

Non-Statin Lipid-Lowering Agents

Modified March 2026

This chart provides lipid effects, outcomes, and cost information for the non-statins. See our FAQ, [Cholesterol Guidelines](#) (United States) and [Canadian Dyslipidemia Recommendations](#) (Canada) for help identifying non-statin candidates based on guidelines. Information is from product labeling (see footnote d) unless otherwise indicated. For a summary of **therapeutic roles** of non-statins, see **footnote c**.

Drugs highlighted in yellow are generally preferred; others have more specialized roles.

Drug/Cost ^a	Lipid Effects ^b	Outcomes Data	Comments (see footnote c for therapeutic role)
Alirocumab (Praluent) (PCSK9 inhibitor) 75 mg/two weeks: US: ~\$520; Canada: ~\$580 300 mg/four weeks: US: ~\$110	75 mg/2 weeks or 300 mg/4 weeks² LDL↓: ~60%	Post-MI, used with maximally-tolerated high-dose statin reduced a composite of CHD death, ischemic stroke, nonfatal MI, and unstable angina (NNT = 63 over 2.8 years vs placebo) [Evidence Level A-1]. ²	<ul style="list-style-type: none"> Subcutaneous injection Injection site reactions in up to 17% of patients.⁴
Bempedoic acid (Nexletol [US], Nexlizet [US; with ezetimibe], Nilemdo [Canada]) (adenosine triphosphate-citrate lyase inhibitor) 180 mg/day: US ~\$420; Canada: ~\$140	180 mg/day^{3,5} LDL↓: ~20% HDL↓: ~4.5% TG: no effect	Reduced a composite of CV death, nonfatal stroke, nonfatal MI, or coronary revascularization in high-risk, statin-intolerant patients (NNT = 63 over three years vs placebo) [Evidence Level A-1]. ³ (~23% of patients in both groups were taking a very low-dose statin)	<ul style="list-style-type: none"> Avoid with simvastatin >20 mg/day or pravastatin >40 mg/day due to increased risk of myopathy.⁴ May cause tendon rupture or cholelithiasis.⁴ Increases uric acid, SCR, and liver enzymes.⁴
Bezafibrate (Canada) (Bezalip SR, generic) (Fibric acid) 400 mg/day: Canada: ~\$70	400 mg/day⁶ (monotherapy) LDL↓: ~5% HDL↑: ~14% TG↓: ~25%	Reduced a composite of MI and sudden death in a subgroup with TG 200 mg/dL (~2.3 mmol/L) or higher. No increase in non-CV death. ⁶ (Patients using other lipid-lowering drugs were excluded).	<ul style="list-style-type: none"> May cause reversible increase in serum creatinine. Max daily dose is 200 mg if CrCl <60 mL/min. Limited data with statins.
