Praluent® (alirocumab)
Repatha® (evolocumab)

INDICATION:

"Praluent is a PCSK9 (proprotein Convertase Subtilisin Kexin Type 9) inhibitor antibody indicated as adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-cholesterol (LDL-C).
Limitations of Use: The effect of Praluent on cardiovascular morbidity and mortality has not been determined."[1]
"Repatha is a PCSK9 (proprotein convertase subtilisin kexin type 9) inhibitor antibody indicated as an adjunct to diet and: Maximally tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low density lipoprotein cholesterol (LDL-C), Other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.
Limitations of Use: The effect of Repatha on cardiovascular morbidity and mortality has not been determined." [2]

Dosage Form/Strength:

Praluent Injection: 75 mg/mL, 150mg/mL pen & syringe
Repatha: 140mg/mL syringe, 140mg/mL SureClick autoinjector

Diagnostic Criteria:

Diagram 1

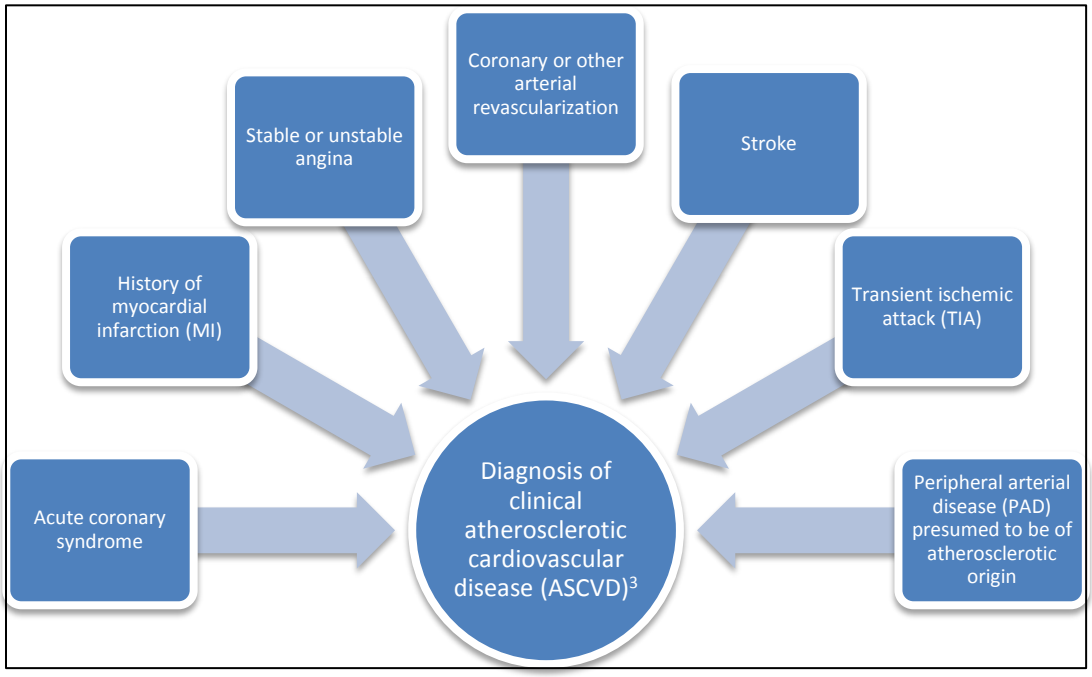


Diagram 2

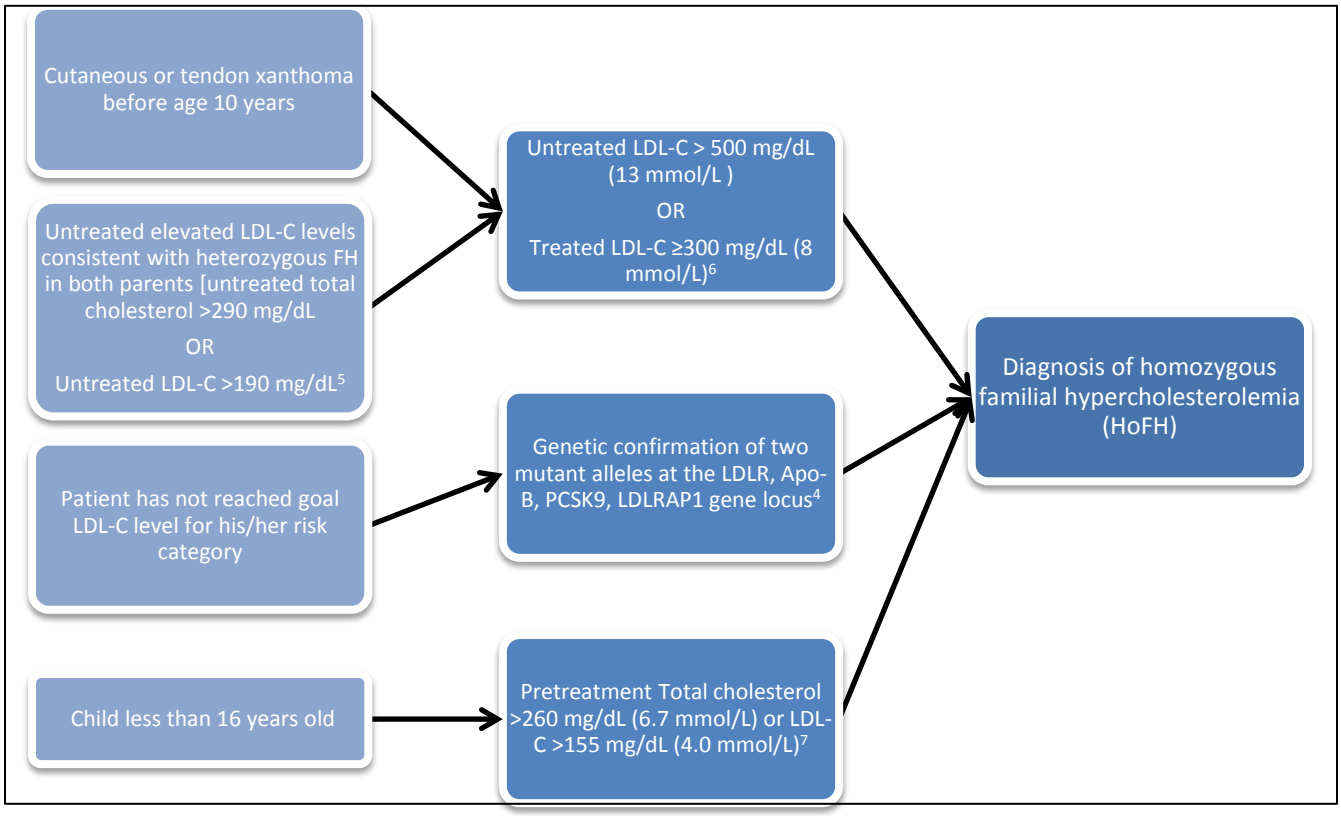
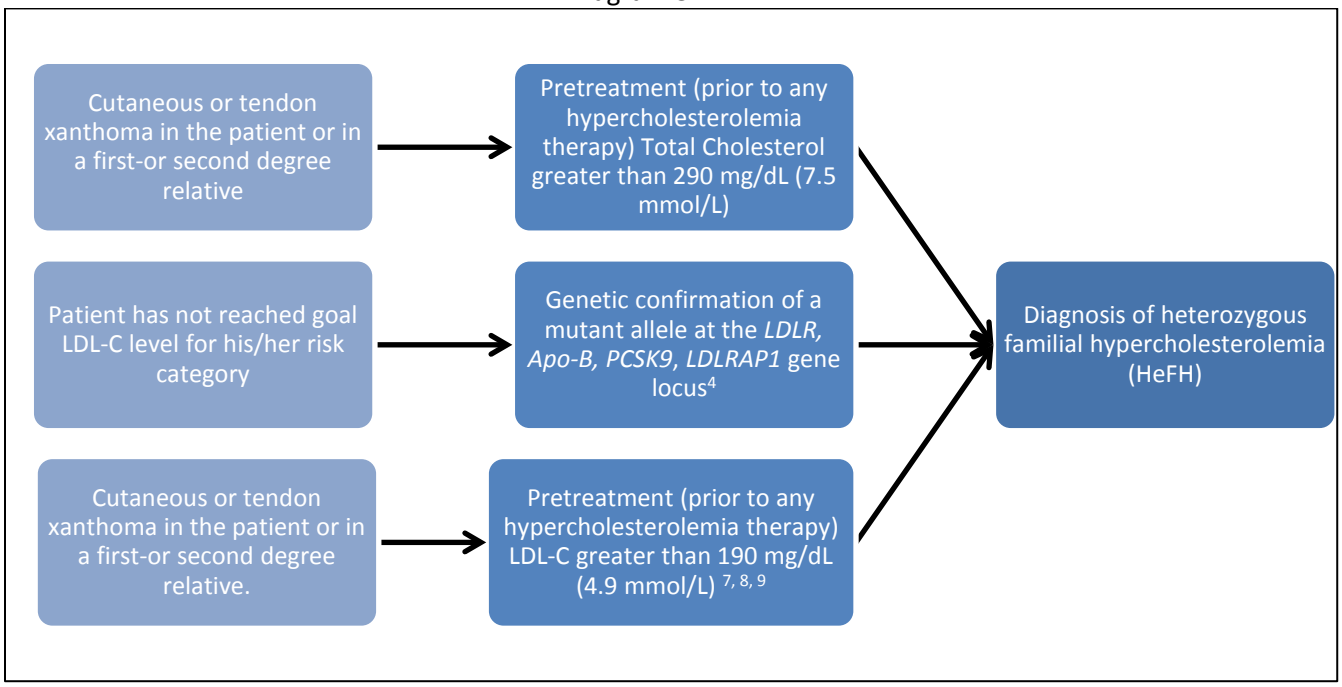


