STEPS

New Drug Reviews

Alirocumab (Praluent) for the Treatment of Hyperlipidemia

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STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

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Alirocumab (Praluent) is a monoclonal antibody labeled for the treatment of hyperlipidemia in patients with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who need additional lowering of low-density lipoprotein (LDL) cholesterol despite treatment with diet and maximally tolerated doses of statins.[1] It is one of two inhibitors of proprotein convertase subtilisin/kexin type 9 (PCSK-9), a protein that binds LDL-receptors on hepatocytes, leading to enhanced clearing of serum LDL by free LDL receptors.

Drug	*Dosage*	*Dose form*	*Cost**
Alirocumab (Praluent)	75 mg via subcutaneous injection every two weeks, increasing to 150 mg every two weeks if needed	Prefilled 75-mg or 150-mg syringe/pen	$1,164*

**—Estimated retail price of one month's treatment based on information obtained at http://www.goodrx.com (accessed July 6, 2016).*

SAFETY

In an 18-month randomized controlled trial, 2,341 patients taking alirocumab did not have increased all-cause mortality, cardiovascular mortality, stroke, or heart failure compared with those taking placebo.[1,2] Alirocumab has been shown to increase adverse neurocognitive effects such as amnesia, memory impairment, and confusional state, but these are rare (number needed to harm [NNH] = 170). Serious adverse effects leading to discontinuation are similar to those with placebo and are infrequent (7.2%).

TOLERABILITY

Common adverse effects of alirocumab include localized injection-site reactions, nasopharyngitis, and flulike illness (4% to 11%).[1] Additionally, myalgia is more common with alirocumab than with placebo (NNH = 40). When alirocumab is used alone, one in 20 patients will discontinue therapy because of adverse effects. However, when combined with maximally tolerated statin therapy, pooled drop-out rates totaled 28% with alirocumab vs. 24% with placebo (NNH = 25).

EFFECTIVENESS

Alirocumab is highly effective at lowering LDL cholesterol, and higher doses produce more profound LDL reductions. It has little effect on serum levels of triglycerides and high-density lipoprotein cholesterol. In five placebo-controlled trials[1,2] enrolling a total of 3,499 patients with either familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, and who were already being treated with maximally tolerated doses of statin therapy, alirocumab reduced serum LDL concentrations by 44% to 61% (from a mean baseline of 122 mg per dL [3.16 mmol per L] to a mean of 52 mg per dL [1.35 mmol per L]) compared with placebo after 18 months of therapy. The effect of alirocumab on clinical outcomes has not been adequately studied. In one clinical trial, a post hoc analysis demonstrated a reduction in the composite outcome of death from coronary disease, death from unknown cause, nonfatal myocardial infarction, stroke, and unstable angina requiring hospitalization (absolute risk reduction = 1.6%; number needed to treat = 63 over 18 months).[2] Nonfatal myocardial infarction accounted for the majority

of difference observed. Alirocumab is not labeled for the primary prevention of hyperlipidemia and has not been studied for this purpose. It also has not been studied as an alternative to statins.

PRICE

A one-month supply of alirocumab costs $1,164. Evolocumab (Repatha), the other injectable monoclonal antibody of the PCSK-9 inhibitors, costs $1,127 per month. This is in addition to statin therapy such as atorvastatin (Lipitor), which costs $12 ($343) for a one-month supply (20 mg per day), or rosuvastatin (Crestor), which costs $195 ($263) for a one-month supply (10 mg per day).

SIMPLICITY

Alirocumab is administered subcutaneously every two weeks via prefilled pens or syringes that must be stored in a refrigerator. The starting dosage of alirocumab is 75 mg every two weeks, increasing to 150 mg every two weeks if LDL goals are not met. No dosing adjustment is required for patients with mild to moderate renal or hepatic impairment.

Bottom Line

Alirocumab is a novel lipid-lowering therapy that is highly effective at lowering LDL cholesterol when used in addition to statin therapy and diet. Its use should be limited to patients with either heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease who do not tolerate an adequate dose of a statin. More data regarding clinically relevant outcomes are needed before alirocumab should be used routinely as adjunctive therapy for the prevention of cardiovascular events.

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