

Table 10. Medications for additional LDL-C reduction in patients taking statins (maximal tolerated doses)

Medication	Mechanism of Action	Dose for LDL-C Reduction	LDL-C Reduction	Major Drug Interactions
Ezetimibe	Binds to Nieman Pick N1L1 receptor and prevents absorption of cholesterol from GI tract	10 mg daily	15–20%	Cyclosporine, fenofibrate, fibrates, cholestyramine
Alirocumab ^a	Prevents degradation of LDL receptor by inhibiting PCSK9	75 mg every 2 wks or 300 mg every 4 wks	56–61% on background of statin	None known
Evolocumab ^a	Prevents degradation of LDL receptor by inhibiting PCSK9	140 mg @ 2 wks subcutaneously or 420 mg subcutaneously once monthly	63–71% on a background of a statin; 41–45% on background of statin + ezetimibe	None known
Cholestyramine	Bile acid sequestrant	8–16 g daily in divided doses, once or twice a day starting with 4 g	12–25%	When given concomitantly with warfarin, thiazide diuretics, thyroxine, estrogens and progestins, tetracycline, phenobarbital, penicillin G, acetaminophen, phosphate supplements
Colesevelam	Bile acid sequestrant	1250–1875 mg by mouth two times daily	15–18%	When given concomitantly with oral contraceptives, levothyroxine, warfarin, glimepiride, glipizide, phenytoin
Bempedoic acid	ATP citrate lyase inhibitor, inhibitor of cholesterol synthesis	180 mg by mouth daily	18% on a background of a statin	Limit simvastatin to 20 mg, pravastatin limit to 40 mg, cyclosporine

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; ATP, adenosine triphosphate; CVD, cardiovascular disease; FH, familial hypercholesterolemia; GI, gastrointestinal; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; N1L1, N1-linker 1; PCSK9, proprotein convertase subtilisin/kexin type 9.

^a Alirocumab and evolocumab are indicated to reduce the risk of ASCVD events in patients with established CVD. They are also indicated as adjunct to diet alone, or in combination with other lipid-lowering therapies to reduce LDL-C in patients with primary hyperlipidemia (eg, heterozygous FH). Evolocumab is also approved alone in combination with other lipid-lowering therapies in patients with homozygous FH who require additional lowering of LDL-C. The other medications in this table are not indicated to reduce ASCVD events.

From the prescribing information for NuCare Pharmaceuticals, Inc. 2020, Esperion Therapeutics 2020, Ohm Laboratories Inc. 2020, Sanofi-Aventis, U.S. LLC 2018, Amgen Inc. 2017, Eon Labs 2020, Daiichi Sankyo 2020 (470, 478–483). All medications are to be used as adjunct to diet and exercise.

increasing hepatic synthesis of bile acids, which reduces the amount of cholesterol in the liver. Reduced hepatic cholesterol leads to the upregulation of LDL receptors.

Bempedoic acid is an adenosine-triphosphate citrate lyase inhibitor approved by the US FDA in 2020 for use as an adjunct to diet and maximally tolerated statin therapy in adults with heterozygous FH or established ASCVD, who require additional reduction in LDL-C (478). The effect of bempedoic acid on CV morbidity and mortality has not been determined but is under investigation.

Treatment for hypertriglyceridemia

In patients with elevated TG, initial management includes the identification and treatment of secondary factors that raise TG, and the initiation or adjustment of lifestyle therapy. Secondary factors include endocrine

diseases discussed in this guideline, chronic liver and kidney disease, and medications (estrogens, glucocorticoids, mitotane, tamoxifen, raloxifene, bile acid resins, protease inhibitors, retinoids, hydrochlorothiazide, propranolol, metoprolol, cyclosporine, tacrolimus, phenothiazine, aripiprazole, olanzapine, quetiapine, and risperidone). For patients with persistent elevation in TG up to 500 mg/dL (5.6 mmol/L) per day, statins are the first choice of pharmacological therapy as adjunct to lifestyle changes. A fibrate may also be used with the caution that the combination of a fibrate and a statin increases the risk of myopathy. This risk is more common with gemfibrozil compared with fenofibrate (see “Hypertriglyceridemia: Fibrates” section). In addition, as noted in this guideline, EPA ethyl ester is recommended to reduce ASCVD risk in statin-treated patients with TG of 150–499 mg/dL