Diagram 3



Praluent & Repatha Criteria for Approval

Table 1:
Praluent & Repatha Criteria for Approval

Medication is being prescribed by, or in consultation with, a specialist (e.g., cardiologist, lipidologist, endocrinologist)

↓

The patient has not reached goal LDL-C level for the patient's risk category, as defined by generally accepted peer-reviewed guidelines. (For example: NCEP ATP III, NLA, or ACC/AHA)

↓

The patient has failed at least two high potency statins (i.e. rosuvastatin or atorvastatin), after a trial of at least 4 weeks each, at the maximum tolerated dose, in combination with Zetia®.

↓

The patient will use the requested medication in conjunction with diet

↓

Baseline (prior to treatment with a PCSK9 inhibitor) LDL and Total Cholesterol levels must be provided

Praluent			Repatha				
Patient has a diagnosis of HeFH confirmed by the diagnostic criteria of Diagram 3	OR ↔	Patient has a diagnosis of clinical ASCVD confirmed by the diagnostic criteria of Diagram 1	The patient has a diagnosis of HoFH confirmed by the diagnostic criteria of Diagram 2	OR ↔	The patient has a diagnosis of HeFH confirmed by the diagnostic criteria of Diagram 3	OR ↔	Patient has a diagnosis of ASCVD confirmed by the diagnostic criteria of Diagram 1
Patient is ≥18 years old			Patient is ≥13 years old		Patient is ≥18 years old		
Patient will use Praluent in conjunction with maximally tolerated statin therapy	OR ↔	Patient has a package labeled contraindication* to all statins	Repatha will be used with other LDL lowering therapies (i.e. statins, Zetia, or LDL apheresis)		Patient will use Repatha in conjunction with maximally tolerated statin therapy	OR ↔	Patient has a package labeled contraindication* to all statins

ASCVD = Atherosclerotic cardiovascular disease, HeFH = heterozygous familial hypercholesterolemia, HoFH = homozygous familial hypercholesterolemia
* Muscle cramps/pain does not count as a contraindication

Praluent & Repatha Criteria for Denial:

Table 2:
Praluent & Repatha Criteria for Denial

Medication is not being prescribed by, or in consultation with, a specialist (e.g., cardiologist, lipidologist, endocrinologist)

↓

The patient is at, or below, goal LDL-C level, as defined by generally accepted peer-reviewed guidelines.

