Protocol for the Safe and Efficient Use of PCSK9 Inhibitors

Approved January 2016
Updated July 2020
Updated January 2022

Addendum:

1. FDA approved use of Praluent as an adjunct to other LDL-C-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C. – April 2021
2. FDA approved use of Repatha in pediatric patients age 10 and older with heterozygous familial hypercholesterolemia (HeFH) – September 2021
3. FDA approved use of Repatha in pediatric patients age 10 and older with homozygous familial hypercholesterolemia (HoFH) – September 2021

Praluent® (alirocumab) is a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor antibody indicated:

a. To reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease; OR

b. As an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low-density lipoprotein cholesterol (LDL-C)

c. As an adjunct to other LDL-C-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.

Repatha® (evolocumab) is a PCSK9 inhibitor antibody indicated:

a. To reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease; OR

b. As an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce LDL-C; OR.

c. As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 10 years and older with HeFH, to reduce LDL-C

d. As an adjunct to other LDL-C-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH), to reduce LDL-C

Criteria for Approval:

Patient's diagnosis must be confirmed by the following:

1. Laboratory documentation of LDL from within the past 30 days must be received and the patient must meet one of the following:
    a. LDL-C ≥ 70 mg/dL for documented ASCVD (Must receive documentation of ASCVD as noted under section C below)
    b. LDL-C ≥ 100 mg/dL for familial hypercholesterolemia without documented ASCVD
2. Patient must not be receiving another PCSK9 inhibitor
3. For HoFH, the patient must not be receiving Juxtapid or Kynamro
4. Patient is not pregnant
5. Patient must have a confirmed diagnosis of one of the following:

A. Homozygous familial hypercholesterolemia (HoFH)

a. Patient is 18 years of age or older for Praluent or 10 years of age or older for Repatha; AND
b. Documentation (medical records, patient's chart) of genetic confirmation of two mutant alleles at the LDLR, Apo-B, PCSK9, or ARH adaptor protein 1/LDLRAP1 gene locus OR
c. Untreated LDL-C >500 mg/dL or treated LDL-C ≥300 mg/dL with ONE of the following:
    i. Cutaneous or tendon xanthoma before age 10 OR
    ii. Untreated LDL-C levels consistent with heterozygous FH in both parents (untreated total cholesterol >290 mg/dL or untreated LDL-C >190 mg/dL; OR

B. Heterozygous familial hypercholesterolemia (HeFH)

a. Patient is 18 years of age or older for Praluent or 10 years of age or older for Repatha; AND
b. Patient has diagnosis of HeFH confirmed by one of the following:
    i. Genetic testing showing a LDL-receptor mutation, familiar defective Apo-B-100, or a PCSK9 mutation
    ii. Pretreatment (prior to any hypercholesterolemia therapy) or highest level on treatment total cholesterol >290 mg/dL (>7.5 mmol/L) AND Tendon xanthomas in patient, patient's first degree relative, or patient's second degree relative

iii. Pretreatment (prior to any hypercholesterolemia therapy) or highest level on treatment LDL-C >190 mg/dL (>4.9 mmol/L) AND Tendon xanthomas in patient, patient's first degree relative, or patient's second degree relative

iv. Patient meets definite FH as determined using the Dutch Lipid Clinic Network criteria by a score of greater than 8 (see table 1); OR

C. Clinical atherosclerotic cardiovascular disease (ASCVD)

a. Patient is 18 years of age or older

b. Patient has a history of ASCVD or cardiovascular event

i. Provide documentation (medical records, patient's chart) of the condition/event

ii. ASCVD is defined as a diagnosis of ONE of the following:

1. Acute coronary syndrome
2. History of myocardial infarction (MI)
3. History of Stable or unstable angina
4. History of Coronary or other arterial revascularization (e.g., PTCA, CABG)
5. History of Stroke
6. History of Transient ischemic attack (TIA)
7. Peripheral arterial disease presumed to be of atherosclerotic origin
8. Findings from CT angiogram or catheterization are consistent with clinical ASCVD; OR
9. Other documented atherosclerotic diseases such as:
    1. coronary atherosclerosis
    2. renal atherosclerosis
    3. aortic aneurysm secondary to atherosclerosis
    4. carotid plaque (≥ 50% stenosis)

c. The prescriber must plan to continue prescribing ezetimibe (unless the patient has a documented contraindication or intolerance to ezetimibe therapy) and a maximally tolerated statin (unless the patient has a documented contraindication or intolerance to statin therapy) together with the requested PCSK-9 inhibitor).

