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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 weeks**[2] 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]	• 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)	• 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/day**[6] (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).	• 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%	• **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], Lodalis [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]	• 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/day**[30] (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	• 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 monthly**[15] 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]	• 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%	• 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]	• 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%	• 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]	• 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%	• 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]	• 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]	• 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	• 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	• 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%	• 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]	• 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%	• 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]	• 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:

a. Wholesale acquisition cost (WAC) of 30-day supply of dose specified (generic, if available). US medication pricing by Elsevier, accessed April 2025.
b. Placebo-subtracted lipid effects as statin add-on or monotherapy.
c. Summary of **therapeutic roles** of non-statins:
   • 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 ≥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]
d. **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.*	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.*	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.
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