FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Primary Hyperlipidemia

PRALUENT® is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C.

1.2 Limitations of Use

The effect of PRALUENT on cardiovascular morbidity and mortality has not been determined.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The recommended starting dose of PRALUENT is 75 mg once every 2 weeks administered subcutaneously, since the majority of patients achieve sufficient LDL-C reduction with this dosage. An alternative starting dosage for patients who prefer less frequent dosing is 300 mg once every 4 weeks (monthly).

For patients receiving PRALUENT 75 mg every 2 weeks, measure LDL-C levels within 4 to 8 weeks of initiating PRALUENT. If the LDL-C response is inadequate, the dosage may be adjusted to the maximum dosage of 150 mg administered every 2 weeks. Reassess LDL-C within 4 to 8 weeks.

For patients receiving PRALUENT 300 mg every 4 weeks, measure LDL-C just prior to the next scheduled dose, since in some patients LDL-C can vary considerably between doses with this regimen [*see Clinical Studies (14)*]. If LDL-C reduction is inadequate, the dosage may be adjusted to 150 mg every 2 weeks, starting the new dose on the next scheduled dosing date. Reassess LDL-C within 4 to 8 weeks.

If an every-2-week dose is missed, instruct the patient to administer the injection within 7 days from the missed dose and then resume the patient's original schedule. If the missed dose is not administered within 7 days, instruct the patient to wait until the next dose on the original schedule.

If an every-4-week dose is missed, instruct the patient to administer the injection within 7 days from the missed dose and then resume the patient's original schedule. If the missed dose is not administered within 7 days, instruct the patient to administer the dose, starting a new schedule based on this date.

The recommended dose of PRALUENT in patients with HeFH undergoing LDL apheresis is 150 mg once every 2 weeks. PRALUENT can be administered without regard to the timing of apheresis.

2.2 Important Administration Instructions

- Provide proper training to patients and/or caregivers on the preparation and administration of PRALUENT prior to use according to the Instructions for Use. Instruct patients and/or caregivers to read and follow the Instructions for Use each time they use PRALUENT.

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

Safety and efficacy in pediatric patients have not been established.

8.5 Geriatric Use

In controlled studies, 1158 patients treated with PRALUENT were ≥65 years of age and 241 patients treated with PRALUENT were ≥75 years of age. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, 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

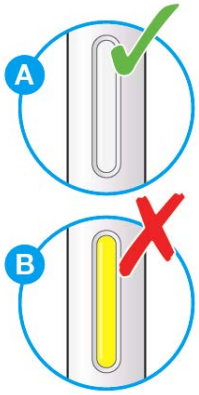
Alirocumab is a human monoclonal antibody (IgG1 isotype) that targets proprotein convertase subtilisin kexin type 9 (PCSK9). Alirocumab is a PCSK9 inhibitor produced by recombinant DNA technology in Chinese Hamster Ovary cell suspension culture. Alirocumab consists of two disulfide-linked human heavy 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 injection. PRALUENT 75 mg/mL or 150 mg/mL solution for subcutaneous injection in a single-dose pre-filled pen or single-dose pre-filled syringe is supplied in a siliconized 1 mL Type-1 clear glass syringe. The needle shield is not made with natural rubber latex.

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

A2: Look at the window.

- Check the liquid is clear, colorless to pale yellow and free from particles (see Figure A).
- You may see an air bubble. This is normal.
- **Do not** use if the window appears solid yellow (see Figure B).
- **Do not** use this medicine if the solution is discolored or cloudy, or if it contains visible flakes or particles.



A3: Let the pen warm up at room temperature for 30 to 40 minutes.

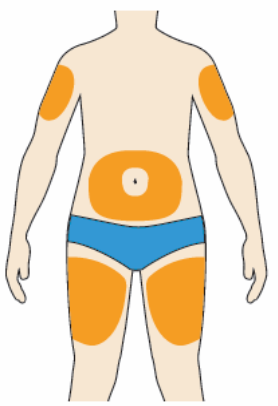
- This is important for administering the entire dose and helps minimize discomfort.
- Take PRALUENT out of the refrigerator to warm up before using.
- **Do not** heat the pen, let it warm up on its own.
- **Do not** put the pen back in the refrigerator.

