



Wellmark Blue Cross and Blue Shield is an independent licensee of the Blue Cross and Blue Shield Association.

Juxtapid and Kynamro

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

This policy document describes the status of medical technology or treatment at the time the document was developed. Since that time, new technology or treatment may have emerged or new medical literature may have been published. This policy will be reviewed regularly and be updated as scientific and medical literature becomes available.

DESCRIPTION

The intent of the Juxtapid and Kynamro drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies. Juxtapid is approved by the Food and Drug Administration (FDA) as an adjunct treatment to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apoB), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH). Kynamro is FDA approved as an adjunct to lipid-lowering medications and diet to reduce LDL-C, apoB, TC, and non HDL-C in patients with HoFH.

POLICY

Criteria for Initial Approval

- A. Juxtapid[®] (lomitapide) or Kynamro[®] (mipomersen) may be considered **medically necessary** when the following criteria are met:**
- 1.) Prescriber must be a lipid specialist or a cardiometabolic specialist, unless the patient resides in an area where access to these specialists are limited, in which case, the prescriber must be a board-certified cardiologist or endocrinologist.
 - 2.) Patient has a diagnosis of homozygous familial hypercholesterolemia confirmed by ONE of the following:

- a. Genetic diagnosis with documented mutations in both alleles at LDL receptor, ApoB, PCSK9, or ARH adapter protein gene locus
OR
 - b. Clinical diagnosis defined as untreated LDL-C greater than 500 mg/dL or treated LDL-C >300 mg/dL **AND** either 1) Tendon or cutaneous xanthomas before age 10; or 2) Diagnosis of definite FH by genetic analysis, Simon-Broome Diagnostic Criteria or Dutch Lipid Clinic Network Criteria in both parents (Appendix A)
- 3.) Patient is engaging in healthy lifestyle changes including a healthy-fat diet (saturated fat <10% of total calories)) emphasizing intake of vegetables, fruits, legumes, nuts, whole grains, and fish and exercise program (150 minutes or more of moderate to vigorous intensity physical activity per week, or engaging as medically appropriate) demonstrated by notable improvement in body mass index (BMI)*, or other clinical indicators of progress (e.g. improvements in fasting blood glucose, lipid profile, exercise tolerability), documented in the medical record
 - 4.) Patient has been unable to achieve an LDL-C reduction of ≥50% despite adherence[†] to the combination of lifestyle changes and at least three months of lipid lowering therapy:
 - a. Trial of BOTH high-intensity statins (atorvastatin 40-80 mg and rosuvastatin 20-40 mg) at a maximum tolerated dose in combination with ezetimibe; OR TWO moderate intensity statins (e.g. pravastatin 40-80 mg, lovastatin 40 mg, fluvastatin 80 mg, pitavastatin 2-4 mg, simvastatin 20-40 mg) in combination with ezetimibe, only in the event the patient is unable to complete either of the high-intensity statin trials at the maximum approved dosing
AND
 - b. A trial of Repatha
 - 5.) Confirmation of provider enrollment in REMS program
 - 6.) If female of childbearing age, documented conversation of no current pregnancy or plans to become pregnant while on treatment (Juxtapid only)
 - 7.) Not to be used in combination with Kynamro, Juxtapid, Repatha or Praluent

OR

- 1.) Prescriber must be a lipid specialist or a cardiometabolic specialist, unless the patient resides in an area where access to these specialists are limited, in which case, the prescriber must be a board-certified cardiologist or endocrinologist.
- 2.) Patient has a diagnosis of homozygous familial hypercholesterolemia confirmed by ONE of the following:
 - a. Genetic diagnosis with documented mutations in both alleles at LDL receptor, ApoB, PCSK9, or ARH adapter protein gene locus
OR
 - b. Clinical diagnosis defined as untreated LDL-C greater than 500 mg/dL or treated LDL-C >300 mg/dL **AND** either 1) Tendon or cutaneous xanthomas before age 10; or 2) Diagnosis of definite FH by genetic analysis, Simon-Broome Diagnostic Criteria or Dutch Lipid Clinic Network Criteria in both parents (Appendix A)
- 3.) Patient is engaging in healthy lifestyle changes including a healthy-fat diet (saturated fat <10% of total calories)) emphasizing intake of vegetables, fruits, legumes, nuts, whole grains, and fish and exercise program (150 minutes or more of moderate to vigorous intensity physical activity per week, or engaging as medically appropriate) demonstrated by notable improvement in body mass index (BMI)*, or other clinical indicators of progress (e.g. improvements in fasting blood glucose, lipid profile, exercise tolerability), documented in the medical record
- 4.) Patient has been unable to achieve an LDL-C reduction of ≥50% despite adherence[†] to the combination of lifestyle changes and at least three months of Repatha
- 5.) Patient has a documented contraindication (e.g., active liver disease, pregnancy, breastfeeding), or medically justifiable reason that precludes statin use (e.g. patients has experienced rhabdomyolysis, CK elevations ≥ 10x ULN, or statin intolerance).

