PRALUENT® (alirocumab) injection, for subcutaneous use

Initial U.S. Approval: 2015

RECENT MAJOR CHANGES

Indications and Usage (1) 3/2024
Dosage and Administration (2.2) 3/2024

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 is a proprotein convertase subtilisin kexin type 9 (PCSK9) 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 adults with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C. (1)
- As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 8 years and older with HeFH to reduce LDL-C. (1)

DOSE AND ADMINISTRATION

- In adults with established cardiovascular disease or with primary hyperlipidemia, including HeFH (2.1):
  - The recommended starting dosage of PRALUENT is either 75 mg once every 2 weeks or 300 mg once every 4 weeks administered subcutaneously. (2.2)
  - For patients receiving PRALUENT 300 mg every 4 weeks, measure LDL-C just prior to the next scheduled dosage, because LDL-C can vary between dosages in some patients.
  - If the LDL-C response is inadequate, the dosage may be adjusted 150 mg subcutaneously every 2 weeks. (2.4)
- In adults with HeFH undergoing LDL apheresis or in adults with HoFH (2.1):
  - The recommended dosage of PRALUENT is 150 mg once every 2 weeks administered subcutaneously. (2.2)
  - PRALUENT can be administered without regard to the timing of LDL apheresis.

- In pediatric patients with HeFH (2.2):
  - The recommended dosage of PRALUENT for patients with a body weight less than 50 kg is 150 mg once every 4 weeks administered subcutaneously. (2.2)
  - The recommended dosage of PRALUENT for patients with a body weight of 50 kg or more is 300 mg once every 4 weeks administered subcutaneously.
  - If the LDL-C response is inadequate, the dosage may be adjusted for patients with a body weight less than 50 kg to 75 mg subcutaneously once every 2 weeks or for patients with a body weight of 50 kg or more to 150 mg subcutaneously once every 2 weeks. (2.4)
  - 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. (2.4)
  - To administer the 300 mg dosage, give two 150 mg PRALUENT injections consecutively at two different injection sites. (2.4)

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: injection site reactions, and influenza. (6) Established cardiovascular disease: 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: 03/2024

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* Sections or subsections omitted from the full prescribing information are not listed.
2.2 Recommended Dosage in Pediatric Patients aged 8 years and older with HeFH

- The recommended dosage of PRALUENT for patients with a body weight less than 50 kg is 150 mg once every 4 weeks administered subcutaneously [see Dosage and Administration (2.4)].
- If the LDL-C lowering response is inadequate, the dosage may be adjusted to 75 mg subcutaneously once every 2 weeks [see Dosage and Administration (2.4)].
- The recommended dosage of PRALUENT for patients with a body weight of 50 kg or more is 300 mg once every 4 weeks administered subcutaneously [see Dosage and Administration (2.4)].
- If the LDL-C lowering response is inadequate, the dosage may be adjusted to 150 mg subcutaneously once every 2 weeks [see Dosage and Administration (2.4)].

2.3 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 dosage, instruct the patient to wait until the next dose on the original schedule.
  - For every 4-week dosage, instruct the patient to administer the dose and start a new schedule based on this date.

2.4 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.

In children aged 12 to 17 years, it is recommended that PRALUENT be given by or under the supervision of a adult. In children aged 8 to 11 years, PRALUENT should be given by a caregiver.

- 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.

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 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.

Adverse Reactions in Adults with Primary Hyperlipidemia

The data in Table 1 are derived from 9 primary hyperlipidemia placebo-controlled trials that included 2,476 adult patients treated with PRALUENT 75 mg and/or 150 mg every 2 weeks, including 2,135 exposed for 6 months and 1,999 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 female, 90% were White, 4% were Black or African American, 1% were Asian, and 3% other races; 6% identified as Hispanic or Latino ethnicity.

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 Adult Patients and >1.4% More Frequently Than with Placebo

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Placebo</th>
<th>PRALUENT*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=1,276)</td>
<td>(N=2,476)</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Influenza</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Contusion</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

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

b 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 816 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.

Adverse Reactions in a Cardiovascular Outcomes Trial in Adults

In a cardiovascular outcomes trial in which 9,451 patients were exposed to PRALUENT for a median of 31 months and 9,443 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 myalgia (6% PRALUENT, 5% placebo).

Adverse Reactions in Pediatric Patients with HeFH

In a 24-week placebo-controlled clinical trial in which 101 pediatric patients aged 8 to 17 years with HeFH were exposed to PRALUENT and 52 pediatric patients with HeFH were exposed to placebo [see Clinical Studies (14.3)], the safety profile of PRALUENT observed in this population was consistent with the safety profile observed in adults with HeFH.

