Clinical Policy Title:	evolocumab, alirocumab
Policy Number:	RxA.264
Drug(s) Applied:	Repatha®, Praluent®
Original Policy Date:	02/07/2020
Last Review Date:	3/15/2024
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

A. Primary Hyperlipidemia, Atherosclerotic Cardiovascular Disease, and Heterozygous Familial Hypercholesterolemia (HeFH) (must meet all):

1. Diagnosis of one of the following (a, b or c):
   a. Primary hyperlipidemia;
   b. Atherosclerotic cardiovascular disease (ASCVD) as evidenced by a history of one (1) of the following conditions:
      i. Coronary or other arterial revascularization;
      ii. Myocardial infarction;
      iii. Peripheral arterial disease presumed to be of atherosclerotic origin;
      iv. Stable or unstable angina;
      v. Stroke or transient ischemic attack (TIA);
   c. Heterozygous Familial Hypercholesterolemia (HeFH)
2. Request meets both of the following (a and b):
   a. Patient has one of the following LDL values while on max tolerated lipid lowering regimen within the last 120 days (i or ii):
      i. LDL greater than or equal to 55 mg/dL with ASCVD;
      ii. LDL greater than or equal to 100 mg/dL without ASCVD;
   b. Patient meets one of the following (i, ii, or iii):
      i. Patient has been receiving at least 12 consecutive weeks of highest tolerable dose of statin therapy;
      ii. Patient is statin intolerant as evidenced by an inability to tolerate at least two statins due to intolerable symptoms or clinically significant biomarker changes of liver function or muscle function (e.g., creatine kinase) and at least one statin is started at the lowest dose;
      iii. Patient has an FDA labelled contraindication to all statins (e.g., active liver disease, persistent elevations in hepatic transaminase levels, hypersensitivity to any component of the medication, pregnancy, lactation)
3. Patient has been receiving at least 12 weeks of ezetimibe (Zetia) treatment as adjunct to max tolerated statin treatment or patient has a history of contraindication or intolerance to ezetimibe.

Approval Duration

All Lines of Business (except Medicare): 12 months

B. Homozygous Familial Hypercholesterolemia (HoFH) (must meet all):

1. Diagnosis of HoFH as confirmed by one of the following (a or b):
   a. Genetic confirmation of 2 mutation in low density lipoprotein receptor (LDLR) gene, PCSK9 gene, ApoB gene, low density lipoprotein receptor adaptor protein 1(LDLRAP1) gene or ARH;
   b. Treated LDL-C greater than 300 mg/dL or untreated LDL-C greater than 500 mg/dL, and one of the following (i or ii):
      i. Xanthoma prior to age 10 years;
      ii. Evidence of HeFH in both parents;
2. Patient meets one of the following (a or b):
   a. Patient is receiving other lipid-lowering treatment (e.g., statin, ezetimibe);
   b. Patient has a documented inability to take other lipid-lowering treatment (e.g., statin, ezetimibe).

Approval Duration

All Lines of Business (except Medicare): 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):

1. Patient is currently receiving medication, excluding manufacturer samples;
2. Patient demonstrates LDL reduction while on treatment or LDL-C values drawn within the past 12 months while on maximally tolerated lipid lowering therapy is within normal limits.
3. Patient meets one of the following (a or b):
   a. Patient continues to receive other lipid-lowering treatment (e.g., statin, ezetimibe);
   b. Patient has a documented inability to take other lipid-lowering treatment (e.g., statin, ezetimibe).

