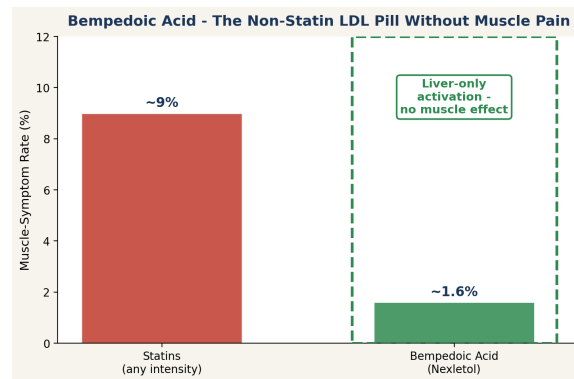


Understanding Bempedoic Acid (Nexletol / Nexlizet)

The non-statin LDL pill that skips your muscles

One pill a day. Drops LDL 18-25% on its own, 25-30% with ezetimibe. The CLEAR Outcomes study showed it cuts heart attacks and strokes in people who cannot take statins.



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

Rias KS Ali, MD FACC

Board Certified in Interventional Cardiology & Cardiovascular Disease

4740 Mile Stretch Drive, Holiday FL 34690 | Office: (727) 943-5200 | Fax: (727) 943-5201 | RiasAliMD.com

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Names & Terms You Will Hear

Term	Meaning
Nexletol (bempedoic acid)	Brand name for the 180 mg bempedoic acid pill. It holds one drug.
Nexlizet (bempedoic acid + ezetimibe)	A combo pill. It holds bempedoic acid 180 mg plus ezetimibe 10 mg.
ACL inhibitor	The drug class name. It blocks a liver enzyme that helps make cholesterol. This lowers LDL.
Prodrug	The pill is turned off when you swallow it. Your liver turns it on. Muscle cells cannot turn it on. That is why it does not cause muscle pain.
Non-statin LDL drug	A drug that lowers LDL but is not a statin. Bempedoic acid is one. So are ezetimibe and the PCSK9 shots.
CLEAR Outcomes	A large study (Nissen, 2023, 13,970 adults). It showed bempedoic acid cuts heart attacks and strokes. It is the first non-statin pill to prove this in people who cannot take statins.



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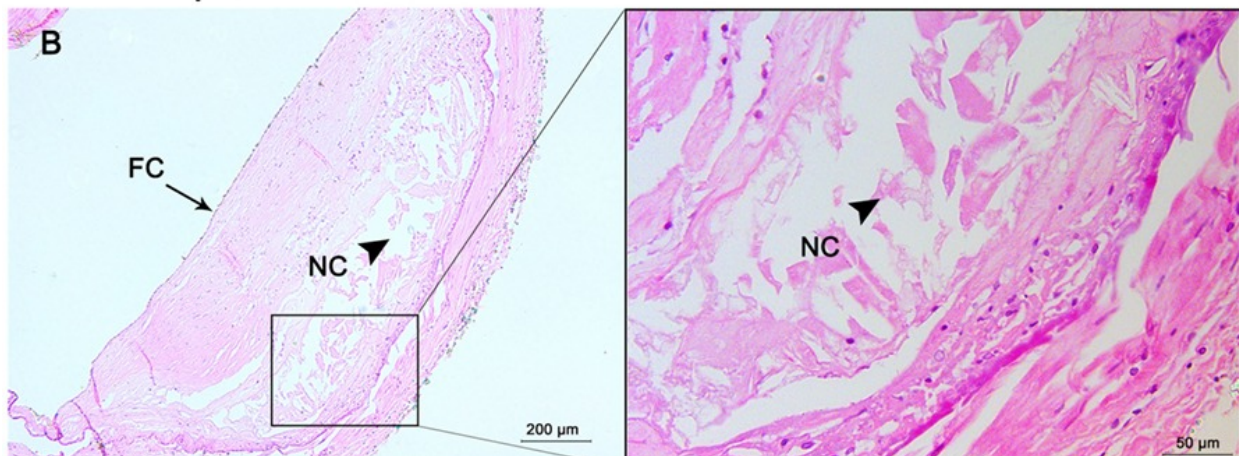


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What Is Bempedoic Acid (Nexletol / Nexlizet)?

