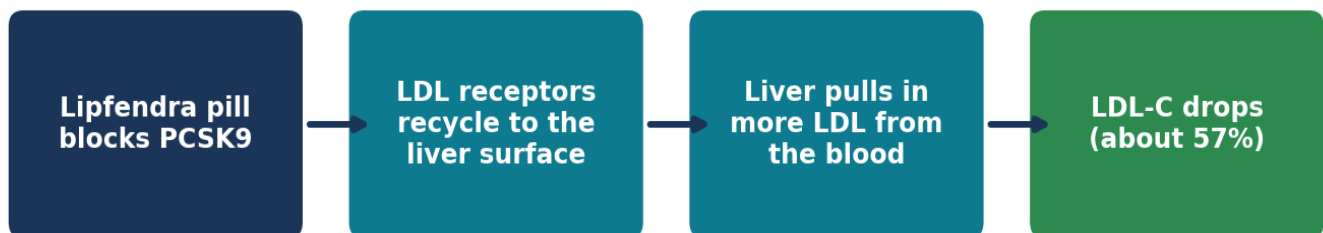


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What Is Lipfendra (Enlicitide)?

- Lipfendra (enlicitide) is a new cholesterol medicine. The FDA approved it in July 2026. It is the **first and only PCSK9 inhibitor you take as a pill**. Every other PCSK9 inhibitor is a shot ([see our PCSK9 Inhibitors guide](#)).
- **What it is for:** it lowers LDL, the 'bad' cholesterol ([see our Understanding Cholesterol guide](#)), in adults. It is used with diet and exercise, on top of a statin, or when statins are not enough or cannot be tolerated. It also helps people with an inherited high-cholesterol condition called HeFH ([see our Familial Hypercholesterolemia guide](#)).
- **How it works:** a protein called PCSK9 makes your liver destroy its LDL receptors. Those receptors are what pull LDL out of the blood. Lipfendra blocks PCSK9. The receptors then recycle back to the liver surface, so your liver clears more LDL and your LDL level falls.
- **How you take it:** one 20 mg tablet, once a day, on an empty stomach. Swallow it whole with water. Then wait before you eat or drink, exactly as your pharmacist tells you. The timing matters for the medicine to work.
- **How well it works:** on top of a statin, Lipfendra lowered LDL by about 57% in studies. That is about as much as the PCSK9 shots. It also lowered other risk markers (non-HDL, ApoB, and lipoprotein(a)).

How Lipfendra Lowers Your LDL Cholesterol



Normally, the PCSK9 protein makes the liver destroy its LDL receptors. Lipfendra blocks PCSK9, so those receptors recycle back to the liver surface. The liver then pulls more LDL out of the blood, and your LDL-C falls.



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Why It Matters

- Many people cannot get their LDL low enough on a statin alone ([see our Statin Therapy guide](#)). Extra LDL lowering closes that gap and can lower heart risk over time.
- Until now, the strongest extra LDL medicines (PCSK9 inhibitors) were all shots. Some people do not want injections or find them hard to keep up. **Lipfendra gives the same kind of LDL drop as a once-a-day pill.**
- People with **familial high cholesterol (HeFH)** have high LDL from a young age. They often need more than a statin. Lipfendra is approved to help lower LDL in HeFH too.
- It works for people who **cannot take a full statin dose** because of side effects. It can be added to a low statin dose or used with other cholesterol pills.
- **Honest limit:** we know Lipfendra lowers LDL a lot. We do **not** yet know if it lowers heart attacks, strokes, or deaths. That study is still going. Your LDL number is a marker, not a promise.
- **Cost:** the list price is about \$315 for a 30-day supply. Merck says most insured patients, including Medicare, pay less. Your out-of-pocket cost depends on your insurance, so ask your pharmacy and our office.