Other Adverse Reactions

Local Injection Site Reactions

In a pool of placebo-controlled trials evaluating PRALUENT 75 mg and/or 150 mg administered every 2 weeks in adults, 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 adults, 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 in adults, 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.

In the trial of pediatric patients with HeFH, local injection site reactions were reported in 5% of patients treated with PRALUENT versus 0% patients treated with placebo; no patients discontinued treatment due to injection site reactions.

Hypersensitivity Reactions in Adults

Hypersensitivity reactions were reported more frequently in adult 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 Adults

In the primary hyperlipidemia trials in adults, 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.
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: Anaphylaxis
- 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 doses 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 breast milk IgG antibodies do not enter the neonatal and infant circulation in substantial amounts.

8.4 Pediatric Use

The safety and effectiveness of PRALUENT as an adjunct to diet and other LDL-C-lowering therapies for the treatment of HeFH have been established in pediatric patients aged 8 years and older. Use of PRALUENT for this indication is based on data from a 24-week, randomized, placebo-controlled, double-blind trial in pediatric patients with HeFH. In this trial, 101 patients received PRALUENT and 52 patients received placebo; 26 patients (17%) were 8 to 9 years of age. This indication is supported by evidence from controlled trials in adults [see Adverse Reactions (6.1) and Clinical Studies (14.3)].

The safety and effectiveness of PRALUENT have not been established in pediatric patients with HeFH who are younger than 8 years of age or in pediatric patients with other types of hyperlipidemia.

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)].
12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the trials described below with the incidence of anti-drug antibodies in other trials, including those of PRALUENT or of other alirocumab products.

In adult patients with cardiovascular disease (Trial 1), the incidence of anti-alirocumab antibody (ADA) formation was 5.5% (504/9,091) in patients treated with PRALUENT 75 mg and/or 150 mg every 2 weeks for up to 5 years (with a median treatment exposure of 31 months). Neutralizing antibody (NAb) responses were observed in 439/9,091 of all patients treated with PRALUENT. Of the patients who developed ADA, 8.5% (43/504) tested positive for NAb.

- While reductions in LDL-C were generally comparable in patients with or without ADA, including NAb, some adult patients treated with PRALUENT with persistent or neutralizing antibodies experienced attenuation in LDL-C efficacy.

- Adult patients who developed ADA had a higher incidence of injection site reactions compared to patients without ADA (7.5% vs 3.6%) [see Adverse Reactions (6.1)].

In a pool of placebo-controlled and active-controlled trials of adult patients treated with PRALUENT 75 mg and/or 150 mg every 2 weeks as well as in a separate clinical trial 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), during the treatment period ranging from 6 to 24 months, the incidence of detecting ADA was 4.8% (147/3,033) and NAb was 1.2% (36/3,033), which was similar to the results from the trial described above.

In pediatric patients aged 8 to 17 years with HeFH (Trial 12), the incidence of ADA for patients treated with PRALUENT was 3% (3/98) with a median treatment exposure of 24 weeks. Patients receiving PRALUENT once every 4 weeks and 23 weeks had ADA, receiving PRALUENT once every 4 weeks with an optional up-titration. Of the 3 pediatric patients who developed ADA, no one tested positive for NAb.

Because of the low occurrence of ADA and the small number of pediatric patients enrolled, the effect of these antibodies on the pharmacokinetics, pharmacodynamics, safety, and/or effectiveness of PRALUENT in pediatric patients is unknown.

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 toxicity 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 toxicity 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 reproductive and teratogenic endpoints (e.g., estrous cyclicity, testicular volume, sperm motility, or total sperm count per ejaculate).

14 CLINICAL STUDIES

14.1 Cardiovascular Outcome Trial in Adult Patients with Established Cardiovascular Disease

Trial 1 (ODYSSEY OUTCOMES, NCT01663402) was a multicenter, double-blind, placebo-controlled trial in 18,924 adult patients (9,462 PRALUENT; 9,462 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 lipid-modifying therapy (LMT) regimens that were statin-intensive (defined as atorvastatin 40 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 were on 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 2,615 (27%) of 9,451 patients treated with PRALUENT required dose adjustment to 150 mg every 2 weeks. Of these, 2,615 patients, 805 (30.8%) were down-titrated to 75 mg every 2 weeks. Overall, 730 (7.7%) of 9,451 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.

Baseline Disease and Demographic Characteristics

The mean age at baseline was 59 years (range 39-92), with 25% female, and 27% at least 65 years old. The trial population was 78% White, 5% Black or African American and 13% Asian. 17% were classified as Hispanic or 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/PIC). Selected additional baseline risk factors included hypertension (65%), diabetes mellitus (25%), New York Heart Association class I or II congestive heart failure (15%), and eGFR <60 mL/min/1.73 m² (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.