- Bempedoic acid is a once-a-day pill that lowers LDL, the "bad" cholesterol. It blocks a liver enzyme called ACL. This enzyme sits one step ahead of the one that statins block.
- It is a **prodrug**. You swallow it turned off, and your liver turns it on. Your muscles cannot turn it on. That is why muscle pain is as rare as with a sugar pill.
- **On its own:** it drops LDL by about 18-25%.
- **With ezetimibe (as Nexlizet):** it drops LDL by about 25-30%.
- **Added to a statin:** it drops LDL by another 15-20%.
- It comes as a 180 mg pill. You take it once a day, with or without food. The dose stays the same. There is no need to step it up.
- It is approved for adults who have heart disease, or a gene that makes LDL run very high. It is for those who still need lower LDL while taking the highest statin dose they can handle.
- The brand costs \$400-600 a month. Your plan will most likely ask for an OK first. There is no generic yet.

Fibrous cap atheroma



A real cross-section of the plaque disease every LDL-lowering drug helps treat. Left: the fibrous cap (FC) sealing in a lipid-rich necrotic core (NC) inside an artery wall. Right: a close-up of that same lipid core. Bempedoic acid lowers LDL one step ahead of where statins work — the goal is the same: shrink this core and thicken the cap that keeps it from rupturing. Image: Yang et al., *Frontiers in Neurology* 2017 (CC BY 4.0).



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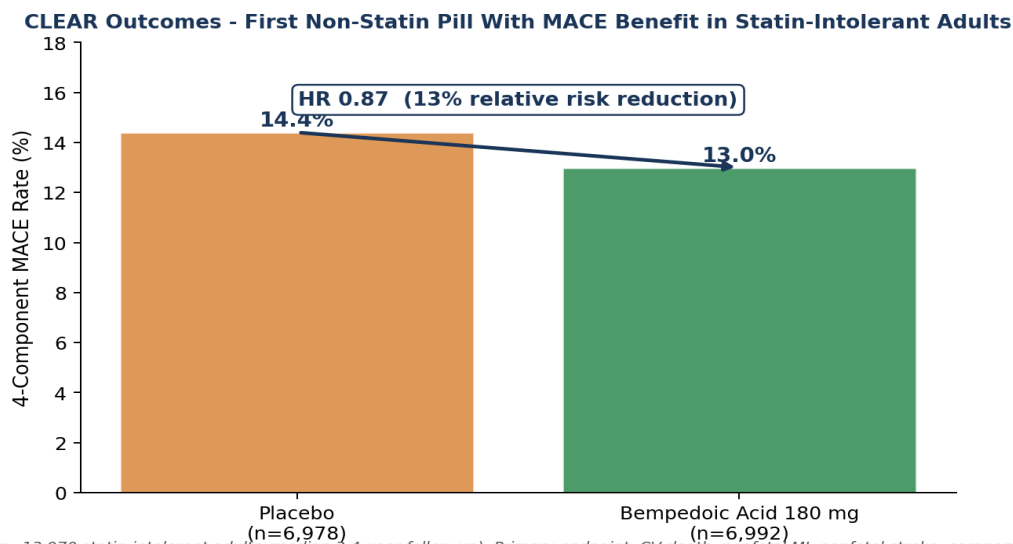
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Why It Matters