How Well It Works

- In the main CORALreef Lipids study (2,909 adults), Lipfendra lowered LDL by **about 57% at 24 weeks** compared with placebo. The drop lasted through 52 weeks.
- In people with familial high cholesterol (HeFH), it lowered LDL by about **59%**.
- It also lowered other markers of heart risk: non-HDL cholesterol, ApoB, and lipoprotein(a) ([see our Lipoprotein\(a\) guide](#)).
- It mainly lowers LDL. It is not a treatment for high triglycerides ([see our Triglycerides guide](#)).
- In the studies, side effects were about the same as placebo. That is a strong safety signal for a brand-new medicine.

An honest word about heart attacks and strokes. Lipfendra clearly lowers LDL cholesterol. But it is **not yet proven** to prevent heart attacks, strokes, or death. The large study that tests this is still underway. We use Lipfendra to lower LDL, which we expect to help over time, and we will share the heart-outcome results when they are known.



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Treatment Options

- **Dose:** one 20 mg tablet, once a day.
- **Empty stomach:** take it on an empty stomach. The prescribing information says to take it in the morning, swallow it whole with water, and wait at least 30 minutes before you eat or drink anything else. Follow the exact instructions from your doctor and pharmacist.
- **Keep taking your statin:** Lipfendra is added on top of your statin (and ezetimibe if you take it). It does not replace them.
- **Follow-up blood test:** plan a cholesterol blood test about 4 to 8 weeks after you start. Expect a big LDL drop.
- **If you miss a dose:** ask your pharmacist or our office what to do. Do not double up unless we tell you to.
- **Tell us your other medicines:** bring your full medicine list, including over-the-counter drugs and supplements, so we can review it with you.



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Lipfendra vs. the PCSK9 Shots -- Same Target, Different Delivery

Medicine	Route	How often	How it is given
Lipfendra (enlicitide)	Pill (oral)	Once a day	Swallow a tablet on an empty stomach
Repatha, Praluent	Injection	Every 2 to 4 weeks	Shot under the skin (self-injected)
Leqvio (inclisiran)	Injection	Twice a year	Shot under the skin, given in the office



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How to Take Lipfendra

- Take **one 20 mg tablet, once a day**. Swallow it whole with water.
- Take it on an **empty stomach**. The label says to take it in the morning and wait at least 30 minutes before eating or drinking anything else.
- The timing is not a small detail. Food in your stomach can lower how much medicine your body absorbs, so follow your pharmacist's instructions closely.
- Keep taking your statin and any other cholesterol medicines unless we tell you otherwise. Lipfendra is an add-on.
- Set a daily reminder so it becomes a habit, like brushing your teeth.

Take it on an empty stomach. Lipfendra works best when your stomach is empty. The prescribing information says to take your 20 mg tablet in the morning with water and then wait at least 30 minutes before you eat or drink anything else. Ask your pharmacist to walk you through the exact timing -- getting it right helps the medicine work.



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Risks, Benefits, and Alternatives

Every choice has trade-offs. Use this table to start the shared decision conversation.

Option	Risks	Benefits	Alternatives
Lipfendra (enlicitide) -- oral PCSK9 inhibitor	A pill taken every day on an empty stomach. Some people get diarrhea (about 7 in 100) or dizziness (about 9 in 100). Not yet proven to lower heart attack or stroke risk.	Lowers LDL by about 57% on top of a statin. No shots. Side effects were like placebo in studies. Also lowers non-HDL, ApoB, and Lp(a).	PCSK9 shots (Repatha, Praluent, Leqvio), ezetimibe, bempedoic acid, or a higher statin dose.
PCSK9 shots (evolocumab, alirocumab, inclisiran)	A shot under the skin every 2 to 4 weeks, or twice a year for Leqvio. Mild shot-site redness in about 5 in 100.	Same big LDL drop. Repatha and Praluent have proven heart-event benefit. Good if you would rather not take a daily pill.	Lipfendra (a daily pill, no shots), ezetimibe, bempedoic acid.
Ezetimibe (a pill)	Lowers LDL by only about 18 to 20% more. May not be enough by itself for high-risk patients.	Cheap, oral, and very well tolerated. Proven small heart-event benefit (IMPROVE-IT trial).	Add or switch to Lipfendra or a PCSK9 shot if LDL stays high.
Higher statin dose only, no add-on	May leave LDL above goal in high-risk patients.	No added cost or new side effects. Statins have decades of proven heart benefit.	Add ezetimibe, Lipfendra, or a PCSK9 shot if you need more LDL lowering.