A4: Prepare the injection site.

- Wash your hands with soap and water and dry with a towel.
- Clean skin in the injection area with an alcohol wipe.
- You can inject into your (see below picture):
  - thighs
  - stomach (except for the 2 inch area around your navel)
  - upper arms
- You can stand or sit to give yourself an injection.

Important:

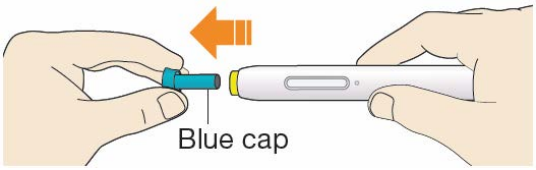
- Change (rotate) your injection site each time you give yourself an injection. If you need to use the same injection site, make sure it is not the same spot on the site you used last time.
- **Do not** inject into areas where the skin is injured, tender, hard, red, or hot. **Do not** inject PRALUENT into areas with visible veins, scars or stretch marks.



Step B: How to give your injection

B1: After completing all steps in "Step A: Getting ready for your injection", pull off the blue cap.

- **Do not** pull off the cap until you are ready to inject.
- **Do not** put the blue cap back on.

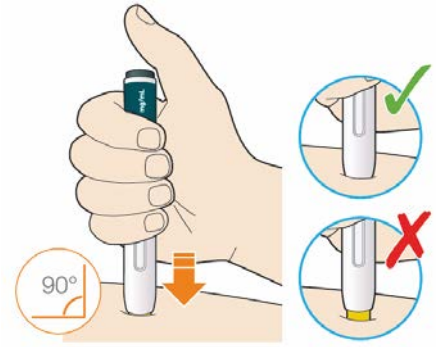


B2: Hold the PRALUENT pen like this.

- **Do not** touch the yellow safety cover.
- Make sure you can see the window.

B3: Press the yellow safety cover on your skin at roughly a 90° angle.

- Press and firmly hold the pen against your body until the yellow safety cover is no longer visible. The pen will not work if the yellow safety cover is not depressed fully.
- If needed, pinch the skin to make sure the injection site is firm.



B4: Push and immediately release the gray button with your thumb.

- You will hear a click. Your injection has now started.
- The window will start to turn yellow.

B5: Keep holding the pen against your skin after releasing the button.

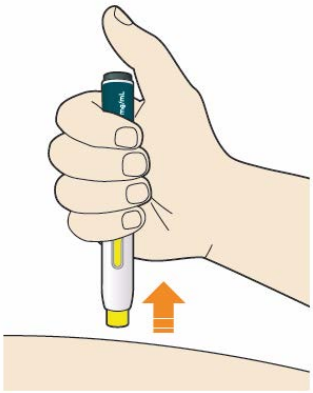
- The injection may take up to 20 seconds.
- The time required for injection to give the entire dose may be longer than for other injectable medicines.

B6: Check the window has turned yellow, before removing the pen.

- **Do not** remove the pen until the entire window has turned yellow.
- Your injection is complete when the window has turned completely yellow, you may hear a second click.
- If the window does not turn completely yellow, call 1-844-772-5836 for help. **Do not** give yourself a second dose without speaking to your healthcare provider.

B7: Pull pen away from your skin.

- **Do not** rub the skin after the injection.
- If you see any blood, press a cotton ball or gauze on the site until the bleeding stops.



B8: Discard pen and cap.

- **Do not** put the blue cap back on.
- Throw away pen and cap in a puncture-resistant container immediately after they have been used.

Disposing of used pens:

- Put your used pens in a FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of) pens and caps in your household trash.**
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:

    - made of a heavy-duty plastic,
    - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
    - upright and stable during use,
    - leak-resistant, and
    - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Keep PRALUENT and all medicines out of the reach of children.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

REGENERON SANOFI

Manufactured by:
sanofi-aventis U.S. LLC
Bridgewater, NJ 08807
A SANOFI COMPANY
U.S. License # 1752

Marketed by: sanofi-aventis U.S. LLC (Bridgewater, NJ 08807)

and Regeneron Pharmaceuticals, Inc. (Tarrytown, NY 10591)

PRALUENT is a registered trademark of Sanofi

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