- **CLEAR Outcomes (Nissen, 2023)** was the first trial to show that a non-statin pill cuts heart attacks and strokes in people who **cannot take statins**. It enrolled 13,970 adults. Bad heart events dropped by 13% (HR 0.87) over about 3.4 years.
- This matters a lot. About 5-10% of people cannot take statins. For years, they had few pill options. Bempedoic acid changed that.
- It is the **only non-statin pill with proof it cuts events** in people who cannot take statins. The ezetimibe proof (the IMPROVE-IT trial) came from people who were also on a statin.
- It spares your muscles because it is turned on only in the liver. Muscle cells cannot turn it on. So even people who get muscle pain easily can take it.
- It fits right into the **LDL ladder**: statin, then add ezetimibe, then add bempedoic acid, then add a PCSK9 shot. People who cannot take statins may use it sooner.
- The combo pill Nexlizet (bempedoic acid + ezetimibe) lets two non-statin pills stand in for a statin. That helps people who cannot take statins at all. One pill covers about 30% of the LDL drop.
- It drops LDL 18-25% on its own, and about 25-30% with ezetimibe. That helps a lot when a statin is only part of the plan, or not an option.



Nissen NEJM 2023 (n=13,970 statin-intolerant adults; median 3.4-year follow-up). Primary endpoint: CV death, nonfatal MI, nonfatal stroke, coronary revascularization.

CLEAR Outcomes (Nissen, 2023; 13,970 adults who could not take statins). Bempedoic acid 180 mg a day vs a sugar pill cut bad heart events (MACE) from 14.4% to 13.0% over about 3.4 years. That is a 13% drop. It is the first non-statin pill proven to cut these events in people who cannot take statins.



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CLEAR Outcomes was a big deal. Until 2023, people who could not take statins had no pill proven to cut heart attacks and strokes. These are millions of people who got muscle pain from every statin they tried. Then CLEAR Outcomes (Nissen, 2023) showed bempedoic acid cuts these events in just these people. Bad heart events dropped by 13% across 13,970 adults. For those who had only ezetimibe or pricey shots before, this is now the first pill that both lowers LDL AND is proven to cut events.



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Treatment Options

- **Dose:** one 180 mg pill a day. The dose stays the same. There is no need to step it up.
- **When to take it:** any time of day, with or without food. Most people take it in the morning or at night.
- **Combo pill (Nexlizet):** bempedoic acid 180 mg plus ezetimibe 10 mg in one pill. You still take it once a day.
- **With statins:** if you can take even a low statin dose, you can add bempedoic acid. But do not pair it with high-dose simvastatin (over 20 mg) or pravastatin (over 40 mg). The mix can raise the risk of muscle harm.
- **Lab check:** get a new lipid panel about 8-12 weeks after you start. Look for an 18-25% LDL drop on the pill alone, and more with ezetimibe.
- **Uric acid check:** get one before you start, and again at 4-12 weeks. The pill can raise uric acid and set off gout in some people.
- **If you have had gout:** tell your cardiologist before you start. You may need a gout-control pill at the same time.
- **Insurance:** your plan will almost always ask for an OK first. Bring notes on the statins you tried and the side effects you had.
- **Pregnancy:** do not take it. Stop the pill before pregnancy, or as soon as you think you may be pregnant.



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The Non-Statin LDL Ladder - Where Bempedoic Acid Fits

Step	Therapy	Additional LDL Drop	Cost / Notes
1	Lifestyle (Mediterranean / DASH, weight, exercise)	5-15%	Free; foundation
2	High-intensity statin (if tolerated)	45-55%	Generic; cheap
3	Add Ezetimibe 10 mg	+18-20%	Generic; \$5-30/month
4	Add Bempedoic acid 180 mg	+15-20%	Brand; \$400-600/month
5	Combination pill Nexlizet (bempedoic + ezetimibe)	+25-30% vs baseline	Brand; covers two mechanisms
6	Add PCSK9i (Repatha / Praluent / Leqvio)	+50-60%	Brand injectable; insurance + copay card



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How Bempedoic Acid Works, and Why Your Muscles Are Spared

