HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PRALUENT safely and effectively. See full prescribing information for PRALUENT.

PRALUENT® (alirocumab) injection, for subcutaneous use

Initial U.S. Approval: 2015

RECENT MAJOR CHANGES

Indications and Usage (1)	4/2021
Dosage and Administration (2.1)	4/2021
Dosage and Administration (2.3)	4/2021
Contraindications (4)	4/2021

INDICATIONS AND USAGE

PRALUENT is a PCSK9 (proprotein convertase subtilisin kexin type 9) inhibitor indicated:

- To reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease. (1)
- As adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C. (1)
- As an adjunct to other LDL-C-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C. (1)

DOSAGE AND ADMINISTRATION

- In adults with established cardiovascular disease or with primary hyperlipidemia, including HeFH (2.1):
  - The recommended starting dose of PRALUENT is either 75 mg once every 2 weeks or 300 mg once every 4 weeks administered subcutaneously.
  - For patients receiving PRALUENT 300 mg every 4 weeks, measure LDL-C just prior to the next scheduled dose, because LDL-C can vary between doses in some patients.
  - If the LDL-C response is inadequate, the dosage may be adjusted 150 mg subcutaneously every 2 weeks.
- In adults with HeFH undergoing LDL apheresis or in adults with HoFH (2.1):
  - The recommended dose of PRALUENT is 150 mg once every 2 weeks administered subcutaneously.
  - PRALUENT can be administered without regard to the timing of LDL apheresis.
- Assess LDL-C when clinically appropriate. The LDL-lowering effect of PRALUENT may be measured as early as 4 weeks after initiation. (2.1)
- Administer PRALUENT subcutaneously into areas of the thigh, abdomen, or upper arm that are not tender, bruised, red, or indurated. Rotate injection sites for each administration. (2.3)
- To administer the 300 mg dose, give two 150 mg PRALUENT injections consecutively at two different injection sites. (2.3)

DOSAGE FORMS AND STRENGTHS

Injection: 75 mg/mL or 150 mg/mL in a single-dose pre-filled pen. (3)

CONTRAINDICATIONS

History of a serious hypersensitivity reaction to alirocumab or any of the excipients in PRALUENT. (4)

WARNINGS AND PRECAUTIONS

Hypersensitivity reactions: hypersensitivity vasculitis, angioedema, and other hypersensitivity reactions requiring hospitalization, have been reported with PRALUENT treatment. If signs or symptoms of serious hypersensitivity reactions occur, discontinue treatment with PRALUENT, treat according to the standard of care, and monitor until signs and symptoms resolve. (5.1)

ADVERSE REACTIONS

Common (>5% of patients treated with PRALUENT and more frequently than placebo) adverse reactions in adults with:
Primary hyperlipidemia: nasopharyngitis, injection site reactions, and influenza. (6)
Established cardiovascular disease: non-cardiac chest pain, nasopharyngitis, and myalgia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Regeneron at 1-844-734-6643 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 04/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

PRALUENT® is indicated:

- To reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease**.**
- As an adjunct to diet, alone or in combination with other low density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C.
- As an adjunct to other LDL-C-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

- In adults with established cardiovascular disease or with primary hyperlipidemia, including HeFH:
  - The recommended starting dose of PRALUENT is either 75 mg once every 2 weeks or 300 mg once every 4 weeks administered subcutaneously *[see Dosage and Administration (2.3)]*.
  - For patients receiving PRALUENT 300 mg every 4 weeks, measure LDL-C just prior to the next scheduled dose, because LDL-C can vary between doses in some patients *[see Clinical Studies (14)]*.
  - If the LDL-C response is inadequate, the dosage may be adjusted 150 mg subcutaneously every 2 weeks.
- In adults with HeFH undergoing LDL apheresis or in adults with HoFH:
  - The recommended dose of PRALUENT is 150 mg once every 2 weeks administered subcutaneously *[see Dosage and Administration (2.3)]*.
  - PRALUENT can be administered without regard to the timing of LDL apheresis.
- Assess LDL-C when clinically appropriate. The LDL-lowering effect of PRALUENT may be measured as early as 4 weeks after initiation.

2.2 Missed Doses

If a dose is missed:

- Within 7 days from the missed dose, instruct the patient to administer PRALUENT and resume the patient's original schedule.
- More than 7 days after the missed dose:
  - For every 2 week dose, instruct the patient to wait until the next dose on the original schedule.
  - For every 4 week dose, instruct the patient to administer the dose and start a new schedule based on this date.

2.3 Important Administration Instructions

- Train patients and/or caregivers on how to prepare and administer PRALUENT, according to the Instructions for Use and instruct them to read and follow the Instructions for Use each time they use PRALUENT.
- Prior to use, allow PRALUENT to warm to room temperature for 30 to 40 minutes if PRALUENT has been refrigerated *[see How Supplied/Storage and Handling (16)]*.
- Visually inspect PRALUENT prior to administration. PRALUENT is a clear, colorless to pale yellow solution. Do not use if the solution is cloudy, discolored, or contains particles.
- Administer PRALUENT subcutaneously into areas of the thigh, abdomen, or upper arm that are not tender, bruised, red, or indurated. Rotate injection sites for each administration.

- To administer the 300 mg dose, give two 150 mg PRALUENT injections consecutively at two different injection sites.

3 DOSAGE FORMS AND STRENGTHS

PRALUENT injection is a clear, colorless to pale yellow solution available as follows:

- 75 mg/mL single-dose pre-filled pen
- 150 mg/mL single-dose pre-filled pen

4 CONTRAINDICATIONS

PRALUENT is contraindicated in patients with a history of a serious hypersensitivity reaction to alirocumab or any of the excipients in PRALUENT. Hypersensitivity vasculitis, angioedema, and hypersensitivity reactions requiring hospitalization have occurred *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions, including hypersensitivity vasculitis, angioedema, and other hypersensitivity reactions requiring hospitalization, have been reported with PRALUENT treatment. If signs or symptoms of serious hypersensitivity reactions occur, discontinue treatment with PRALUENT, treat according to the standard of care, and monitor until signs and symptoms resolve. PRALUENT is contraindicated in patients with a history of a serious hypersensitivity reaction to alirocumab or any excipient in PRALUENT *[see Contraindications (4)]*.

6 ADVERSE REACTIONS

The following adverse reactions are also discussed in the other sections of the labeling:

- Hypersensitivity Reactions *[see Warnings and Precautions (5.1)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data in Table 1 are derived from 9 primary hyperlipidemia placebo-controlled trials that included 2476 patients treated with PRALUENT 75 mg and/or 150 mg every 2 weeks, including 2135 exposed for 6 months and 1999 exposed for more than 1 year (median treatment duration of 65 weeks). The mean age of the population was 59 years, 40% of the population were women, 90% were White, 4% were Black or African American, and 3% were Asian.