Cholestyramine (generics, Olestyr [Canada]) (Bile acid sequestrant) 24 g/day (packets): US: ~\$190 Canada: ~\$180	20 to 24 g/day^{9,12} (monotherapy) LDL↓: ~20% to 30% HDL↑: ~3% to 6% TG↑: ~5 to 6%	<ul style="list-style-type: none"> Primary prevention, men: reduced a composite of CHD death and nonfatal MI (NNT = 59 for 7 years) [Level A-1].⁸ Secondary prevention, men: with diet, reduced cardiac events vs usual care (not placebo-controlled; events not a primary outcome) [Level B-1].¹⁰ Slows progression and increases regression of atherosclerosis.¹⁰ 	Can be difficult to tolerate due to GI side effects such as constipation and gas. ¹¹
Colesevelam (Welchol [US], Lodalix [Canada], generics) (Bile acid sequestrant) 3.8 g/day (tablets): US: ~\$70; Canada: ~\$170	3.8 g/day (monotherapy) LDL↓: ~15% HDL↑: ~4% TG↑: ~5%	Adequate studies of the effects of colesevelam on major CV events or prevention of CVD are lacking. ¹⁴	<ul style="list-style-type: none"> Potential lower risk of GI side effects compared to cholestyramine and colestipol.^{11,13} FDA-approved for glycemic control in type 2 diabetes.
Colestipol (Colestid, generic [US]) (Bile acid sequestrant) 16 g/day (tablets): US: ~\$510; Canada: ~\$200	16 g/day³⁰ (monotherapy) LDL↓: ~25% HDL: no change TG↑: ~22%	Adequate studies of the effects of colestipol on major CV events or prevention of CVD are lacking. ¹⁴	Can be difficult to tolerate due to GI side effects such as constipation and gas. ¹¹
Evinacumab-dgnb (Evkeeza) (angiopoietin-like 3 inhibitor) 1,200 mg every four weeks US: ~\$43,900 Canada: cost not available	15 mg/kg every 4 weeks LDL↓: ~49% HDL↓: ~31% TG↓: 50%	None	<ul style="list-style-type: none"> Indicated for HoFH as an adjunct to other LDL-lowering therapies. One-hour infusion every four weeks.
Evolocumab (Repatha) (PCSK9 inhibitor) 140 mg every two weeks: US: ~\$570; Canada: ~\$630 420 mg once monthly: US: ~\$620	140 mg every two weeks or 420 mg monthly¹⁵ LDL↓: ~60%	Added to a high- or moderate-dose statin, reduced a composite of CV death, MI, or stroke in high-risk CVD patients (most had a prior MI; about one third had diabetes and/or smoked) (NNT = 67 over 2 years vs placebo). CV death as a stand-alone outcome and all-cause mortality were not affected. ¹⁵	<ul style="list-style-type: none"> Subcutaneous injection. Injection site reactions in up to ~6% of patients. Canada: use caution in severe renal or hepatic impairment (no data).