Endpoint Results

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.

14.2 Clinical Trials in Adult Patients with Primary Hyperlipidemia (including HeFH) and HoFH

Primary Hyperlipidemia

Trial 2 (ODYSSEY LONG TERM, NCT01507831) was a multicenter, double-blind, placebo-controlled trial that randomly assigned 1,553 adult patients to PRALUENT 150 mg every 2 weeks and 788 adult 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.

Baseline Disease and Demographic Characteristics

The mean age was 61 years (range 18-89), 38% were female, 93% were White, 3% were Black or African American, and 5% identified as Hispanic or Latino ethnicity. The average LDL-C at baseline was 122 mg/dL.

Endpoint Results

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).

Table 2: Cardiovascular Outcomes in Adult Patients with Established Cardiovascular Disease

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>PRALUENT N=9,462</th>
<th>Placebo N=9,462</th>
<th>Hazard Ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>Incidence Rate per 100 Patient Years (95% CI)</td>
<td>n (%)</td>
</tr>
<tr>
<td><strong>Primary composite endpoint</strong></td>
<td>903 (9.5%)</td>
<td>3.5 (3.3 to 3.8)</td>
<td>1052 (11.1%)</td>
</tr>
<tr>
<td>CHD death</td>
<td>205 (2.2%)</td>
<td>0.8 (0.7 to 0.9)</td>
<td>222 (2.3%)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>626 (6.6%)</td>
<td>2.4 (2.2 to 2.6)</td>
<td>722 (7.6%)</td>
</tr>
<tr>
<td>Fatal or non-fatal ischemic stroke</td>
<td>111 (1.2%)</td>
<td>0.4 (0.3 to 0.5)</td>
<td>152 (1.6%)</td>
</tr>
<tr>
<td>Unstable angina requiring hospitalization</td>
<td>37 (0.4%)</td>
<td>0.1 (0.1 to 0.2)</td>
<td>60 (0.6%)</td>
</tr>
</tbody>
</table>

Components of the Primary Composite Endpoint

- All-cause mortality: 334 (3.5%) vs 392 (4.1%) (HR 0.85 (0.73, 0.98))
- Myocardial infarction (MI): 113 (1.2%) vs 122 (1.3%) (HR 0.91 (0.77, 1.08))
- Unstable angina requiring hospitalization: 35 (0.4%) vs 50 (0.5%) (HR 0.70 (0.53, 0.93))
- Cerebrovascular event: 39 (0.4%) vs 41 (0.4%) (HR 0.95 (0.73, 1.25))
- Cardiovascular death: 107 (1.1%) vs 107 (1.1%) (HR 1.00 (0.75, 1.34))
- Fatal or non-fatal stroke: 126 (1.3%) vs 160 (1.7%) (HR 0.79 (0.65, 0.96))
- Cardiovascular death or stroke: 234 (2.5%) vs 272 (2.9%) (HR 0.86 (0.73, 1.03))
- Non-fatal MI: 626 (6.6%) vs 722 (7.6%) (HR 0.85 (0.73, 0.98))

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

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 TERMa

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>LDL-C</th>
<th>Total-C</th>
<th>Non-HDL-C</th>
<th>Apo B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=788)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>PRALUENT 150 mg (n=1,553)</td>
<td>-58</td>
<td>-36</td>
<td>-49</td>
<td>-50</td>
</tr>
<tr>
<td>Difference from placebo (LS Mean) (95% CI)</td>
<td>-58 (−61, −56)</td>
<td>-36 (−37, −34)</td>
<td>-50 (−52, −47)</td>
<td>-51 (−53, −48)</td>
</tr>
</tbody>
</table>

* Difference is PRALUENT minus Placebo

b 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.

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

d Number of patients with observed data.

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

### Baseline Disease and Demographic Characteristics

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

### Endpoint Results

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). The LDL-C-lowering effect was sustained to week 52.

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

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

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

* Difference is PRALUENT minus Placebo

b 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.

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

d Number of patients with observed data.

Trial 6 (ODYSSEY HIGH FH, NCT01617655) was a multicenter, double-blind, placebo-controlled trial that randomly assigned 72 adult patients to PRALUENT 150 mg every 2 weeks and 35 adult 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.

### Baseline Disease and Demographic Characteristics

The mean age was 51 years (range 18-80), 47% were female, 88% were White, 2% were Black or African American, and 6% identified as Hispanic or Latino ethnicity. The average LDL-C at baseline was 186 mg/dL.