- **The cholesterol line:** your liver makes cholesterol with a long chain of helpers (enzymes). Statins block one of them, called HMG-CoA reductase. Bempedoic acid blocks one just ahead of it, called **ATP-citrate lyase (ACL)**.
- **The prodrug trick:** the pill is turned off when you swallow it. A liver-only helper called ACSVL1 turns it on. Without ACSVL1, the pill does nothing.
- **Why muscles are spared:** your muscle cells do NOT have ACSVL1. So the pill stays off in muscle. No live drug in muscle means no muscle pain.
- **How LDL drops:** the liver now makes less cholesterol. So it pulls more LDL out of your blood to use. That is the same end result as a statin, just one step earlier in the line.
- **Why it adds to a statin:** the two drugs block two spots on the same line. Even on a statin, the liver still makes some cholesterol. Bempedoic acid closes more of the gap.
- **Why it pairs so well with ezetimibe:** ezetimibe blocks the gut from taking cholesterol in. Bempedoic acid blocks the liver from making it. Together they hit both sides. That is why Nexlizet drops LDL 25-30%.

Bempedoic Acid - Four Common Cases

Cannot take statins	On full statin + ezetimibe, LDL still high	High LDL from a gene (HeFH)	Can take only part of a statin dose
• Muscle pain on 2 or more statins • The pill alone drops LDL 18-25% • Or Nexlizet drops it 25-30% • CLEAR Outcomes proves it cuts events	• Add bempedoic acid as the next pill • LDL drops another 15-20% • Costs less than a PCSK9 shot for many • One pill a day, no shot	• You most often need a few drugs • Statin + ezetimibe + bempedoic acid • Add a PCSK9 shot or inclisiran if needed • You take these for life	• A low statin dose every other day • Plus bempedoic acid 180 mg a day • Plus ezetimibe 10 mg if needed • Stack them to reach your LDL goal



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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
Add bempedoic acid to your statin (or take it alone if you cannot take statins)	Higher uric acid (about 10% up). Gout flares (about 3% vs 2% on a sugar pill). A rare risk of a torn tendon. Brand cost. Not safe in pregnancy.	LDL drops another 15-25%. Proven to cut heart attacks and strokes (MACE) in people who cannot take statins (CLEAR Outcomes). One pill a day. No muscle pain.	Raise your statin dose if you can take it. Or add ezetimibe (it costs less). Or add a PCSK9 shot (stronger, but a shot).
Switch to the combo pill Nexlizet (bempedoic acid + ezetimibe)	Same side effects as each drug alone. May cost more than two cheaper generics.	One pill is easier to keep up. Two non-statin drugs that work in two ways. LDL drops about 25-30%.	Take bempedoic acid and generic ezetimibe as two pills (often cheaper).
Take bempedoic acid alone if you cannot take statins	Only about 18-25% LDL drop alone. That may not be enough if your LDL is very high. Brand cost.	The strongest non-statin pill for people who cannot take statins. Proof it cuts heart attacks and strokes (MACE).	Take ezetimibe alone (cheaper, but weaker). Or use a PCSK9 shot (stronger, but a shot).
Skip bempedoic acid and go straight to a PCSK9 shot	A PCSK9 drug means shots, an OK from your plan first, and a higher copay for many people.	The biggest LDL drop (about 50-60%). Strong proof it cuts events. A good fit for very high-risk people.	Try bempedoic acid first as a pill. Move up to a PCSK9 shot if your LDL is still too high.
Do nothing more. Stay on your statin (or part of one, or none) alone	Higher heart risk if your LDL stays above goal.	A simpler plan. No added cost.	Add ezetimibe (the cheapest) first. Then add bempedoic acid if you need more.



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Option	Risks	Benefits	Alternatives
Stop your statin and switch to bempedoic acid alone	You lose the statin's proven benefit. The pill alone drops LDL less than a full statin dose.	It clears up statin side effects. You may stick with one pill you can take instead of one you skip.	Try a low statin dose every other day. Or a low statin dose plus ezetimibe. Or bempedoic acid plus ezetimibe (Nexlizet).