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Ezetimibe (Zetia [US], Ezetrol [Canada], generics) (Cholesterol absorption inhibitor) 10 mg/day: US: ~\$15; Canada: <\$10	10 md/day (monotherapy) LDL↓: ~15% to 20% ³⁷ HDL↑: ~2% to 3% TG↓: ~6% to 11%	<ul style="list-style-type: none"> With simvastatin 40 mg post-ACS, reduced a composite of CV death, nonfatal MI or stroke, unstable angina hospitalization, or revascularization (NNT = 50 over 7 years vs simvastatin alone [Level A-1]).¹⁶ With simvastatin 20 mg, reduces first major atherosclerotic event in chronic renal disease [Level A-1].¹⁷ 	<ul style="list-style-type: none"> In the US, ezetimibe is also available in combination with simvastatin (Vytorin, generics), bempedoic acid (Nexlizet), or amlodipine (Lypqozet, generics). LDL reduction is ~25% with statin.³⁷
Fenofibrate (Antara [US], Lipofen [US], Trilipix [US], Lipidil EZ [Canada], Lipidil Supra [Canada], generics (fibric acid) 130 mg/day: US: ~\$120 145 mg/day: US: ~\$15; Canada: ~\$30 200 mg/day: Canada: ~\$30	150 mg/day (monotherapy) LDL↓: ~18% HDL↑: ~10% TG↓: ~37%	<ul style="list-style-type: none"> Prevention of CV events in type 2 diabetes: did not reduce primary composite outcome (nonfatal MI or CV death). Improved outcomes included nonfatal MI (24%↓), coronary revascularization (21%↓), progression to albuminuria, and reduced laser treatments for retinopathy. Non-significant increase in CV death.¹⁸ As statin add-on, did not lower risk of nonfatal MI, nonfatal stroke, or CV death more than statin alone in patients with type 2 diabetes at high risk for CV disease.¹⁹ 	<ul style="list-style-type: none"> Contraindicated if CrCl <30 mL/min. Associated with reversible increase in SCr. Clinical significance unknown. Risk of cholelithiasis (unknown frequency).⁴ Safer than gemfibrozil for use with statins.²⁰ May cause a paradoxical reduction in HDL.
Gemfibrozil (Lopid [US], generics) (Fibric acid) 1,200 mg/day: US: ~\$15; Canada: ~\$90	1,200 mg/day ²¹ (monotherapy) LDL: no change HDL↑: ~6% TG↓: 31%	<ul style="list-style-type: none"> Primary prevention, men: reduced sudden cardiac death plus fatal/nonfatal MI (NNT = 71 over 5 years) [Level A-1]. Secondary prevention of nonfatal MI plus cardiac death in men with low HDL (NNT = 23 over 5 years) [Level A-1].²¹ 	<ul style="list-style-type: none"> Consider alternative if CrCl <50 mL/min. Avoid if CrCl <10 mL/min.⁴ Avoid with statin.²⁰ No proven mortality benefit. Risk of cholelithiasis (unclear frequency).⁴
Icosapent ethyl (Vascepa, generics [US]) (EPA; about 1 g omega-3s/capsule ²³) 4 g/day US: ~\$180; Canada: ~\$320	TG↓: ~10% (2 g/day), ~22% (4 g/day). ²³ LDL↓: ~6% (4 g/day). ²³	As statin add-on, reduced a composite of CV death, nonfatal MI or stroke, revascularization, or unstable angina in a high-risk, mostly secondary prevention, population (NNT=21 over 5 years). Higher incidence of A-fib in icosapent group (NNH=71) [Level B-1]. ²²	<ul style="list-style-type: none"> Patients in statin add-on study had a mean TG of 216 mg/dL (2.4 mmol/L).²² Safe for use with statin.²³ Use caution with fish or shellfish allergy.⁴
Inclisiran (Leqvio) (siRNA) 284 mg every six months US: \$3,400/6 months Canada: ~\$3,100/6 months	LDL↓: ~50% ²⁴	None	<ul style="list-style-type: none"> Catalyzes the breakdown of the mRNA that codes for PCSK9 (i.e., inhibits PCSK9 production).⁴ Subcutaneous injection given by a healthcare provider at months 0, 3, then every six months.⁴ No long-term safety data.
Lomitapide (Juxtapid) 60mg/day US: ~\$119,000 Canada: pricing unavailable.	LDL↓: ~44%	None	<ul style="list-style-type: none"> US: available only via the Juxtapid REMS (risk of liver toxicity). Indicated for HoFH as an adjunct to other LDL-lowering therapies. Requires supplementation with vitamin E and fatty acids due to impaired absorption. CYP450 drug interactions. Fetal harm.
Niacin (US) (Niacor, Niaspan [generic only; US]) Niacin 1 g/day: \$300 (Niacor), ~\$15 (Niaspan generic)	Niaspan 1,500 to 2,000 mg/day: ²⁵ LDL↓: ~6% HDL↑: ~15% TG↓: ~21%	<ul style="list-style-type: none"> Secondary MI prevention: one less MI for every 30 patients treated for five years (Coronary Drug Project) [Level B-1]. No CV event benefit from combo of niacin + statin vs statin alone in patients with LDL <70 mg/dL (1.81 mmol/L), low HDL, and high TG.²⁵ 	<ul style="list-style-type: none"> Raises HDL more than other agents. Use limited by side effects (e.g., flushing, hyperglycemia, hepatotoxicity, increased uric acid) and need for lab monitoring). No mortality benefit. May increase risk of statin myopathy.

