# OVERVIEW
## *Alirocumab*

### Introduction

Alirocumab is a human monoclonal antibody to PCSK9 (proprotein convertase subtilisin/kexin type 9), a circulating protein that modulates the activity of the LDL cholesterol receptor in the liver. The monoclonal antibody lowers serum LDL cholesterol and is used to treat severe hypercholesterolemia. Alirocumab therapy has been associated with a low rate of serum aminotransferase elevations and has yet to be linked to instances of clinically apparent acute liver injury.

### Background

Alirocumab (al" i rok' ue mab) is a human IgG1 monoclonal antibody to proprotein convertase subtilisin/kexin type 9 (PCSK9), a serine protease that decreases the activity of the LDL cholesterol receptor in the liver. Inhibition of PCSK9 increases the low density lipoprotein (LDL) cholesterol receptor, leading to an increased uptake of LDL particles and a decrease in serum LDL cholesterol. Patients with a genetic deficiency in PCSK9 have low levels of LDL cholesterol, and inhibition of the protein activity with monoclonal antibody leads to a marked lowering of LDL cholesterol. In several controlled trials, alirocumab was shown to lower LDL cholesterol in persons with heterozygosity for familial hypercholesterolemia and in persons at risk for atherosclerosis who have been unable to achieve adequate cholesterol lowering with standard lipid lowering agents (statins). Alirocumab was approved for use in the United States in 2015. The current indications are limited to patients with severe hypercholesterolemia who are heterozygous for familial hypercholesterolemia or who have had clinical complications of atherosclerosis and an inadequate response to standard therapies. Alirocumab should be given in combination with advice on diet and exercise and is usually used in combination with oral lipid lowering agents such as statins. Alirocumab is available in solution in single use syringes or pens of 75 or 150 mg/mL under the brand name Praluent. The recommended initial dose is 75 mg administered subcutaneously every two weeks, which can be raised to 150 mg every two weeks based upon tolerance and response. Side effects are uncommon and rarely serious, but include injection site reactions (7%) and myalgia (4%). Rare, but potentially serious side effects may include memory impairment, neurocognitive defects, confusion and hypersensitivity reactions.

### Hepatotoxicity

In premarketing studies, liver test abnormalities were uncommon in patients taking alirocumab and rates of abnormalities were only slightly higher than in patients receiving placebo injections. Some

degree of ALT elevation was reported in 2.5% with alirocumab vs 1.7% with placebo injections. ALT or AST values greater than 3 times the upper limit of normal (ULN) occurred in 1.7% of persons on alirocumab vs 1.4% on placebo. No instances of acute, clinically apparent liver injury attributed to alirocumab were reported during the prelicensure evaluation and none have been reported since. However, alirocumab has had limited use and has been available commercially for a short time only.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

**Mechanism of Injury**

Alirocumab is a human monoclonal antibody and is metabolized in many tissues to polypeptides and amino acids which are unlikely to be toxic. Monoclonal antibody therapy sometimes causes immune mediated liver injury, but such events have not been described in alirocumab or evolocumab.

**Outcome and Management**

Therapy with alirocumab and other monoclonal antibodies to PCSK9 have been well tolerated with rates of adverse events similar to those with placebo or comparator treatments. Local injection site reactions occur with these agents, but are generally mild and improve with continued therapy. Monoclonal antibodies to PCSK9 has not been linked to significant elevations in serum enzymes or bilirubin or to clinically apparent liver injury. Patients who develop serum aminotransferase elevations above 3 times the upper limit of normal should be evaluated for other causes of liver injury including drug-induced injury from another antilipemic agent.

Drug Class: Antilipemic Agents; Monoclonal Antibodies, Anti-PCSK9

Other Drugs in the Class: Evolocumab

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## PRODUCT INFORMATION
## *Alirocumab*

### REPRESENTATIVE TRADE NAMES

Alirocumab – Praluent®

### DRUG CLASS

Antilipemic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

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## CHEMICAL FORMULA AND STRUCTURE
## *Alirocumab*

| DRUG | CAS REGISTRY NO. | MOLECULAR FORMULA | STRUCTURE |
|---|---|---|---|
| Alirocumab | 1245916-14-6 | Monoclonal Antibody | Not Available |