Approval Duration

All Lines of Business (except Medicare): 12 months

References

1. Backes JM, Ruisinger JF, Gibson CA, et al. Statin-associated muscle symptoms—managing the highly intolerant. J Clin Lipidol. 2017; 11:24-33. Available at: https://pubmed.ncbi.nlm.nih.gov/28391891/. Accessed February 01, 2024.
2. Thompson PD, Panza G, Zaleski A, et al. Statin-associated side effects. JACC 2016;67(20):2395-2410. Available at: https://pubmed.ncbi.nlm.nih.gov/27199064/. Accessed February 01, 2024.
3. Marston NA, Giugliano RP, Park JG, Ruzza A, Sever PS, Keech AC, Sabatine MS. Cardiovascular Benefit of Lowering Low-Density Lipoprotein Cholesterol Below 40 mg/dL. Circulation. 2021 Nov 23;144(21):1732-1734. doi: 10.1161/CIRCULATIONAHA.121.056536. Epub 2021 Aug 27. PMID: 34452583; PMCID: PMC8608715. Accessed March 15, 2024.
4. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, Braun LT, de Ferranti S, Faiella-Tommasino J, Forman DE, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.Circulation. 2019; 139:e1082–e1143. doi: 10.1016/j.jacc.2018.11.002. Accessed March 15, 2024
5. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020702s073lbl.pdf. Accessed March 15, 2024

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was update to all lines of	07/16/2020	09/14/2020

business. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Initial Approval criteria: Commercial and Medicaid approval duration were updated from member's renewal date to 6 months. 6. Trial/failure of Praluent criteria was removed from initial approval criteria. 7. Continued Approval criteria II.A.3 “lab results within the past 3 months” was updated to “lab results within the past 12 months”. 8. Continued Approval criteria: Commercial and Medicaid approval duration were updated from member's renewal date to 6 months. 9. References were updated.		
Policy was reviewed: 1. Initial approval criteria 1.A.1.a verbiage was updated. 2. Continued Therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance..." and length of approval updated. 3. References were reviewed and updated.	04/08/2021	06/10/2021
Policy was reviewed: 1. Initial Approval Criteria, Updated: a. I.A.4: Updated age criteria from age is 18 years or older to Member meets one of the following (a or b): a. For HeFH age ≥ 10 years, b. For all other hyperlipidemias age ≥ 18 years; 2. Continued Therapy Approval Criteria, Updated: a. II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 3. References were reviewed and updated.	01/21/2022	04/18/2022
Policy was reviewed: 1. Initial Approval Criteria, I.A.5: Updated combination therapy criteria from For members on statin therapy, both of the following to For members ≥ 18 years old and on statin therapy, both of the following. 2. Initial Approval Criteria, I.A.6: Updated combination therapy criteria from For members not on statin therapy, member meets one of the following to For members ≥ 18 years old and not on statin therapy, member meets one of the following.	12/29/2022	4/13/2023

3. Initial Approval Criteria, I.A.9 and I.B.6: Updated concurrent therapy criteria to remove brand Kynamro as it is discontinued. 4. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.1.a.i.b).f: Updated diagnosis criteria from Medications which can increase lipid levels including, but not limited to: glucocorticoids, sex hormones, antipsychotics, antiretrovirals, immunosuppressive agents, retinoic acid derivatives to Medications that have had a clinically relevant contributory effect on the current degree of the member's elevated lipid levels including, but not limited to: glucocorticoids, sex hormones, antipsychotics, antiretrovirals, immunosuppressive agents, retinoic acid derivatives. 2. Initial Approval Criteria, I.A.4.b: Updated age criteria from for all other hyperlipidemias age: ≥ 18 years to for all otherprimary hyperlipidemias a (not including HeFH) or ASCVD age: ≥ 18 years. 3. Initial Approval Criteria, I.A.7.b: Updated to include new attestation criteria Provider attestation that member requires > 25% additional lowering of LDL-C. 4. Initial Approval Criteria, I.A and I.B: Updated from 6 months to 3 months for Commercial and Medicaid. 5. Initial Approval Criteria, I.B.3.a and I.B.3.b: Updated duration of therapy in criteria from within the last 30 days to within the last 60 days.	04/04/2023	04/13/2023
Policy was reviewed.	10/19/2023	10/19/2023
Policy was reviewed: 1. Removed requirement for documentation of genetic testing, poor diet, hypothyroidism etc for primary hyperlipidemia. 2. Removed requirement for evidence of history of Acute coronary syndrome and CHD for ASCVD. 3. Removed requirement of WHO/Dutch lipid network familial hypercholesterolemia diagnostic criteria score for HeFH. 4. Added confirmation of some specific LDL range and presence of history of MI and family history of FH, tendinous xanthomas etc for HeFH. 5. Removed prescriber requirement. 6. Removed age requirement. 7. Added requirements for some specific LDL values and previous use of statin treatment for all the indications.	02/01/2024	**MM/DD/YYYY**