Adverse reactions reported in at least 2% of PRALUENT-treated patients, and more frequently than in placebo-treated patients, are shown in Table 1.

Table 1: Adverse Reactions Occurring in >2% of PRALUENT-Treated Patients and More Frequently Than with Placebo

Adverse Reactions	Placebo (N=1276) %	PRALUENT* (N=2476) %
Nasopharyngitis	11.1	11.3
Injection site reactions†	5.1	7.2
Influenza	4.6	5.7
Urinary tract infection	4.6	4.8
Diarrhea	4.4	4.7
Bronchitis	3.8	4.3
Myalgia	3.4	4.2
Muscle spasms	2.4	3.1
Sinusitis	2.7	3.0
Cough	2.3	2.5
Contusion	1.3	2.1
Musculoskeletal pain	1.6	2.1

* 75 mg every 2 weeks and 150 mg every 2 weeks combined

† Includes erythema/redness, itching, swelling, pain/tenderness

Adverse reactions led to discontinuation of treatment in 5.3% of patients treated with PRALUENT and 5.1% of patients treated with placebo. The most common adverse reactions leading to treatment discontinuation in patients treated with PRALUENT were allergic reactions (0.6% versus 0.2% for PRALUENT and placebo, respectively) and elevated liver enzymes (0.3% versus <0.1%).

In an analysis of ezetimibe-controlled trials in which 864 patients were exposed to PRALUENT for a median of 27 weeks and 618 patients were exposed to ezetimibe for a median of 24 weeks, the types and frequencies of common adverse reactions were similar to those listed above.

In a cardiovascular outcomes trial in which 9451 patients were exposed to PRALUENT for a median of 31 months and 9443 patients were exposed to placebo for a median of 32 months, common adverse reactions (greater than 5% of patients treated with PRALUENT and occurring more frequently than placebo) included non-cardiac chest pain (7.0% PRALUENT, 6.8% placebo), nasopharyngitis (6.0% PRALUENT, 5.6% placebo), and myalgia (5.6% PRALUENT, 5.3% placebo).

In the HoFH placebo-controlled trial in which 45 patients were exposed to PRALUENT for a median of 12 weeks and 24 patients were exposed to placebo for a median of 12 weeks, no additional adverse reactions were identified.

Local Injection Site Reactions

In a pool of placebo-controlled trials evaluating PRALUENT 75 mg and/or 150 mg administered every 2 weeks, local injection site reactions including erythema/redness, itching, swelling, and pain/tenderness were reported more frequently in patients treated with PRALUENT (7.2% versus 5.1% for PRALUENT and placebo, respectively). Few patients discontinued treatment because of these reactions (0.2% versus 0.4% for PRALUENT and placebo, respectively), but patients receiving PRALUENT had a greater number of injection site reactions, had more reports of associated symptoms, and had reactions of longer average duration than patients receiving placebo.

In a 48-week placebo-controlled trial evaluating PRALUENT 300 mg every 4 weeks and 75 mg every 2 weeks, in which all patients received an injection of drug or placebo every 2 weeks, local injection site reactions were reported more frequently in patients treated with PRALUENT 300 mg every 4 weeks as compared to those receiving PRALUENT 75 mg every 2 weeks or placebo (16.6%, 9.6%, and 7.9%, respectively). Three patients (0.7%) treated with PRALUENT 300 mg every 4 weeks discontinued treatment due to local injection site reactions versus no patients (0%) in the other 2 treatment groups.

In a cardiovascular outcomes trial, local injection site reactions were reported in 3.8% of patients treated with PRALUENT versus 2.1% patients treated with placebo, and led to permanent discontinuation in 26 patients (0.3%) versus 3 patients (<0.1%), respectively.

Hypersensitivity Reactions

Hypersensitivity reactions were reported more frequently in patients treated with PRALUENT than in those treated with placebo (8.6% versus 7.8%). The most common hypersensitivity reaction was pruritus (1.1% versus 0.4% for PRALUENT and placebo, respectively). The proportion of patients who discontinued treatment due to allergic reactions was higher among those treated with PRALUENT (0.6% versus 0.2%).

Serious allergic reactions, such as hypersensitivity, nummular eczema, and hypersensitivity vasculitis were reported in patients using PRALUENT in controlled clinical trials.

Liver Enzyme Abnormalities

In the primary hyperlipidemia trials, liver-related disorders (primarily related to abnormalities in liver enzymes) were reported in 2.5% of patients treated with PRALUENT and 1.8% of patients treated with placebo, leading to treatment discontinuation in 0.4% and 0.2% of patients, respectively. Increases in serum transaminases to greater than 3 times the upper limit of normal occurred in 1.7% of patients treated with PRALUENT and 1.4% of patients treated with placebo.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity with PRALUENT. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to PRALUENT in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

In a cardiovascular outcomes trial, 5.5% (504/9091) of patients treated with PRALUENT 75 mg and/or 150 mg every 2 weeks had anti-drug antibodies (ADA) detected after initiating treatment compared with 1.6% (149/9097) of patients treated with placebo. Persistent ADA responses, defined as at least 2 consecutive post-baseline samples with positive ADA separated by at least a 16-week period, were observed in 0.7% of patients treated with PRALUENT and 0.4% of patients treated with placebo. Neutralizing antibody (NAb) responses were observed in 0.5% of patients treated with PRALUENT and in <0.1% of patients treated with placebo. Efficacy based on reductions in LDL-C was mostly similar in patients with or without ADA. However, some patients treated with PRALUENT with persistent or neutralizing antibodies experienced attenuation in LDL-C efficacy.

A higher incidence of injection site reactions were observed in patients with treatment-emergent ADA compared to patients who were ADA negative (7.5% vs 3.6%). In a pool of ten placebo-controlled and active-controlled trials of patients treated with PRALUENT 75 mg and/or 150 mg every 2 weeks as well as in a separate clinical study of patients treated with PRALUENT 75 mg every 2 weeks or 300 mg every 4 weeks (including some patients with dose adjustment to 150 mg every 2 weeks), the incidence of detecting ADA and NAb was similar to the results from the trial described above.

The long-term consequences of continuing PRALUENT treatment in the presence of ADA are unknown.

6.3 Postmarketing Experience

The following adverse reactions have been reported during post-approval use of PRALUENT. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Hypersensitivity reactions: Angioedema
- Influenza-like illness

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from clinical trials and postmarketing reports on PRALUENT use in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. In animal reproduction studies, there were no effects on embryo-fetal development when rats were subcutaneously administered alirocumab during organogenesis at dose exposures up to 12-fold the exposure at the maximum recommended human dose of 150 mg every two weeks. In monkeys, suppression of the humoral immune response was observed in infant monkeys when alirocumab was dosed during organogenesis to parturition at dose exposures 13-fold the exposure at the maximum recommended human dose of 150 mg every two weeks. No additional effects on pregnancy or neonatal/infant development were observed at dose exposures up to 81-fold the maximum recommended human dose of 150 mg every two weeks. Measurable alirocumab serum concentrations were observed in the infant monkeys at birth at comparable levels to maternal serum, indicating that alirocumab, like other IgG antibodies, crosses the placental barrier. Monoclonal antibodies are transported across the placenta in increasing amounts especially near term; therefore, alirocumab has the potential to be transmitted from the mother to the developing fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population(s) is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2%-4% and 15%-20%, respectively.