### Endpoint Results

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

Trial 7 (ODYSSEY CHOICE I, NCT01926782) was a multicenter, double-blind, placebo-controlled trial that randomly assigned 456 adult patients with primary hyperlipidemia to PRALUENT 300 mg every 4 weeks, 115 adult patients to PRALUENT 75 mg every 2 weeks, and 230 adult patients to placebo. Patients were stratified based on whether or not they were treated concomitantly with statin.

Baseline Disease and Demographic Characteristics

The mean age was 61 years (range 21-88), 42% were female, 87% were White, 3% were Black or African American, and 3% identified as Hispanic or Latino ethnicity.

Endpoint Results

In the cohort of patients on background statin, the mean LDL-C at baseline was 113 mg/dL. 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/150 mg every 2 weeks and 241 adult patients to ezetimibe 10 mg/day. Patients were taking a maximally tolerated dose of a statin and required additional LDL-C reduction.

Baseline Disease and Demographic Characteristics

The mean age was 60 years (range 45-72), 47% were female, 90% were White and 10% were Black or African American, and 1% identified as Hispanic or Latino ethnicity. Mean baseline LDL-C was 140 mg/dL.

Endpoint Results

At week 12, the mean percent change from baseline in LDL-C was -48% with PRALUENT compared to -34% with ezetimibe, and the treatment difference between PRALUENT and ezetimibe in mean LDL-C percent change was -14% (95% CI: -22%. -6%). 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 -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).

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

Adult Patients with HoFH

Trial 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.

Baseline Disease and Demographic Characteristics

The mean age was 43 years (range 19-81), 51% were female, 78% were White, 3% were Black or African American, 17% were Asian, and 3% identified as Hispanic or Latino ethnicity. Mean baseline LDL-C was 283 mg/dL with 97% on statins, 72% on ezetimibe, and 14% on lomitapide.

Endpoint Results

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. No patient discontinued from the trial prior to the 12-week primary endpoint.

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

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

14.3 Clinical Trials in Pediatric Patients with HeFH

Trial 12 (EFC14643, NCT03510884) was a randomized, multicenter, placebo controlled, double blind, 24 week trial in 153 pediatric patients aged 8 to 17 years with HeFH. Patients were on a low-fat diet and receiving background lipid-lowering therapy. Patients were randomized in a 2:1 ratio to receive PRALUENT or placebo. In the PRALUENT group dosed every 4 weeks, 49 patients received a dose of 40 mg for body weight less than 50 kg or 75 mg for body weight 50 kg or more. The 40 mg dosage every 2 weeks is not approved (see Dosage and Administration (2.2)). In the PRALUENT group dosed every 4 weeks, 52 patients received a dose of 150 mg for body weight less than 50 kg or 300 mg for body weight 50 kg or more. Dose adjustment of PRALUENT to 75 mg every 2 weeks for body weight less than 50 kg or 150 mg every 2 weeks for body weight 50 kg or more occurred at week 12 in patients with LDL-C ≥110 mg/dL.

Baseline Disease and Demographic Characteristics

The diagnosis of HeFH was made based on criteria from Simon Broome Register Group (1991) or by genetic testing. The mean age was 13 years (range: 8 to 17 years); 57% female, 82% White, 2% Black or African American, 10% American Indian or Alaska Native, and <1% not reported, 16% Hispanic/Latino ethnicity. Mean body weight was 53 kg. The mean LDL-C at baseline was 174 mg/dL. Of the patients receiving PRALUENT once every 2 weeks with an optional up-titration, 99% were on statins and 7% were on ezetimibe at baseline. Of the patients receiving PRALUENT once every 4 weeks with an optional up-titration, 31% were on statins and 25% were on ezetimibe at baseline.

Endpoint Results

At week 24 in the group receiving treatment every 4 weeks, the treatment difference between the PRALUENT and placebo groups in LS mean LDL-C percent change from baseline was -31.4% (97.5% CI: -45.0 to -17.9; p<0.0001) (see Table 6 and Figure 6). For the effect of PRALUENT on lipid parameters as compared to placebo see Table 6.

Figure 6: LDL-C LS Mean Percent Change from Baseline Over Time Through Week 24 in Pediatric Patients (aged 8 to 17 years) with HeFH Treated with PRALUENT Every 4 Weeks or Placebo

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.

