JOHNS HOPKINS MEDICINE / JOHNS HOPKINS HEALTHCARE	Johns Hopkins HealthCare LLC **Pharmacy Public** **Pharmacy Management Drug Policies**	*Policy Number*	MEDS095
		Effective Date	10/21/2015
		Review Date	04/20/2022
	Subject **Proprotein convertase Subtilisin Kexin Type 9 (PCSK9) Inhibitors (Praluent, Repatha)**	*Revision Date*	02/04/2022
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This document applies to the following Participating Organizations:

Priority Partners

Keywords: PCSK inhibitors, PCSK9, praluent, repatha

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I. POLICY

A. Praluent (alirocumab) and Repatha (evolocumab) will require prior authorization to ensure appropriate use. The process for initiating a prior authorization request can be found in policy PHARM 20. Praluent and Repatha will require prior authorization for outpatient prescription drug benefit coverage to ensure this medication is used only when clinically appropriate.
   1. PPMCO members are subject to the Priority Partners formulary, available at www.ppmco.org.
   2. USFHP members are subject to prior authorization criteria, step-edits and days-supply limits outlined in the Tricare Policy Manual. Tricare Policy supersedes JHHC Medical/Pharmacy Policies. Tricare limits may be accessed at: http://pec.ha.osd.mil/formulary_search.php?submenuheader=1

II. POLICY CRITERIA

A. **Praluent** (alirocumab) may be approved for patients meeting the following criteria:
   1. Documentation of ONE of the following:
      a. Hypercholesterolemia:
         I. Heterozygous familial hypercholesterolemia (HeFH)
            i. Patient is 18 years of age or older
            ii. Patient has a diagnosis of heterozygous familial hypercholesterolemia (HeFH) documented by medical records and laboratory LDL-C values>190mg/dl prior to statin therapy
         II. Homozygous Familial Hypercholesterolemia (HoFH)
            i. Patient is 18 years of age or older
            ii. Patient has a diagnosis of homozygous familial hypercholesterolemia with ONE of the following:
               a. Confirmation of the condition with evidence of untreated LDL-C concentration greater than 500 mg/dL, or treated LDL-C greater than or equal to 300 mg/dL
               b. Patient has been documented to be at high risk of Acute Coronary Syndrome (ACS) AND has had cutaneous or tendonous xanthoma before the age of 10 years
               c. Patient has been documented to have untreated LDL-C levels consistent with heterozygous familial hypercholesterolemia in both parents (LDL-C >190 mg/dL)
      b. Cardiovascular Event Prevention:

I. Patient is 18 years of age or older
II. Patient has a documented history of clinical atherosclerotic cardiovascular disease (ASCVD) evidenced by at least one of the following:
i. Acute Coronary Syndromes(ACS)
ii. History of myocardial infarction (MI)
iii. Stable or unstable angina
iv. Coronary or other arterial revascularization
v. Stroke, or transient ischemic attack (TIA)
vi. Peripheral arterial disease presumed to be of atherosclerotic origin

2. Documentation of ONE of the following:
a. Documentation of treatment failure with one statin regimen used for at least 90 days, consisting of a high-potency statin at the maximum tolerated dose (i.e. atorvastatin 40 or higher, or rosuvastatin 20mg or higher) in combination with Zetia (ezetimibe), despite optimal compliance with regimen.
I. Treatment failure is defined as:
i. less than 50% reduction LDL-C for individuals where initial LDL-C is known;
ii. LDL-C remains greater than or equal to 70mg/dl for individuals where initial LDL-C is unknown and patient has documented CVD
iii. LDL-C remains greater than or equalt to 100mg/dl and patient has No documented history of CVD;
b. Documentation of a condition that is a contraindication to statin therapy including active liver disease or unexplained persistent elevation of serum transaminases (> 3X upper limit of normal per laboratory reference range (documentation must be provided)
c. Documentation of statin intolerance (defined by the National Lipid Association Statin Intolerance Panel) and includes all the following (documentation must be provided):
I. Inability to tolerate at least 2 statins, with at least one started at the lowest starting daily dose
II. Statin dose reduction is attempted for symptom and biomarker abnormality resolution, rather than discontinuation of statin therapy altogether
III. Intolerable symptoms or abnormal biomarker changes are reversible upon statin discontinuation, but reproducible by re-challenge of statins, if clinically appropriate.
i. Statin re-challenge may be appropriate for individuals with all the following:Symptomatic; **AND** Creatine kinase is <4X upper limit of normal per laboratory reference range; AND AST/ALT are <3X upper limit of normal per laboratory reference range;
ii. Symptoms or biomarker abnormalities are not attributable to established predispositions or conditions recognized to increase the risk of statin intolerance, such as: Hypothyroidism, Drug interactions, Concurrent illness, Significant changes in physical activity/exercise, or Underlying muscle disease;

3. Airocumab will be used in combination with a statin used at the maximum tolerated dose unless statin contraindication or intolerance exists;
4. Documentation that patient has received comprehensive counseling regarding appropriate diet and lifestyle modifications
5. Alirocumab is prescribed by a cardiologist, endocrinologist or lipid specialist

B. **Repatha** (evolocumab) may be approved for patients meeting the following criteria:
1. Documentation of ONE of the following:
a. Hypercholesterolemia:
I. Heterozygous familial hypercholesterolemia (HeFH)

i. Patient is 10 years of age or older
ii. Patient has a diagnosis of heterozygous familial hypercholesterolemia documented by medical records and laboratory LDL-C values>190mg/dl prior to statin therapy