There is a pregnancy safety study for PRALUENT. If PRALUENT is administered during pregnancy, healthcare providers should report PRALUENT exposure by contacting Regeneron at 1-844-734-6643.

Data

Animal data

In Sprague Dawley rats, no effects on embryo-fetal development were observed when alirocumab was dosed at up to 75 mg/kg/dose by the subcutaneous route on gestation days 6 and 12 at exposures 12-fold the maximum recommended human dose of 150 mg every two weeks, based on serum AUC.

In cynomolgus monkeys, suppression of the humoral immune response to keyhole limpet hemocyanin (KLH) antigen was observed in infant monkeys at 4 to 6 months of age when alirocumab was dosed during organogenesis to parturition at 15 mg/kg/week and 75 mg/kg/week by the subcutaneous route, corresponding to 13-fold and 81-fold the human exposure at the maximum recommended human dose of 150 mg every two weeks, based on serum AUC. The lowest dose tested in the monkey resulted in humoral immune suppression; therefore, it is unknown if this effect would be observed at clinical exposure. No study designed to challenge the immune system of infant monkeys was conducted. No additional embryo-fetal, prenatal or postnatal effects were observed in infant monkeys, and no maternal effects were observed, when alirocumab was dosed at up to 75 mg/kg/week by the subcutaneous route, corresponding to maternal exposure of 81-fold the exposure at the maximum recommended human dose of 150 mg every two weeks, based on serum AUC.

8.2 Lactation

Risk Summary

There is no information regarding the presence of alirocumab in human milk, the effects on the breastfed infant, or the effects on milk production. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for PRALUENT and any potential adverse effects on the breastfed infant from PRALUENT or from the underlying maternal condition. Human IgG is present in human milk, but published data suggest that breastmilk IgG antibodies do not enter the neonatal and infant circulation in substantial amounts.

8.4 Pediatric Use

The safety and effectiveness of PRALUENT have not been established in pediatric patients.

8.5 Geriatric Use

In controlled trials, 3663 patients treated with PRALUENT were ≥65 years of age and 734 patients treated with PRALUENT were ≥75 years of age. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Renal Impairment

No dose adjustment is needed for patients with mild or moderately impaired renal function. No data are available in patients with severe renal impairment *[see Clinical Pharmacology (12.3)]*.

8.7 Hepatic Impairment

No dose adjustment is needed for patients with mild or moderate hepatic impairment. No data are available in patients with severe hepatic impairment *[see Clinical Pharmacology (12.3)]*.

11 DESCRIPTION

Alirocumab is a human monoclonal antibody (IgG1 isotype) that targets proprotein convertase subtilisin kexin type 9 (PCSK9). Alirocumab is a PCSK9 inhibitor produced by recombinant DNA technology in Chinese Hamster Ovary cell suspension culture. Alirocumab consists of two disulfide-linked human heavy chains, each covalently linked through a disulfide bond to a human kappa light chain. A single N-linked glycosylation site is located in each heavy chain within the CH2 domain of the Fc constant region of the molecule. The variable domains of the heavy and light chains combine to form the PCSK9 binding site within the antibody. Alirocumab has an approximate molecular weight of 146 kDa.

PRALUENT is a sterile, preservative-free, clear, colorless to pale yellow solution for subcutaneous use. PRALUENT 75 mg/mL or 150 mg/mL solution for subcutaneous injection in a single-dose pre-filled pen is supplied in a siliconized 1 mL Type-1 clear glass syringe.

Each 75 mg/mL pre-filled pen contains 75 mg alirocumab, histidine (8 mM), polysorbate 20 (0.1 mg), sucrose (100 mg), and Water for Injection USP, to pH 6.0.

Each 150 mg/mL pre-filled pen contains 150 mg alirocumab, histidine (6 mM), polysorbate 20 (0.1 mg), sucrose (100 mg), and Water for Injection USP, to pH 6.0.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Alirocumab is a human monoclonal antibody that binds to proprotein convertase subtilisin kexin type 9 (PCSK9). PCSK9 binds to the low-density lipoprotein (LDL) receptors (LDLR) on the surface of hepatocytes to promote LDLR degradation within the liver. By inhibiting the binding of PCSK9 to LDLR, alirocumab increases the number of LDLRs available to clear LDL, thereby lowering LDL-C levels.

12.2 Pharmacodynamics

Alirocumab reduced free PCSK9 in a concentration-dependent manner. Following a single subcutaneous administration of alirocumab 75 or 150 mg, maximal suppression of free PCSK9 occurred within 4 to 8 hours. Free PCSK9 concentrations returned to baseline when alirocumab concentrations decreased below the limit of quantitation.

12.3 Pharmacokinetics

Absorption

After subcutaneous administration of 75 mg to 300 mg alirocumab, median times to maximum serum concentrations (t_{max}) were 3-7 days. The pharmacokinetics of alirocumab after single subcutaneous administration of 75 mg into the abdomen, upper arm, or thigh were similar. The absolute bioavailability of alirocumab after subcutaneous administration was about 85% as determined by population pharmacokinetics analysis. A slightly greater than dose proportional increase was observed, with a 2.1-fold to 2.7-fold increase in total alirocumab concentrations for a 2-fold increase in dose from 75 mg every 2 weeks to 150 mg every 2 weeks. Monthly dose normalized exposure with 300 mg every 4 weeks treatment was similar to that of 150 mg every 2 weeks. Steady state was reached after 2 to 3 doses with an accumulation ratio up to a maximum of about 2-fold.

Distribution

Following intravenous administration, the volume of distribution was about 0.04 to 0.05 L/kg indicating that alirocumab is distributed primarily in the circulatory system.

Elimination

Specific metabolism studies were not conducted, because alirocumab is a protein. Alirocumab is expected to degrade to small peptides and individual amino acids. In clinical studies where alirocumab was administered in combination with atorvastatin or rosuvastatin, no relevant changes in statin concentrations were observed in the presence of repeated administration of alirocumab, indicating that cytochrome P450 enzymes (mainly CYP3A4 and CYP2C9) and transporter proteins such as P-gp and OATP were not affected by alirocumab.

Two elimination phases were observed for alirocumab. At low concentrations, the elimination is predominately through saturable binding to target (PCSK9), while at higher concentrations the elimination of alirocumab is largely through a non-saturable proteolytic pathway.