- a. Statin intolerance shall be defined in accordance with the National Lipid Association definition:
 - i.) Inability to tolerate at least two statins (one at any dose, one at lowest daily dose) due to objectionable symptoms or abnormal biomarkers temporally related to statin use, reversible upon statin discontinuation and reproducible by re-challenge while excluding other known determinants. Other known determinants include low body mass index (BMI), acute infection, untreated or undertreated hypothyroidism, severe renal or hepatic dysfunction, organ transplant, recent severe trauma, HIV infection, Vitamin D deficiency, history of creatine kinase elevation, history of preexisting or unexplained muscle or joint pain, high level of physical activity, illicit drug abuse, excess alcohol use. Each statin trial, both initial and re-challenge shall be at least two weeks duration.
 - ii.) A trial of one statin at lowest starting daily dose
 - Rosuvastatin 5mg
 - Atorvastatin 10mg
 - Simvastatin 10mg
 - Lovastatin 20mg
 - Pravastatin 40mg
 - Fluvastatin 40mg
 - Pitavastatin 2mg
 - iii.) One statin at any daily dose
- 6.) Confirmation of provider enrollment in REMS program
- 7.) If female of childbearing age, documented conversation of no current pregnancy or plans to become pregnant while on treatment (Juxtapid only)
- 8.) Not to be used in combination with Kynamro, Juxtapid, Repatha or Praluent

Approval will be for 6 months

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy for Juxtapid or Kynamro must meet all initial authorization criteria., and have achieved or maintained a LDL-C reduction greater than 20% from the levels immediately prior to initiation of treatment with either Juxtapid or Kynamro after at least 12 months of treatment

Approval will be for 12 months

The aforementioned drugs are considered **not medically necessary** for patients who do not meet the criteria set forth above.

*If patient is within healthy BMI range, documentation must satisfy that he or she is engaging in low fat diet and exercise program

†Please note: Documentation of LDL-C levels are required (untreated baseline and current [within 30 days of prior authorization request]);

Quantity Limits Apply

- Juxtapid 30 capsules per 30 days
- Kynamro 4 syringes per 28 days

APPENDIX

APPENDIX A: Diagnosis of familial hypercholesterolemia (FH)

A definite diagnosis of FH is made when one of the following diagnostic criteria is met:

1. Genetic diagnosis
 - a) An LDL-receptor mutation, familial defective apo B-100, or a PCSK9 gain-of-function mutation
2. Simon-Broome Diagnostic Criteria for definite FH
 - a) Total cholesterol > 290 mg/dL or LDL-C > 190 mg/dL in patients over 16 years of age or total cholesterol > 260 mg/dL or LDL-C > 155 mg/dL in patients less than 16 years of age
AND
 - b) Tendon xanthomas in the patient, first (parent, sibling or child) or second degree relative (grandparent, uncle or aunt)
3. Dutch Lipid Clinic Network Criteria for definite FH
 - a) Total score > 8 points

CLINICAL RATIONALE

Homozygous familial hypercholesterolemia (HoFH) is quite rare, affecting around 1:1,000,000 persons (approximately 300 people in the United States). HoFH is generally identified via severely elevated low density lipoprotein cholesterol (LDL-C) in the absence of secondary causes of hypercholesterolemia; cardiovascular events can occur in the second decade of life. There are two sets of diagnostic criteria used for diagnosis (the World Health Organization/Dutch Lipid Network and Simon-Broome Register); genetic testing is also available. Juxtapid and Kynamro are both approved for the treatment of HoFH patients. Kynamro is an injectable antisense inhibitor of apolipoprotein B synthesis that has been shown to reduce LDL-C levels by an additional 25 percent when combined with other lipid lowering therapies at maximally tolerated doses. Juxtapid is an oral microsomal triglyceride transfer protein inhibitor that can reduce LDL-C by up to 40 percent when combined with maximally tolerated lipid-lowering therapies and LDL apheresis. Both drugs have black box warnings and are available through risk evaluation and mitigation strategy (REMS) because of the risk of hepatotoxicity.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD-CM diagnostic codes.

- Not applicable

REFERENCES

- Juxtapid [package insert]. Cambridge, MA: Aegerion Pharmaceuticals, Inc.; January 2020.
- Kynamro [package insert]. Cambridge, MA: Genzyme Corporation, Inc.; January 2017.
- Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease. Consensus Statement of the European Atherosclerosis Society. *Eur Heart J.* 2013;34:3478–3490.
- Cuchel M, Bruckert E, Ginsberg HN, 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;35:2146-2157.
- National Institute for Health and Clinical Excellence (2008). Identification and management of familial hypercholesterolaemia. NICE clinical guideline 71.
- Raal JF, Santos RD, Blom DJ, et al. Mipomersen, an apolipoprotein B Synthesis inhibitor, for lowering of LDL cholesterol concentrations in patients with homozygous familial hypercholesterolaemia: a randomized, double-blind, placebo-controlled trial. *Lancet.* 2010;375:998-1006.

- Goldberg AC, Hopkins PN, Toth PP, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients. Clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. *J Clin Lipidol*. 2011;5:S1–S8.
- Raal JF, Santos RD. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. *Atherosclerosis*. 2012;223:262-268.
- Liposorber System [package insert]. New York, NY: Kaneka Pharma America, LLC. Available at <http://www.liposorber.com/physician/prescribe/prescribe.htm>. Accessed: December 6, 2017.
- Moriarty PM. LDL-apheresis therapy: current therapeutic practice and potential future use. *Future Lipidol*. 2006;3:299-308.
- Bays HE, Jones PH, Orringer CE, et al. National Lipid Annual Summary of Clinical Lipidology 2016. *J Clin Lipidol* 2016; 10:S1-S43.
- Lloyd-Jones DM, Morris PB, Ballantyne CM, Birtcher KK, Daly DD Jr., DePalma SM, Minissian MB, Orringer CE, Smith SC Jr. 2017 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 risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2017;70:1785–822.

POLICY HISTORY

Policy #: 05.01.91

Policy Creation: December 2015

Reviewed: April 2020

Revised: April 2020

Current Effective Date: June 6, 2020