Table 6: Mean Percent Change from Baseline and Difference from Placebo in Lipid Parameters at Week 24 in Pediatric Patients (aged 8 to 17 years)

<table>
<thead>
<tr>
<th>Treatment Group*</th>
<th>LDL-C</th>
<th>Apo B</th>
<th>Non-HDL-C</th>
<th>Total Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=25)</td>
<td>9.7</td>
<td>10.4</td>
<td>9.7</td>
<td>7.4</td>
</tr>
<tr>
<td>PRALUENT once every 2 weeks (40 mg for body weight less than 50 kg or 75 mg for body weight 50 kg or more)ad</td>
<td>26.6 (-36.6, -27.9)</td>
<td>23.1 (-29.7, -18.0)</td>
<td>23.4 (-30.1, -17.2)</td>
<td>23.4 (-30.1, -17.2)</td>
</tr>
</tbody>
</table>

* A pattern-mixture 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

** Number of patients with observed data

Table 6: Mean Percent Change from Baseline and Difference from Placebo in Lipid Parameters at Week 24 in Pediatric Patients (aged 8 to 17 years)

Table 6: Mean Percent Change from Baseline and Difference from Placebo in Lipid Parameters at Week 24 in Pediatric Patients (aged 8 to 17 years) (continued)

<table>
<thead>
<tr>
<th>Treatment Group*</th>
<th>LDL-C</th>
<th>Apo B</th>
<th>Non-HDL-C</th>
<th>Total Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=25)</td>
<td>9.7</td>
<td>10.4</td>
<td>9.7</td>
<td>7.4</td>
</tr>
<tr>
<td>PRALUENT once every 2 weeks (40 mg for body weight less than 50 kg or 75 mg for body weight 50 kg or more)ad</td>
<td>26.6 (-36.6, -27.9)</td>
<td>23.1 (-29.7, -18.0)</td>
<td>23.4 (-30.1, -17.2)</td>
<td>23.4 (-30.1, -17.2)</td>
</tr>
</tbody>
</table>

a In the PRALUENT group 52 patients received a dose of 150 mg every 4 weeks (body weight less than 50 kg) or 300 mg every 4 weeks (body weight 50 kg or more). At week 12, a total of 15 (28.8%) patients had an automatic blinded dose adjustment to 75 mg every 2 weeks (body weight less than 50 kg) or 150 mg every 2 weeks (body weight 50 kg or more).
b In the PRALUENT group dosed every 2 weeks, 49 patients received a dose of 40 mg for body weight less than 50 kg or 75 mg for body weight 50 kg or more. At week 12, a total of 22 (44.9%) patients had an automatic blinded dose adjustment to 75 mg every 2 weeks (body weight less than 50 kg) or 150 mg every 2 weeks (body weight 50 kg or more).
c The 40 mg dosage every 2 weeks is not approved

d A pattern-mixture 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

e The percent of missing data was 5% in the every 2 week group and 13% in the every 4 week group

16 HOW SUPPLIED/STORAGE AND HANDLING

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

<table>
<thead>
<tr>
<th>Strength</th>
<th>Package Size</th>
<th>NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>75 mg/mL single-dose pre-filled pen</td>
<td>1 pen</td>
<td>61755-020-01</td>
</tr>
<tr>
<td>150 mg/mL single-dose pre-filled pen</td>
<td>1 pen</td>
<td>61755-021-01</td>
</tr>
<tr>
<td>2 pens</td>
<td>61755-020-02</td>
<td></td>
</tr>
<tr>
<td>2 pens</td>
<td>61755-021-02</td>
<td></td>
</tr>
</tbody>
</table>

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

Advertise 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.

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 prefilled pen. Informed 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.

REGENERON

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

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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 [HeFH]), 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.
- along with diet and other LDL-lowering treatments in children aged 8 years and older with HeFH to reduce LDL-C.

It is not known if PRALUENT is safe and effective in children who are younger than 8 years of age or in children with other types of high cholesterol (hyperlipidemias).

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 can harm your unborn baby. Talk to your healthcare provider for information about PRALUENT that is right for you.
- are breastfeeding or plan to breastfeed. You should not do both without talking to your healthcare provider first.
- are allergic to something else, such as other medicines, foods, or certain materials. PRALUENT contains a latex rubber stopper. Ask your healthcare provider how to get PRALUENT if you are allergic to latex.

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 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.
- In children aged 12 to 17 years, it is recommended that PRALUENT be given by or under the supervision of an adult. In children aged 8 to 11 years, PRALUENT should be given by a caregiver.
- PRALUENT is injected under the skin (subcutaneously) every 2 weeks or every 4 weeks (monthly).
- If your healthcare provider prescribes you the monthly dose, give 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.

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
  - trouble breathing
  - swelling of the face, lips, throat or tongue

The common side effects of PRALUENT include:
- redness, itching, swelling, pain, or tenderness at the injection site
- flu or flu-like symptoms
- diarrhea

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: March 2024