Based on a population pharmacokinetic analysis, the median apparent half-life of alirocumab at steady state was 17 to 20 days in patients receiving alirocumab at subcutaneous doses of 75 mg every 2 weeks or 150 mg every 2 weeks.

Specific Populations

A population pharmacokinetic analysis was conducted on data from 2799 patients. Age, body weight, gender, race, and creatinine clearance were found not to significantly influence alirocumab pharmacokinetics.

Renal Impairment

Since monoclonal antibodies are not known to be eliminated via renal pathways, renal function is not expected to impact the pharmacokinetics of alirocumab.

No data are available in patients with severe renal impairment.

Hepatic Impairment

Following administration of a single 75 mg SC dose, alirocumab pharmacokinetic profiles in patients with mild and moderate hepatic impairment were similar to those in patients with normal hepatic function.

No data are available in patients with severe hepatic impairment.

Drug-Drug Interactions

The median apparent half-life of alirocumab is reduced to 12 days when administered with a statin; however, this difference is not clinically meaningful.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been conducted with alirocumab. The mutagenic potential of alirocumab has not been evaluated; however, monoclonal antibodies are not expected to alter DNA or chromosomes.

There were no adverse effects on surrogate markers of fertility (e.g., estrous cyclicity, testicular volume, ejaculate volume, sperm motility, or total sperm count per ejaculate) in a 6-month chronic toxicology study in sexually-mature monkeys subcutaneously administered at 5, 15, and 75 mg/kg/week at systemic exposures up to 103-fold the 150 mg every two weeks subcutaneous clinical dose based on serum AUC. In addition, there were no adverse alirocumab-related anatomic pathology or histopathology findings in reproductive tissues in rat or monkey toxicology studies at systemic exposures up to 11-fold and 103-fold respectively, in the 6-month studies, compared to clinical systemic exposure following a 150 mg every two weeks dose, based on serum AUC.

13.2 Animal Toxicology and/or Pharmacology

During a 13-week toxicology study of 75 mg/kg once weekly alirocumab in combination with 40 mg/kg once daily atorvastatin in adult monkeys, there were no effects of PRALUENT on the humoral immune response to keyhole limpet hemocyanin (KLH) after one to two months at exposures 100-fold greater than the exposure at the maximum recommended human dose of 150 mg every two weeks, based on AUC.

14 CLINICAL STUDIES

Adult Patients with Established Cardiovascular Disease

Study 1 (ODYSSEY OUTCOMES, NTC01663402) was a multicenter, double-blind, placebo-controlled trial in 18,924 adult patients (9462 PRALUENT; 9462 placebo) followed for up to 5 years. Patients had an acute coronary syndrome (ACS) event 4 to 52 weeks prior to randomization and were treated with a lipid-modifying therapy (LMT) regimen that was statin-intensive (defined as atorvastatin 40 or 80 mg, or rosuvastatin 20 or 40 mg) or at maximally tolerated dose of a statin, with or without other LMT. Patients were randomized to receive either PRALUENT 75 mg or placebo once every two weeks.

At month 2, if additional LDL-C lowering was required based on pre-specified LDL-C criteria (LDL-C ≥50 mg/dL), PRALUENT was adjusted to 150 mg every 2 weeks. For patients who had their dose adjusted to 150 mg every 2 weeks and who had two consecutive LDL-C values below 25 mg/dL, down-titration from 150 mg every 2 weeks to 75 mg every 2 weeks was performed. Patients on 75 mg every 2 weeks who had two consecutive LDL-C values below 15 mg/dL were switched to placebo in a blinded fashion. Approximately 2615 (27.7%) of 9451 patients treated with PRALUENT required dose adjustment to 150 mg every 2 weeks. Of these 2615 patients, 805 (30.8%) were down-titrated to 75 mg every 2 weeks. Overall, 730 (7.7%) of 9451 patients switched to placebo.

A total of 99.5% of patients were followed for survival until the end of the trial. The median follow-up duration was 33 months.

The mean age at baseline was 59 years (range 39-92), with 25% women, and 27% at least 65 years old. The trial population was 79% White, 3% Black, and 13% Asian; 17% identified as Hispanic/Latino ethnicity. The index ACS event was a myocardial infarction in 83% of patients and unstable angina in 17% of patients. Prior to the index ACS event, 19% had prior myocardial infarction and 23% had coronary revascularization procedures (CABG/PCI). Selected additional baseline risk factors included hypertension (65%), diabetes mellitus (25%), New York Association class I or II congestive heart failure (15%), and eGFR <60 mL/min/1.73 m^2 (13%). Most patients (89%) were receiving statin-intensive therapy with or without other LMT at randomization. The mean LDL-C value at baseline was 92.4 mg/dL.

PRALUENT significantly reduced the risk for the primary composite endpoint (time to first occurrence of coronary heart disease death, non-fatal myocardial infarction, fatal and non-fatal ischemic stroke, or unstable angina requiring hospitalization: p=0.0003). The results are presented in Table 2.

Table 2: Cardiovascular Outcomes in Patients with Established Cardiovascular Disease

Endpoint	PRALUENT N=9462		Placebo N=9462		Hazard Ratio (95% CI)*
	n (%)	Incidence Rate per 100 Patient Years (95% CI)	n (%)	Incidence Rate per 100 Patient Years (95% CI)	
Primary composite endpoint†	903 (9.5%)	3.5 (3.3 to 3.8)	1052 (11.1%)	4.2 (3.9 to 4.4)	0.85 (0.78, 0.93)

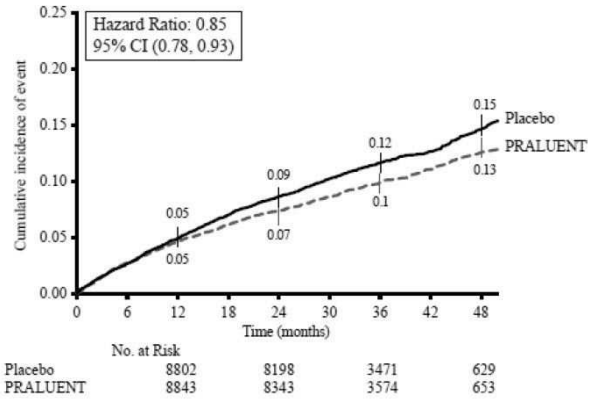
Table 2: Cardiovascular Outcomes in Patients with Established Cardiovascular Disease (continued)