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Common Misconceptions

Myth	Reality
Bempedoic acid is just a new statin.	No. It is NOT a statin. It works one step ahead of where statins work. And it is turned on only in the liver, not in muscle. So it does not cause the muscle pain that statins can.
If I had muscle pain on a statin, bempedoic acid will hurt too.	Most likely no. Muscle is the weak spot for statins. But muscle cannot turn bempedoic acid on. In people who cannot take statins, muscle pain on this pill was as rare as on a sugar pill.
Bempedoic acid is too new to trust.	It was approved in 2020. And the CLEAR Outcomes study (Nissen, 2023) backs it. That study had 13,970 people and showed a 13% drop in heart attacks and strokes. That is real, large, and recent proof.
If I take bempedoic acid I can stop my statin.	Most often no. If you can take even a low statin dose, keep it. The two drugs together drop LDL the most. The pill stands in for a statin only when you truly cannot take one.
Bempedoic acid causes muscle problems like statins.	The trials show none. In CLEAR Outcomes, muscle pain was as rare as on a sugar pill. The reason is that it is turned on only in the liver.
I should wait for a generic.	There is no generic yet, and none is coming soon. If your LDL is far from goal and you have heart disease, waiting may cost you more than the drug. Your plan will most often say yes when you ask.
A small rise in my creatinine means my kidneys are failing.	No. The pill nudges one lab number (creatinine) up a little. But it does NOT lower how well your kidneys work. Your kidneys are fine.
Gout is rare, so I do not need to worry about it.	Bempedoic acid raises uric acid. People who have had gout, or whose uric acid runs high, can flare. Tell your cardiologist if you have ever had gout. It is easy to head off.



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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
High uric acid and gout flares (about 3%)	The pill raises uric acid by about 10%. Most people feel nothing. But those who have had gout, or whose uric acid runs high, can flare. Check uric acid before you start and at follow-up.
Torn tendon (rare)	Trials saw a small rise in torn tendons, such as the Achilles. The risk is higher in older adults, in people on steroids, and in those with past tendon trouble. Stop the pill if you get sudden bad tendon pain.
A lab-only rise in one kidney number	The pill nudges one kidney lab number (creatinine) up a little. But how well your kidneys work (GFR) does not change. Do NOT take this as kidney harm.
Mild belly side effects (about 3%)	Some people get loose stools, belly pain, or an upset stomach. These tend to be brief. They ease as you keep taking it, or if you switch to a different time of day.
Muscle symptoms (as rare as a sugar pill)	In the trials, muscle pain was as rare as on a sugar pill. A few cases of serious muscle breakdown have been seen. Those were almost always when a statin was also used. The pill alone shows no real muscle risk.
Mixing with some statins	Bempedoic acid raises the blood level of simvastatin and pravastatin. While on it, do not take simvastatin above 20 mg a day or pravastatin above 40 mg a day. Atorvastatin and rosuvastatin are most often fine.
Small drop in blood counts (rare)	A few trials saw small drops in red cells and platelets. These were rare and most often did not matter.
Not safe in pregnancy	Animal data show harm to the baby. Stop the pill before a planned pregnancy, or as soon as you find out you are pregnant.



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Points to Know

If you remember nothing else, remember these key points.

- Bempedoic acid drops LDL 18-25% on its own, and 25-30% with ezetimibe.
- CLEAR Outcomes (Nissen, 2023) showed it cuts heart attacks and strokes in people who cannot take statins.
- One 180 mg pill a day. The dose stays the same. Take it any time.
- It is turned on only in the liver. That is why there is no muscle pain. This is its big edge over statins.
- The combo pill Nexlizet (bempedoic acid + ezetimibe) puts two non-statin drugs in one pill.
- Watch for a rise in uric acid and for gout. Check labs before you start and at follow-up.
- A small rise in one kidney lab number (creatinine) is normal here. It does NOT mean kidney harm.
- Do not take it in pregnancy.
- Brand cost is \$400-600 a month. Your plan most often says yes when you have tried statins or your LDL is still high.



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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.

