# Lipid modifying medicines

## Comparison table

| Class<br>Active ingredients | LDL-C lowering (monotherapy compared to placebo)[1] | Adverse effects | Considerations | Outcome data |
|---|---|---|---|---|
| **Statins**<br>• atorvastatin<br>• fluvastatin<br>• pravastatin<br>• rosuvastatin<br>• simvastatin | 25–55% | Myalgia, mild transient gastrointestinal symptoms, headache, sleep disturbance (e.g. insomnia, nightmares), dizziness, elevated aminotransferase concentrations. | **Precautions and/or contraindications:** severe intercurrent illness (infection, metabolic disorder), myopathy with other lipid-modifying medicine, renal and hepatic impairment, pregnancy, breastfeeding, concurrent sodium fusidate use.<br>Simvastatin: concurrent use with some CYP3A4 inhibitors, gemfibrozil, cyclosporin or danazol is contraindicated.<br>Rosuvastatin 40 mg: contraindicated with Asian ancestry.<br>**Dosing:** daily dosing. Pravastatin and simvastatin may be slightly more effective taken in the evening.<br>**Dose increases:** allow at least four weeks between dose increases to optimize effects from current dose. More than 80% of the LDL-lowering effect of a statin is achieved with 50% of maximum dose. | Cholesterol Treatment Triallists meta-analyses: each 1 mmol/L reduction in LDL-C reduces risk of major vascular events by 21%.[2] |
| **Ezetimibe** | 15–25% | Headache, diarrhoea. | **Precautions:** concurrent fenofibrate use, moderate-severe hepatic impairment and pregnancy. | IMPROVE-IT trial: addition of ezetimibe to statin therapy was associated with a 6.4% reduction in the primary composite end point of cardiovascular death, major coronary events, or nonfatal stroke.[3] |
| **PCSK9 (proprotein convertase subtilisin/ kexin type 9) inhibitors**<br>• alirocumab<br>• evolocumab | 30–60% | Injection site reactions (mild pain, redness), nasopharyngitis, upper respiratory tract infections, influenza. | **Precautions:** allergic reactions. If signs or symptoms of serious allergic reactions occur, stop treatment with PCSK9is and initiate appropriate symptomatic treatment. Monitor until signs and symptoms resolve.<br>Pregnancy: Category B1.<br>Lactation: unknown whether these are excreted in human milk. A clinical decision should be made whether to discontinue breastfeeding or discontinue the drug, taking into account the potential benefit of the drug to the mother and the potential benefit of breastfeeding to the infant.<br>**Administration:** fortnightly or monthly subcutaneous injection. | FOURIER trial: addition of evolocumab to statin therapy +/- ezetimibe was associated with a 15% relative risk reduction in the composite of cardiovascular death, MI, stroke, hospitalisation for unstable angina or coronary revascularisation.[4]<br>ODYSSEY trial: addition of alirocumab to statin therapy in patients with a history of acute coronary syndrome was associated with a 15% relative risk reduction in the composite of coronary heart disease death, MI, stroke or unstable angina.[5] |

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|---|---|---|---|---|
| **Fibrates**<br>• fenofibrate<br>• gemfibrozil | 5–15%<br>(>25% with fenofibrate) | GI disturbances (e.g. dyspepsia, abdominal pain), increased creatinine concentration (reversible), myopathy (concurrent statin use; fenofibrate less risk than gemfibrozil).<br>Gemfibrozil: headache, dry mouth, myalgia.<br>Fenofibrate: increased aminotransferase concentration (reversible). | **Contraindications:** severe renal or hepatic impairment, primary biliary cirrhosis, gallstones, gall bladder disease, photosensitivity due to a fibrate.<br>Gemfibrozil: concurrent simvastatin use.<br>Fenofibrate: pancreatitis unless due to hypertriglyceridaemia, concurrent fibrate or ketoprofen use.<br>**Precautions:**<br>Fenofibrate: concurrent ezetimibe use may increase risk of gallbladder disease.<br>**Sun exposure:** avoid skin exposure (use protective clothing and sunscreen).<br>**Biochemistry:** complete blood count and liver function at baseline and during treatment; CK at baseline, repeat if clinically indicated. | Fibrates have been shown to improve lipid levels but there is no evidence that their addition to statin therapy reduces mortality, fatal MI or stroke in patients with dyslipidaemia.<br>FIELD study: fenofibrate delayed progression of existing diabetic retinopathy in trial subgroup analyses but did not prevent its development.[6] |
| **Bile acid-binding resins**<br>• colestyramine | 15–25% | Constipation, abdominal pain, dyspepsia, flatulence, nausea, vomiting, diarrhoea, anorexia.<br>Gastrointestinal adverse effects are common, which often limits their practical use; minimise by starting with a low dose and increasing gradually. | **Precautions:** triglycerides > 3 mmol/L, complete biliary obstruction, constipation, diverticular disease, severe haemorrhoids, Phenylketonuria.<br>**Vitamin supplementation:** consider fat-soluble vitamin supplements for high doses over an extended period.<br>**Timing:** can reduce effect of other medicines; take other medicines at least 1 hour before or 4–6 hours after. | Bile acid-binding resins have been shown to reduce LDL-C but evidence to support their addition to statin therapy to improve cardiovascular outcomes is limited. |



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**References:**

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