PHARMACY POLICY STATEMENT
(Kentucky Medicaid)

Original Effective Date	Next Annual Review	Last Revision
07/29/2013	09/26/2017	03/03/2017
Policy Name		**Policy Number**
Biologic Cholesterol Agents		SRx-0067
Policy Type		
Medical	Administrative	**PHARMACY**	Reimbursement

Pharmacy Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) are derived from literature based on and supported by clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any Evidence of Coverage documents, Pharmacy Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Pharmacy Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Pharmacy Policy Statement. If there is a conflict between the Pharmacy Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination.

Contents of Policy

A. INTRODUCTION

Familial hypercholesterolemia (FH) is an inherited condition that causes high levels of low density lipoprotein (LDL) cholesterol levels beginning at birth, and premature cardiovascular disease. For individuals with familial hypercholesterolemia, diet and lifestyle are important but they are not the cause of high LDL as patients with familial hypercholesterolemia have genetic mutations that make the liver incapable of metabolizing excess LDL. There are two forms of familial hypercholesterolemia: heterozygous familial hypercholesterolemia (HeFH), where there is a genetic mutation inherited from one parent, and homozygous familial hypercholesterolemia (HoFH), where a genetic mutation is inherited from both parents.

The intent of CareSource Pharmacy Policy Statements is to encourage appropriate selection of patients for therapy according to product labeling, clinical guidelines, and/or clinical studies as well as to encourage use of preferred agents. The CareSource Pharmacy Policy Statement is a guideline for determining health care coverage for our patients with benefit plans covering prescription drugs. Pharmacy Policy Statements are written on selected prescription drugs requiring prior authorization or step therapy. The Pharmacy Policy Statement is used as a tool to be interpreted in conjunction with the member's specific benefit plan.

NOTE: The Introduction section is for your general knowledge and is not to be construed as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals and is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider can also be a place where medical care is given, like a hospital, clinic or lab. This policy informs providers about when a service may be covered.

B. DEFINITIONS

1. None applicable.

C. POLICY COVERAGE CRITERIA

1. Site of Service

Site of Service Administration	Coverage Criteria
Office, Outpatient, Home	**Preferred place of service is in the home.**

2. Coverage Criteria

CareSource will approve the use of Repatha (evolocumab), Praluent (alirocumab), Juxtapid (lomitapide) and Kynamro (mipomersen), and consider its use medically necessary when the criteria have been met for each condition listed below. Prior authorization should be submitted with chart notes and documentation supporting medical necessity.

Condition	Repatha (evolocumab) Coverage criteria:
Homozygous Familial Hypercholesterolemia	1) Member has diagnosis of homozygous familial hypercholesterolemia confirmed by one of the following: a. LDL-R DNA sequencing test or APOB (hypercholesterolemia) mutation analysis confirmation of two mutant alleles at LDLR, Apo-B, PCSK9, ARH adaptor protein 1/LDLRAP1 gene locus b. Pre-treatment LDL-C greater than 500mg/dl with one or more of the following i. Elevated LDL levels before lipid lowering therapy consistent with heterozygous familial hypercholesterolemia in both parents where LDL levels are known 1. LDL > 190 in members under age 20 2. LDL > 220 for members age 20 to 29 3. LDL > 250 for patients age 30 or older ii. History of early vascular disease (men < 55 years, women < 60 years) on both side of family if LDL levels are unknown 2) Member is 13 years of age or older 3) Prescribed by a cardiologist, endocrinologist, or lipid specialist 4) Failed to achieve an LDL level of ≤ 130mg/dl or a greater than 50% reduction in LDL level from baseline with 30 day trial of two different treatment regimens of high-potency statins (atorvastatin, simvastatin, or rosuvastatin) plus ezetimibe (Zetia) or monotherapy with Vytorin, unless patient has documented intolerance to all three high-potency statins 5) Triglycerides ≤ 400 mg/dL 6) Required co-administration with maximally tolerated statin or other lipid lowering therapy or patient has documented contraindication or intolerance to satin therapy

Heterozygous Familial Hypercholesterolemia	1) Member has diagnosis of heterozygous familial hypercholesterolemia confirmed by one of the following: a. Single mutation in the PCSK9, LDLR, LDLRAP or APOB gene b. Clinical criteria as "definite FH" using WHO/Dutch Lipid Network. (Score of 9 or higher) 2) Member is 18 years of age or older 3) Prescribed by a cardiologist, endocrinologist, or lipid specialist 4) Pre-treated LDL level of ≥190 mg/dl 5) Triglycerides ≤400 mg/dl 6) Failure to achieve LDL ≤100mg/dl or a greater than 50% reduction in LDL levels from baseline with at least a 30 day trial of two different treatment regimens of high-potency statins (atorvastatin, simvastatin, or rosuvastatin) plus ezetimibe (Zetia) or monotherapy with Vytorin, unless patient has documented intolerance to all three high-potency statins 7) Required co-administration with a statin at maximum tolerated dose or patient has documented contraindication or intolerance to satin therapy 8) Member has been instructed to eat a low fat diet, and documented diet modifications provided in chart notes