- New or worse joint pain or swelling, above all in a big toe. Call us this week. It may be a gout flare.
- Sudden bad tendon pain, swelling, or trouble using a joint. Call us today. A torn tendon is rare but real.
- Bad muscle pain or dark-colored urine. Call us today. This is rare, and most often only when you also take a statin.
- New tiredness, yellow skin or eyes, or pain on the right side under your ribs. Call us this week. A liver effect is rare.
- A bad allergic reaction (hives, swelling, trouble breathing). Call 911.
- You plan to get pregnant, or you are pregnant. Call us. You must stop the pill.
- You have not had your lipid or uric acid labs redone 8-12 weeks after you start. Call to set them up.
- Your plan said no, or the cost worries you. Call us. We can often get it covered with the right notes.

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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.

- [AHA - Cholesterol Medications](#) - AHA patient overview of LDL-lowering drug classes including bempedoic acid.
- [Cleveland Clinic - Bempedoic Acid Tablets](#) - Cleveland Clinic patient drug guide for bempedoic acid (Nexletol).
- [Mayo Clinic - Cholesterol-Lowering Medications](#) - Mayo overview of all cholesterol drug classes including bempedoic acid.
- [MedlinePlus - Bempedoic Acid](#) - NIH/NLM patient drug information.
- [National Lipid Association - Patient Tools](#) - NLA patient education on lipid management and non-statin add-on therapy.



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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.

- [CLEAR Outcomes Trial — Bempedoic Acid in Statin-Intolerant Patients \(Nissen et al., NEJM 2023; PMID 36876740\)](#) [Clinical Trial]
Pivotal MACE-outcome trial — 13,970 statin-intolerant patients; bempedoic acid cut MACE 13% (HR 0.87) over ~3.4 years. The first non-statin oral with proven outcome benefit in the statin-intolerant population.
- [CLEAR Wisdom Trial — Bempedoic Acid Add-On to Statin in ASCVD/HeFH \(Goldberg et al., JAMA 2019; PMID 31634091\)](#) [Clinical Trial]
Phase 3 efficacy trial — bempedoic acid added to maximally tolerated statin cut LDL ~17% beyond statin baseline over 52 weeks in ASCVD or HeFH adults.
- [CLEAR Serenity Trial — Bempedoic Acid in Statin-Intolerant Adults \(Laufs et al., JACC 2019; PMID 30922930\)](#) [Clinical Trial]
Phase 3 trial in statin-intolerant patients — bempedoic acid monotherapy reduced LDL ~21% vs placebo without excess muscle symptoms.
- [2022 ACC ECDP on the Role of Nonstatin Therapies for LDL-C Lowering \(Lloyd-Jones et al., JACC\)](#) [Guideline]
ACC expert consensus pathway: where bempedoic acid fits — after ezetimibe in many patients, or before PCSK9i in statin-intolerant patients.
- [2018 AHA/ACC/AACVPR Guideline on the Management of Blood Cholesterol \(Grundy et al.\)](#) [Guideline]
Primary US cholesterol guideline; defines threshold-based escalation of non-statin LDL-lowering therapy.
- [AHA — Cholesterol Medications](#) [Clinical]
AHA patient overview of LDL-lowering drug classes including bempedoic acid.
- [Cleveland Clinic — Bempedoic Acid](#) [Clinical]
Cleveland Clinic patient drug guide for bempedoic acid (Nexletol).
- [Mayo Clinic — Cholesterol-Lowering Medications](#) [Clinical]
Mayo overview of all cholesterol drug classes including bempedoic acid.
- [National Lipid Association — Patient Tools](#) [Clinical]
NLA patient education on lipid management and non-statin add-on therapy.



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About This Guide

Rias KS Ali, MD FACC | Board Certified in Interventional Cardiology & Cardiovascular Disease

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Reviewer note: Reviewed against AHA, NLA, Cleveland Clinic, Mayo Clinic, and the CLEAR Outcomes, CLEAR Wisdom, and CLEAR Serenity studies. Ours adds the muscle-pain chart, the CLEAR Outcomes bar graph, and plain next steps for people who cannot take statins.

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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