Endpoint	PRALUENT N=9462		Placebo N=9462		Hazard Ratio (95% CI)*
	n (%)	Incidence Rate per 100 Patient Years (95% CI)	n (%)	Incidence Rate per 100 Patient Years (95% CI)	
Components of the Primary Composite Endpoint‡					
CHD death	205 (2.2%)	0.8 (0.7 to 0.9)	222 (2.3%)	0.8 (0.7 to 0.9)	0.92 (0.76, 1.11)
Non-fatal MI§	626 (6.6%)	2.4 (2.2 to 2.6)	722 (7.6%)	2.8 (2.6 to 3.0)	0.86 (0.77, 0.96)
Fatal or non-fatal ischemic stroke§	111 (1.2%)	0.4 (0.3 to 0.5)	152 (1.6%)	0.6 (0.5 to 0.7)	0.73 (0.57, 0.93)
Unstable angina requiring hospitalization§	37 (0.4%)	0.1 (0.1 to 0.2)	60 (0.6%)	0.2 (0.2 to 0.3)	0.61 (0.41, 0.92)
Mortality Endpoint (not statistically significant per pre-specified method to control for type I error)					
All-cause mortality	334 (3.5%)	1.2 (1.1 to 1.4)	392 (4.1%)	1.5 (1.3 to 1.6)	0.85 (0.73, 0.98)

* Cox-proportional hazards model with treatment as a factor and stratified by geographic region
† Primary composite endpoint defined as: time to first occurrence of coronary heart disease death, non-fatal myocardial infarction, fatal and non-fatal ischemic stroke, or unstable angina requiring hospitalization
‡ First occurrence of specified event at any time; patients may have experienced more than one adjudicated event
§ Statistical testing performed outside hierarchy; therefore not considered statistically significant

The Kaplan-Meier estimates of the cumulative incidence of the primary endpoint over time is presented in Figure 1.

Figure 1: Primary Composite Endpoint Cumulative Incidence over 4 Years in ODYSSEY OUTCOMES



Primary Hyperlipidemia

Study 2 (ODYSSEY LONG TERM, NCT01507831) was a multicenter, double-blind, placebo-controlled trial that randomly assigned 1553 patients to PRALUENT 150 mg every 2 weeks and 788 patients to placebo. All patients were taking maximally tolerated doses of statins with or without other lipid-modifying therapy, and required additional LDL-C reduction. The mean age was 61 years (range 18-89), 38% were women, 93% were White, 3% were Black, and 5% were Hispanic/Latino. The average LDL-C at baseline was 122 mg/dL.

The proportion of patients who prematurely discontinued study drug prior to the 24-week primary endpoint was 8% among those treated with PRALUENT and 8% among those treated with placebo.

At week 24, the treatment difference between PRALUENT and placebo in mean LDL-C percent change was -58% (95% CI: -61%, -56%; p-value: <0.0001).

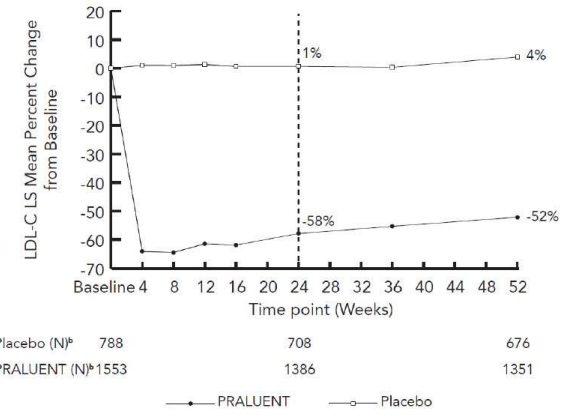
For additional results see Table 3 and Figure 2.

Table 3: Mean Percent Change from Baseline and Difference* from Placebo in Lipid Parameters at Week 24 in ODYSSEY LONG TERM†

Treatment Group	LDL-C	Total-C	Non-HDL-C	Apo B
Week 24 (Mean Percent Change from Baseline)				
Placebo (n=788)	1	0	1	1
PRALUENT 150 mg (n=1553)	-58	-36	-49	-50
Difference from placebo (LS Mean) (95% CI)	-58 (-61, -56)	-36 (-37, -34)	-50 (-52, -47)	-51 (-53, -48)

* Difference is PRALUENT minus Placebo
† A pattern-mixture model approach was used with multiple imputation of missing post-treatment values based on a patient's own baseline value and multiple imputation of missing on-treatment values based on a model including available on-treatment values

Figure 2: Mean Percent Change from Baseline in LDL-C Over 52 Weeks in Patients on Maximally Tolerated Statin Treated with PRALUENT 150 mg Every 2 Weeks and Placebo Every 2 Weeks (ODYSSEY LONG TERM)[a]



[a] The means were estimated based on all randomized patients, with multiple imputation of missing data taking into account treatment adherence
[b] Number of patients with observed data

Study 3 (ODYSSEY COMBO I, NCT01644175) was a multicenter, double-blind, placebo-controlled trial that randomly assigned 209 patients to PRALUENT and 107 patients to placebo. Patients were taking maximally tolerated doses of statins with or without other lipid-modifying therapy, and required additional LDL-C reduction.

The mean age was 63 years (range 39-87), 34% were women, 82% were White, 16% were Black, and 11% were Hispanic/Latino. Mean baseline LDL-C was 102 mg/dL.

The proportion of patients who prematurely discontinued study drug prior to the 24-week primary endpoint was 11% among those treated with PRALUENT and 12% among those treated with placebo.

At week 12, the mean percent change from baseline in LDL-C was -45% with PRALUENT compared to 1% with placebo, and the treatment difference between PRALUENT 75 mg every 2 weeks and placebo in mean LDL-C percent change was -46% (95% CI: -53%, -39%).

At week 12, if additional LDL-C lowering was required based on pre-specified LDL-C criteria, PRALUENT was up-titrated to 150 mg every 2 weeks for the remainder of the trial. The dose was up-titrated to 150 mg every 2 weeks in 32 (17%) of 191 patients treated with PRALUENT for at least 12 weeks. At week 24, the mean percent change from baseline in LDL-C was -44% with PRALUENT and -2% with placebo, and the treatment difference between PRALUENT and placebo in mean LDL-C percent change was -43% (95% CI: -50%, -35%; p-value: <0.0001).

Studies 4 (ODYSSEY FH I, NCT01623115) and 5 (ODYSSEY FH II, NCT01709500) were multicenter, double-blind, placebo-controlled trials that, combined, randomly assigned 490 patients to PRALUENT and 245 patients to placebo. The trials were similar with regard to both design and eligibility criteria. All patients had HeFH, were taking a maximally tolerated dose of statin with or without other lipid-modifying therapy, and required additional LDL-C reduction. The diagnosis of HeFH was made either by genotyping or clinical criteria ("definite FH" using either the Simon Broome or WHO/Dutch Lipid Network criteria). The mean age was 52 years (range 20-87), 45% were women, 94% were White, 1% were Black, and 3% were Hispanic/Latino. The average LDL-C at baseline was 141 mg/dL.

Considering both trials together, the proportion of patients who prematurely discontinued study drug prior to the 24-week primary endpoint was 6% among those treated with PRALUENT and 4% among those treated with placebo.

At week 12, the treatment difference between PRALUENT 75 mg every 2 weeks and placebo in mean LDL-C percent change was -48% (95% CI: -52%, -44%).

