

Statin Intolerance: Facts & Options

High cholesterol is a major risk factor for heart disease. 1 out of every 4 cardiovascular deaths is connected to long term exposure to high LDL (“bad”) cholesterol. For decades, statins have been the first line of defense. However, many people stop taking them due to side effects.

What is statin intolerance?

Statin intolerance happens when side effects (most often muscle pain or weakness) make it hard to continue therapy.

According to the National Lipid Association (NLA), statin intolerance occurs when a patient experiences adverse effects that improve when the dose is lowered or stopped. It falls into two categories:

- **Partial intolerance:** You can handle a low dose, but not enough to reach your cholesterol goals (most common).
- **Complete intolerance:** You cannot tolerate any dose of any statin. (uncommon, <5%).

To be clinically classified as “statin intolerant,” a patient should have tried at least two different statins, including one at the lowest dose.

How common is it?

A major 2022 meta-analysis of 176 studies including over 4 million patients found:

- Self-reported statin intolerance ranges from 5–30%
- True worldwide prevalence is 9.1%
- Complete intolerance occurs in <5% of patients

The Nocebo Effect

Research suggests that some muscle pain is due to the “nocebo effect”, where negative expectations amplify symptoms (up to 50-90% of muscle complaints in trials). But this doesn’t mean symptoms aren’t real; they’re absolutely real and should be taken seriously.

While these feelings are real to the patient, they often mean the body can actually handle a statin if the right one is chosen.

Theories on why some people experience side effects

Common issues include muscle aches, fatigue, or mild liver enzyme rises. Here are some theories:

- **CoQ10 depletion:** Statins block an enzyme needed for cholesterol and CoQ10. CoQ10 is involved in energy production in muscles and the brain. When statins deplete CoQ10, it may contribute to muscle symptoms for some people.
- **Drug interactions:** Some statins are processed by liver pathways (CYP450 enzymes) that are used for many other drugs. This overlap can lead to drug–drug interactions, raising statin levels in the blood and increasing the risk of side effects. Interestingly, CBD products use the same pathway, so taking a statin with CBD may further increase this risk.
- **High doses:** Higher statin doses increase the risk of muscle symptoms, liver enzyme elevations, and blood sugar changes.
- **Genetics and metabolic differences:** Variability in metabolism can make certain statins harder to tolerate than others.

Who is at higher risk?

Certain factors raise the odds, based on the large 2022 meta-analysis:

- Women (+48%)
- Age ≥ 65 (+31%)
- Obesity (+31%)
- Diabetes (+27%)
- Hypothyroidism (+38%)
- Certain drugs (e.g., calcium channel blockers: +35.5%, antiarrhythmics: +31.2%)
- Race (Asian: +25.4%, Black: +29.3%)
- Chronic conditions (e.g., kidney failure: +25.2%, liver disease: +24.3%)
- High statin doses
- Heavy alcohol use or intense exercise

Factors **not** associated: Smoking, high blood pressure, or long-term statin use. Depression may even lower risk (-12.2%).

What to do if you experience side effects

Because complete intolerance is uncommon, many people regain tolerance by:

- Lowering the dose
- Switching to a different statin
- Trying non-daily dosing (e.g., every other day)

Zypitamag® (pitavastatin): A different option

Not all statins are the same. There are 7 statins (e.g., atorvastatin, rosuvastatin, pitavastatin). They differ in how they're processed, interacting, and side effects.

If you've had issues with other statins, consider Zypitamag. Data shows it is one of the best-tolerated statins, especially for those who've had trouble with others.

Clinical findings:

- Muscle pain: Only 3.1% at 4 mg
- Minimal CoQ10 depletion: Zypitamag: -7.7% vs. atorvastatin: -26.1%
- Fewer drug interactions: Zypitamag avoids major CYP pathways where 80% of drugs are processed
- Strong LDL-C reduction: Up to 45% at 4 mg
- Blood sugar: Minimal rise (+2.1%, non-significant) vs. atorvastatin (+7.2%)

If someone has "failed" multiple statins, Zypitamag may still work because it behaves differently from other statins like atorvastatin or simvastatin. Before giving up on statins entirely, try Zypitamag.

ZYPITAMAG IS IDEAL FOR THOSE WHO:

- Have had issues with other cholesterol lowering medications
- Take multiple medications
- Need LDL-C lowering without high doses
- Are concerned about blood sugar increases
- Want well tolerated treatment backed by clinical evidence

Non-statin options vs Zypitamag

If you can't tolerate statins or you need extra help reaching your goals with Zypitamag, several non-statin options exist.

Medication	How it works	LDL-C reduction	Cost
Zypitamag	Blocks liver cholesterol production	↓ 45%	\$39/month or less at Marley Drug
Ezetimibe	Blocks cholesterol absorption from the intestine	↓ 15-25%	\$37 for 6 months at Marley Drug
Nexletol (bempedoic acid)	Blocks ACL enzyme in the liver (upstream from statins)	↓ 15-25%	\$231 - \$390/month
PCSK9 Inhibitors (e.g., Repatha, Praluent, Inclisiran)	Increase LDL receptor recycling so the liver removes more LDL	↓ 50-60%	\$240 - \$520/month

Stay on therapy if possible

Lowering LDL-C prevents plaque buildup (this takes years or decades without symptoms), cutting heart attack, stroke risk ~1% per 1% LDL-C drop.

Statins have the strongest evidence for this; stopping them raises preventable events. Talk to your doctor. Options like Zypitamag or combination therapy (ie: Zypitamag with ezetimibe) can get you there affordably and safely.

Why order Zypitamag through Marley Drug

Zypitamag is available with insurance or at a low cash price. When you choose the cash option, you can access Zypitamag without step therapy, and the maximum you'll pay is \$39 per month.

What you get:

- \$39/month or less
- Free shipping (average delivery time: 2 days)
- Direct pharmacy support
- Cholesterol education program: Evidence-based education through our YouTube channel, blogs, and email updates

Talk your doctor about Zypitamag.