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Common Misconceptions

Myth	Reality
Lipfendra replaces my statin.	No. It works on top of a statin. The studies added it to a statin. Keep taking your statin unless your doctor tells you to stop.
Because it is a pill, it must be weaker than the shots.	Not true. In studies Lipfendra lowered LDL by about 57%, about as much as the injectable PCSK9 inhibitors.
Lipfendra is proven to prevent heart attacks and strokes.	Not yet. It lowers LDL a lot, but the study to see if it cuts heart attacks, strokes, and deaths is still going. We do not yet know that answer.
I can take it with food, like most pills.	No. Take it on an empty stomach, then wait before you eat or drink, exactly as your pharmacist tells you. Food can change how well it works.
It is only for people with sky-high cholesterol.	It is for adults whose LDL stays high on a statin, including people with familial high cholesterol (HeFH). Your overall risk, not just your number, guides the choice.
A brand-new drug must be unsafe.	In studies, side effects and drop-outs were about the same as placebo. The most common were mild diarrhea and dizziness. Long-term heart-outcome data is still being collected.



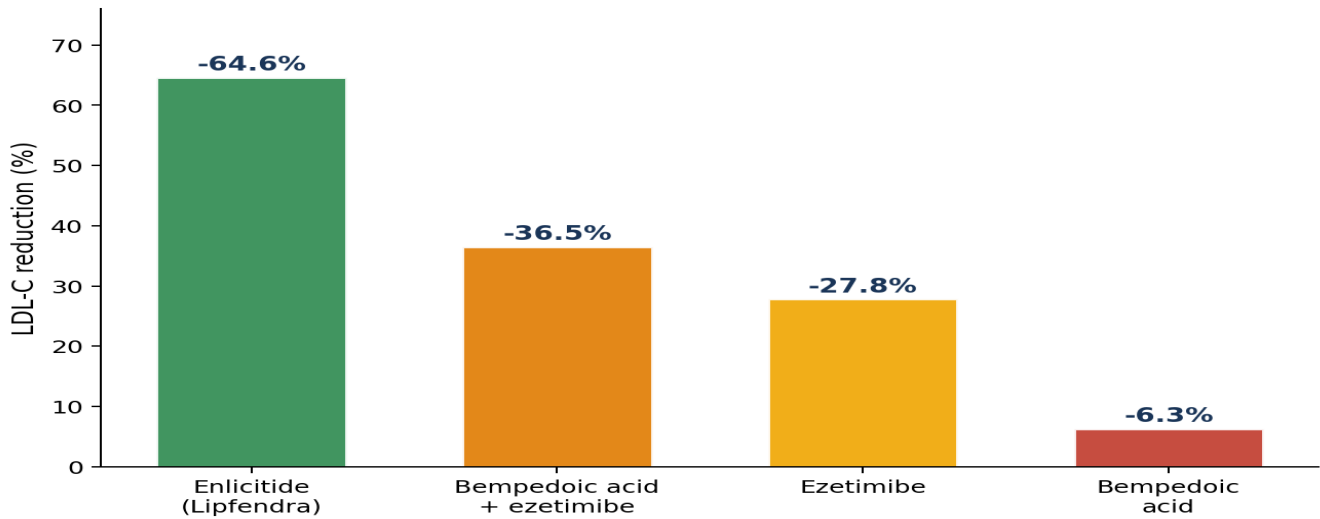
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LDL-C Reduction on Top of a Statin (CORALreef AddOn)



In the CORALreef AddOn trial, enlicitide (Lipfendra) lowered LDL-C by 64.6% -- far more than bempedoic acid plus ezetimibe (36.5%), ezetimibe alone (27.8%), or bempedoic acid alone (6.3%). Its LDL drop is about as strong as the injectable PCSK9 inhibitors.