At week 12, if additional LDL-C lowering was required based on pre-specified LDL-C criteria, PRALUENT was up-titrated to 150 mg every 2 weeks for the remainder of the trials. The dose was up-titrated to 150 mg every 2 weeks in 196 (42%) of 469 patients treated with PRALUENT for at least 12 weeks. At week 24, the mean treatment difference between PRALUENT and placebo in mean LDL-C percent change from baseline was -54% (95% CI: -59%, -50%; p-value: <0.0001). The LDL-C-lowering effect was sustained to week 52.

For additional results see Table 4 and Figure 3.

Table 4: Mean Percent Change from Baseline and Difference* from Placebo in Lipid Parameters at Week 12 and Week 24 in Patients with HeFH (ODYSSEY FH I and FH II Pooled)†

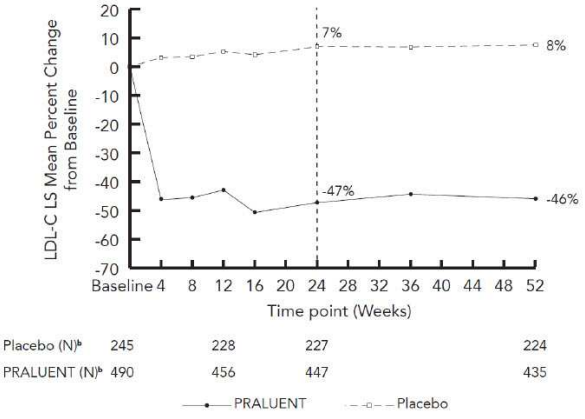
Treatment Group	LDL-C	Total-C	Non-HDL-C	Apo B
Week 12 (Mean Percent Change from Baseline)				
Placebo (n=245)	5	4	5	2
PRALUENT 75 mg (n=490)	-43	-27	-38	-34
Difference from placebo (LS Mean) (95% CI)	-48 (-52, -44)	-31 (-34, -28)	-42 (-46, -39)	-36 (-39, -33)
Week 24 (Mean Percent Change from Baseline)				
Placebo (n=245)	7	5	7	2
PRALUENT 75 mg/150 mg‡ (n=490)	-47	-30	-42	-40
Difference from placebo (LS Mean) (95% CI)	-54 (-59, -50)	-36 (-39, -33)	-49 (-53, -45)	-42 (-45, -39)

* Difference is PRALUENT minus Placebo

† A pattern-mixture model approach was used with multiple imputation of missing post-treatment values based on a patient's own baseline value and multiple imputation of missing on-treatment values based on a model including available on-treatment values

‡ Dose was up-titrated to 150 mg every 2 weeks in 196 (42%) patients treated for at least 12 weeks

Figure 3: Mean Percent Change from Baseline in LDL-C Over 52 Weeks in Patients with HeFH on Maximally Tolerated Statin Treated with PRALUENT 75/150 mg Every 2 Weeks and Placebo every 2 weeks (ODYSSEY FH I and FH II Pooled)[a]



[a] The means were estimated based on all randomized patients, with multiple imputation of missing data taking into account treatment adherence

[b] Number of patients with observed data

Study 6 (ODYSSEY HIGH FH, NCT01617655) was a multicenter, double-blind, placebo-controlled trial that randomly assigned 72 patients to PRALUENT 150 mg every 2 weeks and 35 patients to placebo. Patients had HeFH with a baseline LDL-C ≥160 mg/dL while taking a maximally tolerated dose of statin with or without other lipid-modifying therapy. The mean age was 51 years (range 18-80), 47% were women, 88% were White, 2% were Black, and 6% were Hispanic/Latino. The average LDL-C at baseline was 198 mg/dL.

The proportion of patients who discontinued study drug prior to the 24-week primary endpoint was 10% among those treated with PRALUENT and 0% among those treated with placebo.

At week 24, the mean percent change from baseline in LDL-C was -43% with PRALUENT and -7% with placebo, and the treatment difference between PRALUENT and placebo in mean LDL-C percent change was -36% (95% CI: -49%, -24%; p-value: <0.0001).

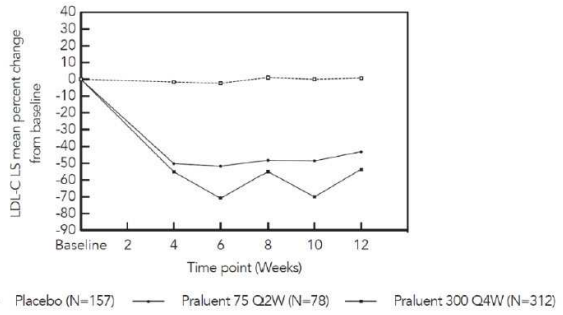
Study 7 (ODYSSEY CHOICE I, NCT01926782) was a multicenter, double-blind, placebo-controlled trial that randomly assigned 458 patients with primary hyperlipidemia to PRALUENT 300 mg every 4 weeks, 115 patients to PRALUENT 75 mg every 2 weeks, and 230 patients to placebo. Patients were stratified based on whether or not they were treated concomitantly with statin.

The mean age was 61 years (range 21-88), 42% were women, 87% were White, 11% were Black, and 3% were Hispanic/Latino.

The proportion of patients who discontinued study drug prior to the 24-week primary endpoint was 12% among those treated with PRALUENT 300 mg every 4 weeks, 14% among those treated with PRALUENT 75 mg every 2 weeks, and 15% among those treated with placebo.

In the cohort of patients on background statin, the mean LDL-C at baseline was 113 mg/dL. At week 12, the treatment difference between PRALUENT 300 mg every 4 weeks and placebo in mean percent change in LDL-C from baseline was -54% (97.5% CI: -61%, -48%), and the treatment difference between PRALUENT 75 mg every 2 weeks and placebo in mean percent change in LDL-C was -44% (97.5% CI: -53%, -35%) (Figure 4).

Figure 4: Mean Percent Change from Baseline in LDL-C up to Week 12 in Patients on Concomitant Statin Treated with PRALUENT 75 mg Every 2 Weeks, PRALUENT 300 mg Every 4 Weeks or Placebo*



* The means were estimated based on all randomized patients, with multiple imputation of missing data taking into account treatment adherence

At week 12, if additional LDL-C lowering was required based on pre-specified LDL-C criteria, PRALUENT was adjusted to 150 mg every 2 weeks for the remainder of the trial. The dose was adjusted to 150 mg every 2 weeks in approximately 20% of patients treated with PRALUENT 75 mg every 2 weeks or 300 mg every 4 weeks for at least 12 weeks. At week 24, the treatment difference between initial assignment to PRALUENT 300 mg every 4 weeks and placebo in mean percent change in LDL-C from baseline was -56% (97.5% CI: -62%, -49%; p-value: <0.0001), and the treatment difference between initial assignment to PRALUENT 75 mg every 2 weeks and placebo in mean percent change in LDL-C from baseline was -48% (97.5% CI: -57%, -39%).