II. Homozygous Familial Hypercholesterolemia (HoFH)
i. Patient is 10 years of age or older
ii. Patient has a diagnosis of homozygous familial hypercholesterolemia with ONE of the following:
a. Confirmation of the condition with evidence of untreated LDL-C concentration greater than 500 mg/dL, or treated LDL-C greater than or equal to 300 mg/dL
b. Patient has been documented to be at high risk of Acute Coronary Syndrome (ACS) AND has had cutaneous or tendonous xanthoma before the age of 10 years
c. Patient has been documented to have untreated LDL-C levels consistent with heterozygous familial hypercholesterolemia in both parents (LDL-C >190 mg/dL)

b. Cardiovascular Event Prevention:
I. Patient is 18 years of age or older
II. Patient has a documented history of clinical atherosclerotic cardiovascular disease (ASCVD) evidenced by at least one of the following:
i. Acute Coronary Syndromes(ACS)
ii. History of myocardial infarction (MI)
iii. Stable or unstable angina
iv. Coronary or other arterial revascularization,
v. Stroke, or transient ischemic attack (TIA)
vi. Peripheral arterial disease presumed to be of atherosclerotic origin

2. Documentation of ONE of the following:
a. Documentation of treatment failure with one statin regimen used for at least 90 days, consisting of a high-potency statin at the maximum tolerated dose (i.e. atorvastatin 40 or higher, or rosuvastatin 20mg or higher) in combination with Zetia (ezetimibe), despite optimal compliance with regimens.
I. Treatment failure is defined as:
i. Less than 50% reduction LDL-C for individuals where initial LDL-C is known
ii. LDL-C remains greater than or equal to 70mg/dl for individuals where initial LDL-C is unknown and patient has documented CVD
iii. LDL-C remains greater than or equal to 100mg/dl and patient has No documented history of CVD
b. Documentation of a condition that is a contraindication to statin therapy including active liver disease or unexplained persistent elevation of serum transaminases (> 3X upper limit of normal per laboratory reference range (documentation must be provided)
c. Documentation of statin intolerance (defined by the National Lipid Association Statin Intolerance Panel) and includes all the following (documentation must be provided):
I. Inability to tolerate at least 2 statins, with at least one started at the lowest starting daily dose
II. Statin dose reduction is attempted for symptom and biomarker abnormality resolution, rather than discontinuation of statin therapy altogether
III. Intolerable symptoms or abnormal biomarker changes are reversible upon statin discontinuation, but reproducible by re-challenge of statins, if clinically appropriate.
i. Statin re-challenge may be appropriate for individuals with all the following: Symptomatic; **AND** Creatine kinase is <4X upper limit of normal per laboratory reference range; AND AST/ALT are <3X upper limit of normal per laboratory reference range;

ii. Symptoms or biomarker abnormalities are not attributable to established predispositions or conditions recognized to increase the risk of statin intolerance, such as: Hypothyroidism, Drug interactions, Concurrent illness, Significant changes in physical activity/exercise, or Underlying muscle disease;

3. Evolocumab will be used in combination with a statin used at the maximum tolerated dose unless statin contraindication or intolerance exists
4. Patient has received comprehensive counseling regarding appropriate diet;
5. Evolocumab is prescribed by a cardiologist, endocrinologist or lipid specialist

III. AUTHORIZATION PERIOD/LIMITATIONS

A. Length of initial authorization- 3 months
B. Length of authorization for continuation of therapy: 12 months. Continuaion of therapy request must meet all the following criteria:
   1. Criteria outlined for initial Prior Authorization has been satisfied
   2. Adherence with therapy and documentation of >45% reduction of LDL-C from baseline
   3. Documentation of LDL reduction has been provided.
C. The quantity requested must be within FDA approved labeling
D. Praluent® (75mg & 150mg)- limited to 2 syringes per 28 days
E. Repatha® (140mg) –limited to 2 syringes per 28 days
F. Repatha®(420mg)-limited to 3 x140mg syringes per 28 days

IV. EXCLUSIONS

A. Concurrent use of Praluent and Repatha
B. Concurrent use of Praluent or Repatha with Juxtapid (lomitapide) or Kynamro (mipomersen)
C. Contraindication to therapy with the requested drug
D. The use of physician samples, or manufacturer product discounts, does not guarantee coverage under the provisions of the medical and/or pharmacy benefit. All pertinent criteria must be met in order to be eligible for benefit coverage.

V. REFERENCES

1. Praluent [prescribing information]. Tarrytown, NY; Regeneron Pharmaceuticals Inc.; April 2021
2. Repatha [prescribing information]. Thousand Oaks, CA; Amgen Inc.; September 2021
3. Raal FJ, Santos RD. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. Atherosclerosis. 2012;223:262-8.
4. McGowan MP, Hosseini Dehkordi SH, Moriarty PM, Duell PB. Diagnosis and Treatment of Heterozygous Familial Hypercholesterolemia. J Am Heart Assoc. 2019 Dec 17;8(24):e013225.

VI. APPROVALS

Signature on file at JHHC

DATE OF REVISION	SUMMARY OF CHANGE
10/21/2015	New Policy

07/27/2017	Updated Exclusions policy regarding physician samples
07/01/2018	Removed EHP Line of Business
07/22/2019	Clarification of criteria
02/10/2020	Updated criteria layout (no clinical criteria changes instituted)
11/16/2021	Updated Repatha criteria based on new FDA-approved prescribing information
02/04/2022	Updated Praluent criteria based on FDA-approved prescribing information update

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