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How It Compares to the Shots and Other Cholesterol Pills

- **Vs. the PCSK9 shots:** Lipfendra gives about the same LDL drop as the injectable PCSK9 inhibitors ([see our PCSK9 Inhibitors guide](#)), but as a daily pill instead of a shot.
- **Vs. ezetimibe:** in a head-to-head study, Lipfendra lowered LDL by 64.6%, while ezetimibe lowered it by about 27.8% ([see our Ezetimibe guide](#)).
- **Vs. bempedoic acid:** bempedoic acid lowered LDL by only about 6.3%, and bempedoic acid plus ezetimibe by 36.5% ([see our Bempedoic Acid guide](#)). Lipfendra beat all of these.
- **Trade-off:** the pill must be taken every day on an empty stomach. A shot is less frequent but is an injection. The best choice depends on what fits your life and your insurance.



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Possible Complications

Knowing what can go wrong helps you spot problems early. Most complications are uncommon, especially with treatment.

Where / What	What Can Happen
Diarrhea (about 7 in 100)	Loose stools were the most common side effect in the familial-high-cholesterol study, a bit more often than with placebo (about 2 in 100). It was usually mild. Drink fluids and call us if it will not stop.
Dizziness (about 9 in 100)	Some people felt dizzy, more than with placebo (about 4 in 100). Stand up slowly. Tell us if it keeps happening or you feel faint.
Allergic reactions (uncommon)	As with any medicine, an allergic reaction is possible. Serious reactions are rare. Get emergency help for swelling of the face or throat or trouble breathing.
No proven heart-event benefit yet	Lipfendra lowers LDL, but we do not yet have proof it lowers heart attack, stroke, or death. Do not stop your other heart medicines expecting that benefit.
Cost and access	The list price is about \$315 for a 30-day supply. Most insured patients, including Medicare, pay less. Your out-of-pocket cost depends on your plan. Ask your pharmacy and our office.
Pregnancy and children	Lipfendra is not approved for children, and its safety in pregnancy or breastfeeding is not established. Talk with your doctor if this applies to you.



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What Is Still Being Studied

- **Heart outcomes:** the big question -- does Lipfendra prevent heart attacks, strokes, and deaths? -- is still being tested in an ongoing trial. We do not have that answer yet.
- **Children:** Lipfendra is not approved for children. A study in younger patients is underway.
- **Pregnancy and breastfeeding:** safety has not been established. Tell us if you are pregnant, planning a pregnancy, or breastfeeding.
- **Long-term use:** the medicine is new, so doctors are still learning about very long-term use. We will keep you updated as more information comes in.



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Points to Know

If you remember nothing else, remember these key points.

- Lipfendra (enlicotide) is the first PCSK9 inhibitor you take as a pill, not a shot.
- It is one 20 mg tablet, once a day, on an empty stomach.
- It lowers LDL by about 57% on top of a statin -- about as much as the PCSK9 shots.
- It also lowers non-HDL, ApoB, and lipoprotein(a).
- In studies, side effects were like placebo; the most common were mild diarrhea and dizziness.
- It is NOT yet proven to prevent heart attacks or strokes. That study is still going.
- It is used on top of a statin, or when statins are not enough or cannot be tolerated.
- It is not approved for children. Talk with us before use in pregnancy or breastfeeding.



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When to Call Us - and When to Call 911

If you are not sure, call. We would rather hear from you twice than miss a real problem.

- Signs of an allergic reaction (rash, swelling of the face or throat, trouble breathing) -- call 911.
- Diarrhea that will not stop or is making you weak or lightheaded -- call us this week.
- New or ongoing dizziness that worries you -- call us.
- You are pregnant, planning a pregnancy, or breastfeeding -- call us before you keep taking it.
- You cannot get the medicine because of insurance or cost -- call our office. We can help.
- You are not sure how to take it on an empty stomach -- call your pharmacist or our office.
- You started Lipfendra and have not had a follow-up cholesterol test -- call us to set one up (usually 4 to 8 weeks after starting).

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Trusted Resources

The links below are the trusted resources Dr. Ali used to write this guide and that he recommends you visit for more information. Each is a clickable link in the digital version and a Short.io tracked URL on the printed version.