d. The patient must meet one of the following for ezetimibe:

i. Patient is currently on ezetimibe AND has documented adherence to ezetimibe for at least the past 90 continuous days (dates and length of therapy must be provided) OR
ii. The patient has a documented contraindication or intolerance to ezetimibe therapy

e. Patient has documented adherence to maximally tolerated statins for a combined total of at least the past 90 continuous days (drug names, daily dosages, dates and length of therapy must be provided) AND has tried TWO maximally tolerated statins unless the patient has a documented contraindication or intolerance to statin therapy. Two maximally tolerated statin therapies are defined as one of the following:
   i. Two high-intensity statin therapies (i.e. rosuvastatin 20-40 mg, atorvastatin 40-80 mg) OR
   ii. Documentation that the patient was not able to tolerate two high-intensity statins, but used a high-intensity statin and a lower daily dose of statin OR two lower intensity statins AND the prescriber provides a documented reason for not using the higher dose.
f. For a patient with a diagnosis of HoFH without ASCVD and who has a documented contraindication/intolerance to ezetimibe AND statin therapy, the patient must be using Evolocumab (Repatha) together with another LDL-C lowering therapy (e.g., LDL apheresis).
g. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Lexi-Drugs, national guidelines, or other peer-reviewed evidence

Initial Approval Duration: Six months

Criteria for Reauthorization:

1. The patient must not be receiving more than one PCSK-9 inhibitor.
2. For homozygous familial hypercholesterolemia, the patient must not be concurrently receiving Juxtapid or Kynamro.
3. The patient must not be pregnant.
4. The patient has been adherent to and must plan to continue using PCSK-9 inhibitor, maximally tolerated statin, and ezetimibe therapy (unless patient has a contraindication or intolerant to statin and/or ezetimibe therapy) for the past 90 continuous days with documentation provided AND demonstrated by the following:

Subsequent Requests:

The patient has experienced at least a 35%* reduction in LDL-C compared to the initial request (laboratory documentation of LDL-C must be received from within the past 30 days).

Will be approved for 1 year if patient meets criteria

** If the patient has HeFH with a baseline LDL-C > 160 mg/dl, patient has experienced at least a 24% reduction in LDL-C compared to the initial request.*

5. For a patient with a diagnosis of HoFH without ASCVD and who has a documented contraindication/intolerance to ezetimibe AND statin therapy, the patient must be using Evolocumab (Repatha) together with another LDL-C lowering therapy (e.g., LDL apheresis).

6. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Lexi-Drugs, national guidelines, or other peer-reviewed evidence

Table 1. Dutch Lipid Clinic Network Diagnostic criteria**

Criteria	Points
Family History	
1st degree relative with known premature* coronary and vascular disease, OR 1st degree relative with known LDL-C level above the 95th percentile	1
1st degree relative with tendinous xanthomata and/or arcus cornealis, OR Children aged	2
Clinical History	
Patient with premature* coronary artery disease	2
Patient with premature* cerebral or peripheral vascular disease	1
Physical Examination	
Tendinous xanthomata	6
Arcus cornealis prior to age 45 years	4
Cholesterol levels mg/dL (mmol/liter)	
LDL-C ≥ 330 mg/dL (≥ 8.5 mmol/L)	8
LDL-C 250-329 mg/dL (6.5-8.4 mmol/L)	5
LDL-C 190-249 mg/dL (5.0-6.4 mmol/L)	3
LDL-C 155-189 mg/dL (4.0-4.9 mmol/L)	1
DNA Analysis	
Functional mutation in the LDLR, apo B, or PCSK9 gene	8

References:

1. Praluent. Prescribing Information. Sanofi-Aventis. Bridgewater, NJ. 4/2021.
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3. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically.
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5. Evolocumab. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. URL: http://www.clinical pharmacology.com. Updated 8/2018

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8. Szarek M, White HD, Schwartz GG, et al. Alirocumab Reduces Total Nonfatal Cardiovascular and Fatal Events: The ODYSSEY OUTCOMES Trial. J Am Coll Cardiol 2019;73:387-96.
9. Murphy SA, Pedersen TR, Gaciong ZA, et al. Effect of the PCSK9 Inhibitor Evolocumab on Total Cardiovascular Events in Patients With Cardiovascular Disease: A Prespecified Analysis From the FOURIER
10. Trial. JAMA Cardiol. 2019;4(7):613-619. doi:10.1001/jamacardio.2019.088