↓

The patient has not failed at least two high potency statins (i.e. rosuvastatin or atorvastatin), after a trial of at least 4 weeks each, at the maximum tolerated dose, in combination with Zetia®.

↓

The patient will not use the requested medication in conjunction with diet

↓

Baseline (prior to treatment with a PCSK9 inhibitor) LDL and Total Cholesterol levels have not been provided

Medication will be used in combination with Juxtapid® (lomitapide) or Kynamro® (mipomersen).

↙ ↘

Praluent			**Repatha**				
↙		↘	↙	↓	↘		
Patient does not have a diagnosis of HeFH confirmed by the diagnostic criteria of Diagram 3	OR ↔	Patient does not have a diagnosis of clinical ASCVD confirmed by the diagnostic criteria of Diagram 1	Patient does not have a diagnosis of HoFH confirmed by the diagnostic criteria of Diagram 2	OR ↔	Patient does not have a diagnosis of HeFH confirmed by the diagnostic criteria of Diagram 3	OR ↔	Patient does not have a diagnosis of ASCVD confirmed by the diagnostic criteria of Diagram 1
↘		↙	↓		↘		↙
Patient is <18 years old			Patient is <13 years old		Patient is <18 years old		
↙		↘	↓		↙		↘
Patient will not use Praluent in conjunction with maximally tolerated statin therapy	OR ↔	Patient does not have a package labeled contraindication* to all statins	Repatha will not be used with other LDL lowering therapies (i.e. statins, Zetia, or LDL apheresis)		Patient will not use Repatha in conjunction with maximally tolerated statin therapy	OR ↔	Patient does not have a package labeled contraindication* to all statins

ASCVD = Atherosclerotic cardiovascular disease, HeFH = heterozygous familial hypercholesterolemia, HoFH = homozygous familial hypercholesterolemia
* Muscle cramps/pain does not count as a contraindication

Praluent & Repatha Criteria for Reauthorization Approval:

- Patient meets all of the criteria for the initial authorization.
  - WITH THE EXCEPTION OF: "The patient has not reached goal LDL-C level for the patient's risk category, as defined by generally accepted peer-reviewed guidelines."; **AND**
- There is documented evidence of a positive clinical response to therapy. Both baseline (prior to treatment with a PCSK9 inhibitor), and current LDL-C and Total Cholesterol levels must be submitted with any reauthorization request.

Praluent & Repatha Criteria for Reauthorization Denial:

- Patient does not meet all of the criteria for the reauthorization approval; **OR**
- There is no documented evidence of a positive clinical response to therapy. Both baseline (prior to treatment with a PCSK9 inhibitor), and current LDL-C and Total Cholesterol levels must be submitted with any reauthorization request.

Length of Authorization:

1. Initial coverage may be approved for up to three months.
2. Subsequent re-authorizations may be issued for up to a year.

Quantity Limit:

- The Praluent dispensing limit is 2 pens or syringes per 30 days.
- The Repatha dispensing limit is 2 syringes or autoinjectors per 30 days for a diagnosis of heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD).
- The Repatha dispensing limit is 3 syringes or autoinjectors per 30 days for a diagnosis of homozygous familial hypercholesterolemia (HoFH).