In the cohort of patients not treated with a concomitant statin, the mean LDL-C at baseline was 142 mg/dL. The treatment difference between PRALUENT and placebo were similar to the cohort of patients treated with a concomitant statin.

Study 8 (ODYSSEY ESCAPE, NCT02326220) was a multicenter, double-blind, placebo-controlled trial that randomly assigned patients with HeFH who were undergoing LDL apheresis to PRALUENT 150 mg every 2 weeks (N=41) or placebo (N=21). Patients were treated in combination with their usual LDL apheresis schedule for 6 weeks. The mean age was 59 years (range 27-79), 42% were women, 97% were White, 3% were Black, and 0% were Hispanic/Latino. The mean LDL-C at baseline, measured before the apheresis procedure, was 181 mg/dL. The proportion of patients who discontinued study drug prior to the 6-week endpoint was 2% among those treated with PRALUENT 150 mg every 2 weeks and 5% among those treated with placebo. At week 6, the mean percent change from baseline in pre-apheresis LDL-C was -53% in patients in the PRALUENT group compared to 1% in patients who received placebo.

Study 9 (ODYSSEY COMBO II, NCT01644188) was a multicenter, double-blind, ezetimibe-controlled trial that randomly assigned 479 patients to PRALUENT 75 mg every 2 weeks/150 mg every 2 weeks and 241 patients to ezetimibe 10 mg/day. Patients were taking a maximally tolerated dose of a statin and required additional LDL-C reduction.

The mean age was 62 years (range 29-88), 26% were women, 85% were White, 4% were Black, and 3% were Hispanic/Latino. Mean baseline LDL-C was 107 mg/dL.

The proportion of patients who prematurely discontinued study drug prior to the 24-week primary endpoint was 9% among those treated with PRALUENT and 10% among those treated with ezetimibe.

At week 12, the mean percent change from baseline in LDL-C was -50% with PRALUENT compared to -22% with ezetimibe, and the treatment difference between PRALUENT and ezetimibe in mean LDL-C percent change was -28% (95% CI: -32%, -23%).

At week 12, if additional LDL-C lowering was required based on pre-specified LDL-C criteria, PRALUENT was up-titrated to 150 mg every 2 weeks for the remainder of the trial. The dose was up-titrated to 150 mg every 2 weeks in 82 (18%) of 446 patients treated with PRALUENT for at least 12 weeks. At week 24, the mean percent change from baseline in LDL-C was -48% with PRALUENT and -20% with ezetimibe, and the treatment difference between PRALUENT and ezetimibe in mean LDL-C percent change was -28% (95% CI: -33%, -23%; p-value: <0.0001).

Study 10 (ODYSSEY MONO, NCT01644474) was a multicenter, double-blind, ezetimibe-controlled trial in patients with a moderate CV risk, not taking statins or other lipid-modifying therapies, and a baseline LDL-C between 100 mg/dL to 190 mg/dL that randomly assigned 52 patients to PRALUENT 75 mg every 2 weeks and 51 patients to ezetimibe 10 mg/day.

The mean age was 60 years (range 45-72), 47% were women, 90% were White and 10% were Black. Mean baseline LDL-C was 140 mg/dL.

The proportion of patients who prematurely discontinued study drug prior to the 24-week endpoint was 15% among those treated with PRALUENT and 14% among those treated with ezetimibe.

At week 12, the mean percent change from baseline in LDL-C was -48% with PRALUENT compared to -19% with ezetimibe, and the treatment difference between PRALUENT 75 mg every 2 weeks and ezetimibe in mean LDL-C percent change was -29% (95% CI: -37%, -22%). At week 12, if additional LDL-C lowering was required based on pre-specified LDL-C criteria, PRALUENT was up-titrated to 150 mg every 2 weeks for the remainder of the trial. The dose was up-titrated to 150 mg every 2 weeks in 14 (30%) of 46 patients treated with PRALUENT for at least 12 weeks. At week 24, the mean percent change from baseline in LDL-C was -45% with PRALUENT and -14% with ezetimibe, and the treatment difference between PRALUENT and ezetimibe in mean LDL-C percent change was -31% (95% CI: -40%, -22%; p-value: <0.0001).

HoFH

Study 11 (ODYSSEY HoFH, NCT03156621) was a multicenter, double-blind, placebo-controlled trial that randomly assigned 45 adult patients to PRALUENT 150 mg every 2 weeks and 24 adult patients to placebo. Patients were taking maximally tolerated doses of statins with or without other lipid-lowering therapy and required additional LDL-C reduction.

Randomization was stratified by LDL apheresis treatment status. The diagnosis of HoFH was made by either clinical diagnosis, which included a history of an untreated total cholesterol concentration >500 mg/dL together with either xanthoma before 10 years of age or with a history of total cholesterol >250 mg in both parents, or by genetic testing. The mean age was 43 years (range 19-81), 51% were women, 78% were White, 3% were Black, 17% were Asian, and 3% were identified as Hispanic/Latino ethnicity. Mean baseline LDL-C was 283 mg/dL with 97% on statins, 72% on ezetimibe, and 14% on lomitapide. No patient discontinued from the study prior to the 12-week primary endpoint. At week 12, the treatment difference between PRALUENT and placebo in mean LDL-C percent change from baseline was -36% (95% CI: -51% to -20%; p <0.0001) (see Figure 5). For the effect of PRALUENT on lipid parameters as compared to placebo, see Table 5.

Patients with two LDL-receptor negative alleles (little to no residual function) had a minimal to absent response to PRALUENT.

Figure 5: LS Mean Percent Change from Baseline in LDL-C Over 12 Weeks in Patients with HoFH (ODYSSEY HoFH)

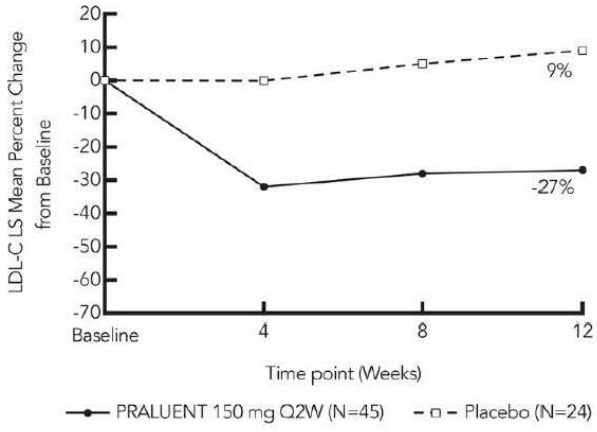


Table 5: Effect of PRALUENT on Lipid Parameters in Patients with HoFH (LS Mean Percent Change from Baseline to Week 12 in ODYSSEY HoFH)

Treatment Group	LDL-C	Apo B	Non-HDL-C	Total Cholesterol
Placebo (n=24)	9	7	8	7
PRALUENT 150 mg every 2 weeks (n=45)	-27	-23	-25	-20
Difference from placebo (LS Mean) (95% CI)	-36 (-51, -20)	-30 (-42, -17)	-33 (-48, -18)	-27 (-39, -14)

16 HOW SUPPLIED/STORAGE AND HANDLING

PRALUENT injection is a clear, colorless to pale yellow solution, supplied as follows:

Strength	Package Size	NDC
75 mg/mL single-dose pre-filled pen	1 pen	61755-020-01
	2 pens	61755-020-02
150 mg/mL single-dose pre-filled pen	1 pen	61755-021-01
	2 pens	61755-021-02

The needle shield is not made with natural rubber latex.