- [Merck -- Lipfendra \(enlicitide\) Announcement](#) - The maker's approval announcement, with the once-daily oral dosing and LDL-lowering summary.
- [AHA -- Cholesterol Medications](#) - American Heart Association overview of cholesterol-lowering medicines.
- [Cleveland Clinic -- PCSK9 Inhibitors](#) - Patient-friendly explanation of how PCSK9 inhibitors work and who they are for.
- [MedlinePlus -- Cholesterol Medicines](#) - NIH/NLM plain-language overview of the medicines used to lower cholesterol.
- [National Lipid Association -- Patient Resources](#) - Patient education on lipid disorders and newer LDL-lowering agents.



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Sources Used to Build This Guide

Every recommendation in this guide is grounded in one or more of the studies, guidelines, or trusted resources below. Short links are tracked so Dr. Ali can see which references patients are reading; nothing personally identifying is captured.

- [Merck — Lipfendra \(enlicotide\) Is the First and Only Once-Daily Oral PCSK9 Inhibitor Approved by the U.S. FDA \(Press Release, July 16, 2026\)](#) *[Press Release]*
Primary source for FDA approval date, first-and-only oral PCSK9 inhibitor claim, 20 mg once-daily indication, and the ~56% (up to 60% post-hoc) LDL-C figure.
- [U.S. FDA — Novel Drug Approvals](#) *[Regulatory]*
Confirms FDA regulatory action and the indication as an adjunct to diet to lower LDL-C in adults with hypercholesterolemia, including HeFH.
- [CORALreef Lipids — Enlicotide for LDL-C Lowering \(N Engl J Med 2026;394\(6\):529-539; NCT05952856\)](#) *[Clinical Trial]*
Pivotal phase-3 trial (2,909 adults): LDL-C -57.1% at week 24 vs placebo, sustained to 52 weeks; also lowered non-HDL-C, ApoB, and lipoprotein(a); side effects like placebo.
- [CORALreef AddOn — Enlicotide vs Oral Nonstatin Therapies \(J Am Coll Cardiol 2026;88\(3\):340-352; NCT06450366\)](#) *[Clinical Trial]*
Head-to-head trial (301 statin-treated adults): enlicotide -64.6% vs bempedoic acid -6.3%, ezetimibe -27.8%, bempedoic acid + ezetimibe -36.5% (P<0.001 for all).
- [Enlicotide Phase-3 CORALreef Program Summary \(Med 2026\)](#) *[Clinical Trial]*
Cross-trial summary of the CORALreef phase-3 program, including the HeFH result (LDL-C -59% at week 24) and pooled safety.
- [MK-0616 \(Enlicotide\): An Oral PCSK9 Inhibitor — Pharmacology Review \(Expert Opin Investig Drugs 2023\)](#) *[Review]*
Mechanism and pharmacology source: macrocyclic peptide that binds PCSK9, oral bioavailability, and renal excretion.
- [American Heart Association — Cholesterol Medications](#) *[Clinical]*
Plain-language framing of LDL cholesterol and cholesterol-lowering medicine classes for patients.
- [Cleveland Clinic — PCSK9 Inhibitors](#) *[Clinical]*
Patient-friendly explanation of how PCSK9 inhibitors work and who they are for.
- [MedlinePlus — Cholesterol Medicines](#) *[Clinical]*
NIH/NLM patient overview of cholesterol medicines used to set expectations and complement the LDL-lowering discussion.



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About This Guide

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Reviewer note: Reviewed the Merck approval release, the CORALreef trial reports, and AHA, Cleveland Clinic, and MedlinePlus patient pages. This guide adds a plain-language mechanism diagram, a pill-versus-shots table, a CORALreef AddOn bar chart, and an honest note that heart-attack and stroke benefit is not yet proven.

Disclaimer

This guide is for educational purposes only and does not replace medical advice from your physician. Recommendations may not apply to every patient. Always follow the specific instructions of Dr. Ali and your care team. In an emergency call 911 or go to the nearest emergency department.



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