Mechanism of Action:

"Alirocumab is a human monoclonal antibody that binds to proprotein convertase subtilisin kexin type 9 (PCSK9). PCSK9 binds to the low-density lipoprotein receptors (LDLR) on the surface of hepatocytes to promote LDLR degradation within the liver. LDLR is the primary receptor that clears circulating LDL, therefore the decrease in LDLR levels by PCSK9 results in higher blood levels of LDL-C. By inhibiting the binding of CPSK9 to LDLR, alirocumab increases the number of LDLRs available to clear LDL, thereby lowering LDL-C levels." [1]

"Evolocumab is a human monoclonal IgG2 directed against human proprotein convertase subtilisin kexin 9 (PCSK9). Evolocumab binds to PCSK9 and inhibits circulating PCSK9 from binding to the low density lipoprotein (LDL) receptor (LDLR), preventing PCSK9-mediated LDLR degradation and permitting LDLR to recycle back to the liver cell surface. By inhibiting the binding of PCSK9 to LDLR, evolocumab increases the number of LDLRs available to clear LDL from the blood, thereby lowering LDL-C levels." [2]

REFERENCES / FOOTNOTES:

[1] Praluent® Prescribing Information. Sanofi-Aventis U.S. LLC. Bridgewater, NJ. October 2015. < http://products.sanofi.us/praluent/praluent.pdf > Accessed 11/30/2015.

[2] Repatha® Prescribing Information. Amgen Inc. Thousand Oaks, CA. September 2015. < http://pi.amgen.com/united_states/repatha/repatha_pi_hcp_english.pdf > Accessed 11/30/2015.

[3] Stone NJ, Robinson J, Lichtenstein AH, Merz CNB, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, McBride P, Schwartz JS, Shero ST, Smith Jr SC, Watson K and Wilson PWF. "2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines." Circulation. November 12, 2013; American Heart Association, Inc. http://circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437738.63853.7a . Accessed 12/2/2015.

[4] Izar, M., Machado, V., Fonseca, F. "Genetic screening for homozygous and heterozygous familial hypercholesterolemia." Appl Clin Genet. 2010; 3: 147-157. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3681171/> Accessed 11/30/2015.

[5] Santos R. "Homozygous Familial Hypercholesterolemia: New Insights and Guidance to Improve Detection and Management." American college of Cardiology. December 10, 2014. <http://www.acc.org/latest-in-cardiology/articles/2014/12/10/11/25/homozygous-familial-hypercholesterolemia?w_nav=LC>. Accessed 12/2/2015.

[6] Cuchel M, Bruckert E, Ginsberg HN, Raal FJ, Santos RD, Hegele RA, Kuivenhoven JA, Nordestgaard BG, Descamps OS, Steinhagen-Thiessen E, Tybjærg-Hansen A, Watts GF, Averna M, Boileau C, Borén J, Catapano AL, Defesche JC, Hovingh GK, Humphries SE, Kovanen PT, Masana L, Pajukanta P, Parhofer KG, Ray KK, Stalenhoef AFH, Stroes E, Taskinen MR, Wiegman A, Wiklund O, and Chapman MJ, *et al*. "Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society." Eur Heart J. 2014 Aug 21; 35(32): 2146–2157.

[7] Identification and Management of Familial Hypercholesterolemia. Simon Broome Diagnostic criteria for index individuals and relatives. Available at: http://www.ncbi.nlm.nih.gov/books/NBK53810/. Accessed 12/3/2015.

[8] Qureshi N, Humphries S, Seed M, Rowlands P, Minhas R. "Identification and management of familial hypercholesterolaemia: what does it mean to primary care?" Br J Gen Pract. 2009 Oct 1; 59(567): 773–778. Published online 2009 Sep 16. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2751920/ Accessed 12/3/2015.

[9] NICE Guidelines. "Familial hypercholesterolaemia: identification and management." National Institute for Health and Clinical Excellence. Manchester, UK. Published 2008.

[10] Lipinski MJ, Benedetto U, Escarcega RO, Biondi-Zoccai G, Lhermusier T, Baker NC, Torguson R, Brewer Jr HB, Waksman R. "The impact of proprotein convertase subtilisin-kexin type 9 serine protease inhibitors on lipid levels and outcomes in patients with primary hypercholesterolaemia: a network meta-analysis." Eur Heart J. First published online: 17 November 2015. < http://dx.doi.org/10.1093/eurheartj/ehv563 >.