Condition	**Praluent (alirocumab) Coverage criteria:**
Heterozygous Familial Hypercholesterolemia	1) Member has diagnosis of heterozygous familial hypercholesterolemia confirmed by one of the following: a. Single mutation in the PCSK9, LDLR, LDLRAP or APOB gene b. Clinical criteria as "definite FH" using WHO/Dutch Lipid Network. (Score of 9 or higher) 2) Member is 18 years of age or older 3) Prescribed by a cardiologist, endocrinologist, or lipid specialist 4) Pre-treated LDL level of ≥190 mg/dl 5) Triglycerides ≤400 mg/dl 6) Failure to achieve LDL ≤100mg/dl or a greater than 50% reduction in LDL levels from baseline with at least a 30 day trial of two different treatment regimens of high-potency statins (atorvastatin, simvastatin, or rosuvastatin) plus ezetimibe (Zetia) or monotherapy with Vytorin,

	unless patient has documented intolerance to all three high-potency statins 7) Required co-administration with a statin at maximum tolerated dose or patient has documented contraindication or intolerance to satin therapy 8) Member has been instructed to eat a low fat diet, and documented diet modifications provided in chart notes 9) Clinical reason to why patient cannot use Repatha (evolocumab) or treatment failure after at least a 30 days of Repatha

Condition	Juxtapid (lomitapide) Coverage criteria:
Homozygous Familial Hypercholesterolemia	1) Member has diagnosis of homozygous familial hypercholesterolemia confirmed by one of the following: a. LDL-R DNA sequencing test or APOB (hypercholesterolemia) mutation analysis confirmation of two mutant alleles at LDLR, Apo-B, PCSK9, ARH adaptor protein 1/LDLRAP1 gene locus b. Pre-treatment LDL-C greater than 500mg/dl with one or more of the following i. Elevated LDL levels before lipid lowering therapy consistent with heterozygous familial hypercholesterolemia in both parents where LDL levels are known 1. LDL > 190 in members under age 20 2. LDL > 220 for members age 20 to 29 3. LDL > 250 for patients age 30 or older ii. History of early vascular disease (men < 55 years, women < 60 years) on both side of family if LDL levels are unknown 2) Member is 18 years of age or older 3) Prescribed by a cardiologist, endocrinologist, or lipid specialist 4) Medication is adjunct to other lipid-lowering therapies (a statin or ezetimibe) 5) Member has been instructed to eat a low fat diet, and documented diet modifications provided in chart notes

	6) Clinical reason to why patient cannot use Repatha (evolocumab) or treatment failure after at least a 30 days of Repatha

Condition	Kynamro (mipomersen) Coverage criteria:
Homozygous Familial Hypercholesterolemia	1) Member has diagnosis of homozygous familial hypercholesterolemia confirmed by one of the following: a. LDL-R DNA sequencing test or APOB (hypercholesterolemia) mutation analysis confirmation of two mutant alleles at LDLR, Apo-B, PCSK9, ARH adaptor protein 1/LDLRAP1 gene locus b. Pre-treatment LDL-C greater than 500mg/dl with one or more of the following i. Elevated LDL levels before lipid lowering therapy consistent with heterozygous familial hypercholesterolemia in both parents where LDL levels are known 1. LDL > 190 in members under age 20 2. LDL > 220 for members age 20 to 29 3. LDL > 250 for patients age 30 or older ii. History of early vascular disease (men < 55 years, women < 60 years) on both side of family if LDL levels are unknown 2) Member is 12 years of age or older 3) Prescribed by a cardiologist, endocrinologist, or lipid specialist 4) Medication is adjunct to other lipid-lowering therapies (a statin or ezetimibe) 5) Member has been instructed to eat a low fat diet, and documented diet modifications provided in chart notes 6) Clinical reason to why patient cannot use Repatha (evolocumab) or treatment failure after at least a 30 days of Repatha

All other uses of Repatha (evolocumab), Praluent (alirocumab), Juxtapid (lomitapide) and Kynamro (mipomersen) are considered experimental/investigational; and therefore, will follow CareSource's off-label policy. Clinical atherosclerotic cardiovascular disease is an excluded diagnosis for Repatha and Praluent.

Please note that this policy is reviewed on an annual basis. New drugs and indications receiving FDA approval may not be reflected in this policy immediately.

Notes:

- The dose of statin should be rosuvastatin 20 mg or higher, atorvastatin 40 mg or higher, simvastatin 40 mg or higher unless one of the following conditions exists: adverse effects occurred at higher doses, age over 65, BMI < 18.5, impaired glucose tolerance or elevated fasting glucose exists, concomitant use of interacting medications (cyclosporine, protease inhibitors, ritonavir, clarithromycin, itraconazole, ketoconazole, erythromycin, nefazodone, simeprevir, verapamil, diltiazem, dronedarone, amiodarone, amlodipine, or ranolazine.
- Documented diagnosis must be confirmed by portions of the individual's medical record which need to be supplied with prior authorization request. These medical records may include, but are not limited to test reports, chart notes from provider's office, or hospital admission notes.
- Patient is required to have completed the trial(s) listed in the above criteria unless the patient is unable to tolerate or has a contraindication to trial medications. Documentation such as chart notes or pharmacy claims may be requested to verify trial(s), intolerance, or contraindication(s).
- Refer to the product package insert for dosing, administration and safety guidelines.