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Omega-3 ethyl esters (US) (Lovaza, generics) (EPA/DHA; about 1 g omega-3s/capsule) 4 g/day: US: ~\$30	4 g/day: ²⁹ LDL↑: ~4% HDL↑: ~5% TG↓: ~23%	<ul style="list-style-type: none"> • Secondary prevention: reduces CV death, sudden death, and composite of death, nonfatal MI, and nonfatal stroke [Level B-1].²⁶ • Secondary prevention in patients with, or at risk for, type 2 diabetes: did not reduce CV events. About half of patients were taking a statin.²⁷ • Primary prevention: no benefit for composite of MI, stroke, or CV death [Level A-1].²⁸ 	<ul style="list-style-type: none"> • Safe for use with statin.²⁹ • Associated with an increase in risk for recurrence of symptomatic A-fib/flutter, especially within first three months of therapy. • Use with caution with fish or shellfish allergy.

Footnotes:

- Wholesale acquisition cost (WAC) of 30-day supply of dose specified (generic, if available). US medication pricing by Elsevier, accessed April 2025.
- Placebo-subtracted lipid effects as statin add-on or monotherapy.
- Summary of **therapeutic roles** of non-statin:
 - Ezetimibe, bempedoic acid, and PCSK9 inhibitors are the preferred add-ons for CV risk reduction for patients who cannot meet LDL goals with a statin.^{3,5,33,31,32}
 - » Ezetimibe is preferred first-line in primary prevention patients.³²
 - » In very high-risk secondary prevention patients, ezetimibe and/or a PCSK9 inhibitor is preferred.³²
 - Inclisiran is an alternative to PCSK9 inhibitors for secondary prevention patients with very high risk, and for patients with severe hypercholesterolemia.^{24,32}
 - Bile acid sequestrant use is limited by tolerability and dosing issues.³² Preferred for pregnant patients because they are not systemically absorbed.³² May increase TG if used without a statin.¹²
 - Fenofibrate or gemfibrozil are first-line for triglycerides ≥ 500 mg/dL (5.7 mmol/L), especially if $\geq 1,000$ mg/dL (11.3 mmol/L), but gemfibrozil cannot be used with a statin.³²
 - Icosapent ethyl is used for certain patients (CVD and age ≥ 50 years, or diabetes plus other risk factors) with triglycerides 150 to 499 mg/dL (1.7 to 5.6 mmol/L) plus LDL < 100 mg/dL (< 2.6 mmol/L) on optimized statin.³²
 - Omega-3 acid ethyl esters (US): first-line option for triglycerides ≥ 500 mg/dL (≥ 5.65 mmol/L).³²
 - Niacin: Role as statin-add-on not supported by RCTs.³² FDA indication for niacin extended-release (ER) use with statins revoked in April 2016 due to lack of CV benefit/safety.³⁴ Last-line for severe hypertriglyceridemia.³²
- US product information** used in creation of this chart: Evkeeza (March 2023), Juxtapid (January 2024), Lopid (August 2023), Lipofen (September 2021), Lovaza (February 2021), niacin extended-release (Lannett, January 2025), Niacor (June 2020), Repatha (November 2024), Welchol (January 2024), Zetia (February 2024). **Canadian product monographs** used in creation of this chart: Bezalip SR (October 2019), Evkeeza (September 2023), Ezetrol (January 2024), Juxtapid (February 2024), Lipidil EZ (February 2021), Repatha (October 2024)

Abbreviations: ACS = acute coronary syndrome; A-fib = atrial fibrillation; CHD = coronary heart disease; CrCl = creatinine clearance; CV = cardiovascular; CVD = cardiovascular disease; EPA = eicosapentaenoic acid; GI = gastrointestinal; HDL = high-density lipoprotein; HoFH = homozygous familial hypercholesterolemia; LDL = low-density lipoprotein; MI = myocardial infarction; mRNA = messenger ribonucleic acid; NNT = number needed to treat; PCSK9 = proprotein convertase subtilisin/kexin type 9; SCr = serum creatinine; siRNA = small interfering ribonucleic acid; TG = triglycerides.

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Levels of Evidence:

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	<ol style="list-style-type: none"> 1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	<ol style="list-style-type: none"> 1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. <https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html>.]

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