8. Removed Age specific criteria related to requirements of use of statin therapy in conjunction with Repatha or intolerance to statin. 9. Removed coadministration criteria. 10. Removed dosing criteria. 11. Updated approval duration. 12. Added reauthorization requirement of continued use of lipid lowering treatment unless documented inability to take lipid lowering treatment. 13. References were reviewed and updated.		
Policy was reviewed: 1. Removed requirement for HeFH diagnosis 2. Revised criteria 2: a. Patient meets both of the following (i and ii): i. Patient has one of the following LDL values while on max tolerated lipid lowering regimen within the last 120 days (a or b): a) LDL greater than or equal to 100 mg/dL with ASCVD; b) LDL greater than or equal to 130 mg/dL without ASCVD; ii. Patient meets one of the following (a, b, c or d): a) Patient has been receiving at least 12 weeks of one high-intensity (HI) statin therapy (treatment) and will continue to receive a HI statin [i.e., atorvastatin 40-80 mg, rosuvastatin 20-40 mg] at max tolerated dose; b) Patient meets both of the following (1 and 2): 1) Patient is unable to tolerate HI statin as evidenced by intolerable and persistent (i.e., more than 2 weeks) myalgia (muscle symptoms w/o CK elevations) or myositis (muscle symptoms with CK elevations less than 10 times ULN); 2) Patient meets one of the following (a or b): a. Patient has been receiving at least 12 weeks of one moderate-intensity (MI) or low-intensity (LI) statin treatment and will continue to receive a MI or LI statin [i.e., atorvastatin 10-20 mg, rosuvastatin 5-10 mg, simvastatin 10-40 mg, pravastatin 10-80 mg, lovastatin 20-40 mg, Lescol XL (fluvastatin XL) 80 mg, fluvastatin 20-40 mg, or Livalo (pitavastatin) 1-4 mg] at max tolerated dose; b. Patient is unable to tolerate MI or LI statin as evidenced by intolerable and persistent (i.e., more than 2 weeks) myalgia (muscle symptoms without CK elevations) or myositis (muscle symptoms with CK elevations ≤ 10 times ULN);	3/15/2024	**MM/DD/YYYY**

c) Patient has a labelled contraindication to all statins; d) Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations ≥ 10 times ULN on one statin treatment; b. Patient meets both of the following (i and ii): i. Patient has one of the following LDL values while on max tolerated lipid lowering regimen within the last 120 days (a or b): a) LDL between 55 and 99 mg/dL with ASCVD; b) LDL between 100 and 129 mg/dL without ASCVD; ii. Patient meets both of the following (a and b): a) Patient meets one of the following (1, 2, 3 or 4): 1) Patient has been receiving at least 12 weeks of one max-tolerated statin treatment and will continue to receive a statin at max tolerated dose; 2) Patient is unable to tolerate statin treatment as evidenced by intolerable and persistent (i.e., more than 2 weeks) myalgia (muscle symptoms without CK elevations) or myositis (muscle symptoms with CK elevations ≤ 10 times ULN; 3) Patient has a labelled contraindication to all statins; 4) Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations ≥ 10 times ULN on one statin treatment; b) Patient has been receiving at least 12 weeks of ezetimibe (Zetia) treatment as adjunct to max tolerated statin treatment or patient has a history of contraindication or intolerance to ezetimibe. 3. Added to criteria II.A.2: "LDL-C values drawn within the past 12 months while on maximally tolerated lipid lowering therapy is within normal limits" 4. Added references		