3. Dosage and Quantity Limits (listed if applicable)

Information for patients with renal or hepatic impairment is not included. See package insert for individual agents.

Condition	Dosage and Quantity Limit of Repatha (evolocumab)
Homozygous Familial Hypercholesterolemia	420 mg once monthly (1 injection per 28 days)
Heterozygous Familial Hypercholesterolemia	140 mg every 2 weeks (2 injections per 28 days) or 420 mg once monthly (1 injection per 28 days)

Condition	Dosage and Quantity Limit of Praluent (alirocumab)
Homozygous Familial Hypercholesterolemia	75 mg or 150 mg every 2 weeks (2 injections per 28 days)

Condition	Dosage and Quantity Limit of Juxtapid (lomitapide)
Homozygous Familial Hypercholesterolemia	5 to 60 mg daily (30 tablets per 30 days)

Condition	Dosage and Quantity Limit of Kynamro (mipomersen)
Homozygous Familial Hypercholesterolemia	200 mg weekly (4 injections per 28 days)

4. Authorization Period

Condition	Approval Period
Homozygous Familial Hypercholesterolemia	The initial authorization Repatha, Juxtapid, or Kynamro is valid for 6 months. Continued treatment may be considered when at least 25% reduction in LDL compared to baseline has been observed and ongoing concomitant lipid lowering therapies is available. A reauthorization after successful initiation period will be placed for 12 months. **ALL** authorizations are subject to continued eligibility.
Heterozygous Familial Hypercholesterolemia	The initial authorization Repatha valid for 6 months. Continued treatment may be considered when at least 25% reduction in LDL compared to baseline has been observed and ongoing concomitant statin therapy is available. A reauthorization after successful initiation period will be placed for 12 months. **ALL** authorizations are subject to continued eligibility.

5. Coding

None applicable.

D. RELATED POLICIES

AD-0004: Medical Necessity - Off-Label, Approved Orphan and Compassionate Use Drugs

E. REVIEW/REVISION HISTORY

DATE	ACTION/DESCRIPTION
7/29/2013	Issued, reviewed.
9/26/2014	Reviewed and revised.
7/26/2015	Reviewed and revised.
10/20/2015	Add Repatha and Praluent, updated format, statin intolerance defined, additional step therapy for Juxtapid and Kynamro.

3/3/2017	Additional step therapy for Juxtapid, Kynamro, and Praluent. Updated criteria and format.

F. REFERENCES

1. Repatha [package insert]. Thousand Oaks, CA. Amgen Inc. August 2015.
2. Praluent [package insert]. Bridgewater, NJ: Regeneron Pharmaceuticals; April 2015.
3. Juxtapid [package insert]. Cambridge, MA: Aegerion Pharmaceuticals; May 2014.
4. Kynamro [package insert]. Cambridge, MA: Genzyme Corporation; January 2013.
5. Pijlman AH, Huijgen R, Verhagen SN, et al. Evaluation of cholesterol lowering treatment of patients with familial hypercholesterolemia: a large cross-sectional study in The Netherlands. Atherosclerosis.;209: 189-194.
6. National Lipid Association Annual Summary of Clinical Lipidology 2015
7. Homozygous familial hypercholesterolemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolemia of the European Atherosclerosis Society
8. Identification and management of familial hypercholesterolemia NICE guidelines
9. Al-Rasadi K, Al-Waili K, Al-Sabti HA, et al. Criteria for Diagnosis of Familial Hypercholesterolemia: A Comprehensive Analysis of the Different Guidelines, Appraising their Suitability in the Omani Arab Population. Oman Medical Journal. 2014;29(2):85-91. doi:10.5001/omj.2014.22.
10. Robinson JG, Nedergaard BS, Rogers WJ, et al. Effect of Evolocumab or Ezetimibe Added to Moderate- or High-Intensity Statin Therapy on LDL-C Lowering in Patients With Hypercholesterolemia: The LAPLACE-2 Randomized Clinical Trial. JAMA. 2014;311(18):1870-1883
11. Blom DJ, Hala T, Bolognese M, et al. A 52 week placebo controlled trial of evolocumab in hyperlipidemia. N Engl J Med 2014; 370:1809-1819.
12. Raal FJ, Stein EA, Dufour R, et al. PCSK9 inhibition with evolocumab (AMG 145) in heterozygous familial hypercholesterolaemia (RUTHERFORD-2): a randomised, double-blind, placebo-controlled trial. Lancet 2015; 385:331-340.
13. Raal FJ, Honarpour N, Blom DJ, et al. Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolaemia (TESLA Part B): a randomised, double-blind, placebo-controlled trial. Lancet 2015; 385: 341–50.

The Pharmacy Policy detailed above has received due consideration and is approved.

Independent medical review – October 2015