DRUG DETERMINATION POLICY

Title: DDP-26 PCSK9 Inhibitors

Effective Date: 11/10/2020

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are specialty drugs indicated for a couple of diagnoses and are associated with some side effects. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of side effects, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

A. Diagnosis and severity.

1. Homozygous Familial Hypercholesterolemia (HoFH) [must meet one listed below]:

   a. Genetic testing: confirmed presence of the LDLR, APOB, PCSK9 or LDLRAP1 gene.

   b. Untreated with low-density lipoprotein (LDL) above 500 mg/dL or treated LDL-C above 300 mg/dL [must meet one listed below]:

      - Cutaneous or tendon xanthoma at less than ten years old.

      - Increased LDL-C consistent with HoFH in both parents.

2. Heterozygous Familial Hypercholesterolemia (HeFH) [must meet one listed below]:

a. Dutch Lipid Clinical Network criteria: defined by total score greater than 8.

b. Simon Broome diagnostic criteria:

- Adult: total cholesterol above 290 mg/dL or LDL-C above 190 mg/dL.
- Child (less than 16 years old.): total Cholesterol above 260 mg/dL or LDL-C above 155 mg/d.

3. Clinical Atherosclerotic Cardiovascular Disease (ASCVD) [must meet one listed below]:

a. History of ASCVD or cardiovascular (CV) event: acute coronary syndromes, myocardial infarction, angina, coronary or other arterial revascularization procedure, stroke, transient ischemic attack, peripheral arterial disease.

B. Other therapies [must meet both listed below]:

1. Non-pharmacological: lifestyle modifications (e.g., diet, alcohol use, tobacco cessation, or exercise) attestation from practitioner.

2. Pharmacological: statin therapy [must meet one listed below]:

a. Contraindication: chronic active liver disease diagnosis for greater than three months and/or unexplained persistent increased serum transaminases.

b. Inadequate response to high intensity statins and combination therapy for three months [must meet all listed below]:

- Atorvastatin 40 to 80 mg per day and rosuvastatin 20 to 40 mg per day.
- High intensity statin with additional lipid lowering agent such as fibrate or ezetimibe.
- LDL-C within the last month: 100 mg/dL or above with ASCVD or 130 mg/dL or above without ASCVD.

c. Significant adverse effects lasting two weeks [must meet both listed below]:

- Muscle symptoms: myalgia, myositis or rhabdomyolysis.
- High intensity statin dosage reduction or statin re-challenge with low intensity statin and reappearance of muscle symptoms.

C. Dosage regimen.

1. Praluent (alirocumab SQ): 75mg every two weeks or 300mg every four weeks; max 150mg every two weeks.

2. Repatha (evolocumab SQ): 140mg every two weeks or 420mg every month; HoFH: maximum dose 420mg every two weeks.

D. Approval.

1. Initial: six months.

2. Re-approval: one year [must meet one listed below]:

a. Absolute reduction LDL-C at least 40mg/dL.

b. Reduced LDL-C at or below than 100mg/dL with ASCVD or at or below 130mg/dL without ASCVD and maintain LDL above an acceptable threshold level dependent on the current standard of practice.

E. Exclusions:

1. Pregnant or breast-feeding.

2. Women of childbearing potential **not** using effective contraceptive methods for the duration of PCSK9 inhibitor therapy.

3. Triglycerides above 400 mg/dL.

4.0 Coding:

None.

5.0 References, Citations & Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Repatha & Praluent accessed Septermber 2020.
2. Efficacy and safety of alirocumab in reducing lipids and cardiovascular events. *NEJM* 2015; 372(16):1489-99.
3. Efficacy and safety of evolocumab in reducing lipids and cardiovascular events. *NEJM* 2015; 372(16)1500-9.
4. American Association of Clinical Endocrinologists and American College of Endocrinology guidelines for the management of dyslipidemia and prevention of cardiovascular disease. Endocr Pract 2017; 23:1-87.
5. Focused Update of the 2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease.

6.0 Appendices:

See page 4.

7.0 Revision History:

Original Effective Date: 08/25/2015

Next Review Date: 10/01/2021

Revision Date	Reason for Revision
7/19	Moved to new format; replaced abbreviations
12/19	Off cycle review; removal of specialist-only prescribing requirement; add bottom LDL threshold level for re-approval as per standard of practice
8/20	Annual review, formatting, added other therapies language, replaced abbreviations, simplified text on target lipid levels

Appendix I: Monitoring & Patient Safety

Drug	Adverse Reaction	Monitoring Parameters	REMS
Praluent	• Local: injection site reactions (7-17%) • Pregnancy: adverse events not observed in animal studies;	• Lab: LDL-C within 4-8 weeks of start or dose titration. • Miscellaneous: hypersensitivity to rx.	Not needed
Repatha	• Respiratory: nasopharyngitis (6-11%), URI (9%) • Pregnancy: adverse events not observed in animal studies	• Lab: LDL-C within 4-8 weeks of start; Lipid profile (HeFH) • Miscellaneous: hypersensitivity to rx.	Not needed