Store in a refrigerator at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light. Do not freeze. Do not shake.

PRALUENT may be kept at room temperature up to 77°F (25°C) in the original carton for 30 days. If not used within the 30 days, discard PRALUENT.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-Approved Patient Labeling (Patient Information and Instructions for Use).

Pregnancy

Advise women who are exposed to PRALUENT during pregnancy that there is a pregnancy safety study that monitors pregnancy outcomes. Encourage these patients to report their pregnancy to Regeneron at 1 844-734-6643 *[see Use in Specific Populations (8.1)].*

Hypersensitivity Reactions

Inform patients that serious hypersensitivity reactions (e.g., angioedema) have been reported in patients treated with PRALUENT. Advise patients on the symptoms of hypersensitivity reactions and instruct them to discontinue PRALUENT and seek medical attention promptly, if such symptoms occur.

Administration

Provide guidance to patients and caregivers on proper subcutaneous injection technique and how to use the pre-filled pen. Inform patients that it may take up to 20 seconds to inject PRALUENT. Inform patients the pre-filled pen should be allowed to warm to room temperature for 30 to 40 minutes prior to use if refrigerated.

Manufactured by:
Regeneron Pharmaceuticals, Inc.
Tarrytown, NY 10591
U.S. License # 1760

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Patient Information
PRALUENT® (PRAHL-u-ent)
(alirocumab)
injection, for subcutaneous use

What is PRALUENT?

PRALUENT is an injectable prescription medicine used:

- in adults with cardiovascular disease to reduce the risk of heart attack, stroke, and certain types of chest pain conditions (unstable angina) requiring hospitalization.
- along with diet, alone or together with other cholesterol-lowering medicines in adults with high blood cholesterol levels called primary hyperlipidemia (including a type of high cholesterol called heterozygous familial hypercholesterolemia), to reduce low-density lipoprotein cholesterol (LDL-C) or bad cholesterol.
- along with other LDL-lowering treatments in adults with a type of high cholesterol called homozygous familial hypercholesterolemia, who need additional lowering of LDL-C.

It is not known if PRALUENT is safe and effective in children.

Who should not use PRALUENT?

Do not use PRALUENT if you are allergic to alirocumab or to any of the ingredients in PRALUENT. See the end of this leaflet for a complete list of ingredients in PRALUENT.

What should I tell my healthcare provider before using PRALUENT?

Before you start using PRALUENT, tell your healthcare provider about all of your medical conditions, including allergies, and if you:

- are pregnant or plan to become pregnant. It is not known if PRALUENT will harm your unborn baby. Tell your healthcare provider if you become pregnant while taking PRALUENT.
- are breastfeeding or plan to breastfeed. You and your healthcare provider should decide if you will take PRALUENT or breastfeed. You should not do both without talking to your healthcare provider first.

If you are pregnant during PRALUENT treatment, you are encouraged to call Regeneron at 1-844-734-6643 to share information about the health of you and your baby.

Tell your healthcare provider or pharmacist about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I use PRALUENT?

- **See the detailed "Instructions for Use" that comes with this Patient Information about the right way to prepare and give your PRALUENT injections.**
- Use PRALUENT exactly as your healthcare provider tells you to use it.
- PRALUENT comes as a single-dose (1 time) pre-filled pen (autoinjector). Your healthcare provider will prescribe the dosage that is best for you.
- If your healthcare provider decides that you or a caregiver can give the injections of PRALUENT, you or your caregiver should receive training on the right way to prepare and give PRALUENT. **Do not** try to inject PRALUENT until you have been shown the right way by your healthcare provider or nurse.
- PRALUENT is injected under the skin (subcutaneously) every 2 weeks or every 4 weeks (monthly).
- If your healthcare provider prescribes you the monthly dose, you will give yourself 2 separate injections in a row, using a different pen for each injection and 2 different injection sites.
- **Do not** inject PRALUENT together with other injectable medicines at the same injection site.
- Always check the label of your pen to make sure you have the correct medicine and the correct dose of PRALUENT before each injection.
- If you forget to use PRALUENT or are not able to take the dose at your regular time, inject your missed dose as soon as you remember, within 7 days. **Then,** if you inject every 2 weeks take your next dose in 2 weeks from the day you missed your dose **or** if you inject every 4 weeks take your next dose in 4 weeks from the day you missed your dose. This will put you back on your original schedule.
- If you missed a dose by more than 7 days and you inject every 2 weeks wait until your next scheduled dose to re-start PRALUENT **or** if you inject every 4 weeks start a new schedule from the time you remember to take your dose. If you are not sure when to re-start PRALUENT, ask your healthcare provider or pharmacist.
- If you use more PRALUENT than you should, talk to your healthcare provider or pharmacist.
- **Do not** stop using PRALUENT without talking with your healthcare provider. If you stop using PRALUENT, your cholesterol levels can increase.

What are the possible side effects of PRALUENT?

PRALUENT can cause serious side effects, including:

- **allergic reactions**. PRALUENT may cause allergic reactions that can be severe and require treatment in a hospital. Stop using PRALUENT and call your healthcare provider or go to the nearest hospital emergency room right away if you have any symptoms of an allergic reaction including:
  - a severe rash
  - redness
  - hives
  - severe itching
  - trouble breathing
  - swelling of the face, lips, throat or tongue

The most common side effects of PRALUENT include:

- redness, itching, swelling, pain, or tenderness at the injection site
- symptoms of the common cold
- flu or flu-like symptoms

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.
These are not all of the possible side effects of PRALUENT. Ask your healthcare provider or pharmacist for more information.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of PRALUENT.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. **Do not** use PRALUENT for a condition for which it was not prescribed. **Do not** give PRALUENT to other people, even if they have the same symptoms that you have. It may harm them.
This Patient Information summarizes the most important information about PRALUENT. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about PRALUENT that is written for health professionals.
For more information about PRALUENT, go to www.PRALUENT.com or call 1-844-PRALUENT (1-844-772-5836).

What are the ingredients in PRALUENT?

- Active ingredient: alirocumab
- Inactive ingredients: histidine, polysorbate 20, sucrose, and Water for Injection, USP.

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This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: April 2021

PRA.21.03.0015