Medical Policy

BlueCross BlueShield of Kansas
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Title: Statin Therapy

- **Prime Therapeutics will review Prior Authorization requests.**
  Prior Authorization Form:
  http://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-6082KS-STQL.pdf

  Link to Drug List (Formulary):
  https://www.bcbsks.com/drugs/

Professional
Original Effective Date: January 1, 2010
Revision Date(s): May 20, 2011; August 30, 2012; January 1, 2013; July 1, 2013; January 1, 2014; October 28, 2014; October 1, 2015; September 1, 2016; May 15, 2017; October 15, 2017; April 16, 2018; October 1, 2018
Current Effective Date: October 1, 2018

Institutional
Original Effective Date: January 1, 2010
Revision Date(s): May 20, 2011; August 30, 2012; January 1, 2013; July 1, 2013; January 1, 2014; October 28, 2014; October 1, 2015; September 1, 2016; May 15, 2017; October 15, 2017; April 16, 2018; October 1, 2018
Current Effective Date: October 1, 2018

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

The intent of the Statin Prior Authorization program is to encourage the use of cost-effective generic statins (HMG Co-A reductase inhibitors) prior to the use of brand statins for the management of high blood cholesterol. This 1-step program includes all brand statin or statin combination products as targets requiring use of a generic statin or statin combination prior to their use. The program will evaluate use of a brand statin or statin combination product through the prior authorization process when patients are unable to take a generic statin or statin combination due to documented intolerance, FDA labeled contraindication, or hypersensitivity. Requests for brand statins or statin combinations will be reviewed when patient-specific documentation has been provided.

Target Agents (brands only)

- **Advicor**® (niacin extended release/lovastatin) [b]
- **Altoprev**® (lovastatin extended release)
- **Crestor**® (rosuvastatin) [a]
- **Lescol XL®** (fluvastatin extended release) [a]
- **Liptruzet**™ (ezetimibe/atorvastatin) [b]
- **Livalo**® (pitavastatin)
- **Simcor**® (niacin extended release/simvastatin) [b]
- **Vytorin**® (ezetimibe/simvastatin) [a]
- **Zypitamag** (pitavastatin)

a - currently available as a generic; included as a prerequisite in step therapy program
b – discontinued

FDA Approved Indications and Dosage[1-12, 21, 22]

Single Ingredient Products

Drug	Indication	Limitations of Use	Dosage
Altoprev® (lovastatin extended release) tablets	Adjunctive therapy to diet to: • Reduce the risk of MI, revascularization procedures, and angina in patients without CHD, but with multiple risk factors. • Slow the progression of coronary atherosclerosis in patients with CHD as part of a treatment strategy to lower Total-C and LDL-C. • Reduce elevated Total-C, LDL-C, Apo B, and TG levels and increase HDL-C in adult patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia.	Not studied in Fredrickson Types I, III, and V dyslipidemias.	20-60 mg once daily

Drug	Indication	Limitations of Use	Dosage
Crestor® * (rosuvastatin) tablets	• Adult patients with primary hyperlipidemia and mixed dyslipidemia as an adjunct to diet to reduce elevated total-C, LDL-C, ApoB, nonHDL-C, and TG levels and to increase HDL-C • Pedatric patients 8 to 17 years of age with heterozygous familial hypercholesterolemia (HeFH) to reduce elevated total-C, LDL-C and ApoB after failing an adequate trial of diet therapy • Pediatric patients 7 to 17 years of age with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C, total-C, nonHDL-C and ApoB as an adjunct to diet, either alone or with other lipid-lowering treatments • Adult patients with hypertriglyceridemia as an adjunct to diet • Adult patients with primary dysbeta-lipoproteinemia (Type III hyperlipoproteinemia) as an adjunct to diet • Adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C, total-C, and ApoB • Slowing the progression of atherosclerosis as part of a treatment strategy to lower total-C and LDL-C as an adjunct to diet • Risk reduction of MI, stroke, and arterial revascularization procedures in patients without clinically evident CHD, but with multiple risk factors	Not studied in Fredrickson Type I and V dyslipidemias.	5-40 mg once daily
Lescol® * (fluvastatin) capsules	Adjunctive therapy to diet to: • Reduce elevated TC, LDL-C, Apo B, and TG, and to increase HDL-C in adult patients with primary hypercholesterolemia and mixed dyslipidemia • Reduce elevated TC, LDL-C, and Apo B levels in boys and post-menarchal girls, 10 to 16 years of age, with heterozygous familial hypercholesterolemia after failing an adequate trial of diet therapy • Reduce the risk of undergoing revascularization procedures in patients with clinically evident CHD • Slow the progression of atherosclerosis in patients with CHD	Not studied in conditions where the major abnormality is elevation of chylomicrons, VLDL, or IDL (i.e., hyperlipoproteinemia Types I, III, IV, or V)	40 mg to 80 mg once daily or in two divided doses
Lescol XL® * (fluvastatin) tablets ER			80 mg once daily
Lipitor® * (atorvastatin) tablets	Adjunct therapy to diet to: • Reduce the risk of MI, stroke, revascularization procedures, and angina in patients without CHD, but with multiple risk factors • Reduce the risk of MI and stroke in patients with type 2 diabetes without CHD, but with multiple risk factors • Reduce the risk of non-fatal MI, fatal and non-fatal stroke, revascularization procedures, hospitalization for CHF, and angina in patients with CHD • Reduce elevated total-C, LDL-C, apo B, and TG levels and increase HDL-C in adult patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia • Reduce elevated TG in patients with hypertriglyceridemia and primary dysbeta-lipoproteinemia • Reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH) • Reduce elevated total-C, LDL-C, and apo B levels in boys and postmenarchal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia after failing an adequate trial of diet therapy	Not studied in Fredrickson Types I and V dyslipidemias.	10-80 mg once daily

Drug	Indication	Limitations of Use	Dosage
Livalo® (pitavastatin) tablets	Patients with primary hyperlipidemia or mixed dyslipidemia as an adjunctive therapy to diet to reduce elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and to increase high-density lipoprotein cholesterol (HDL-C)	-Doses of LIVALO greater than 4 mg once daily were associated with an increased risk for severe myopathy in premarketing clinical studies. Do not exceed 4 mg once daily dosing of LIVALO. The effect of LIVALO on cardiovascular morbidity and mortality has not been determined. LIVALO has not been studied in Fredrickson Type I, III, and V dyslipidemias.	1-4 mg once daily
Mevacor® * (lovastatin) tablets	Adjunctive therapy to diet for: • Primary prevention of coronary heart disease • To slow the progression of coronary atherosclerosis in patients with coronary heart disease as part of a treatment strategy to lower total-C and LDL-C to target levels. • Reduction of elevated total-C and LDL-C levels in patients with primary hypercholesterolemia (Types IIa and IIb2) • To reduce total-C, LDL-C and apolipoprotein B levels in adolescent boys and girls who are at least one year post-menarche, 10-17 years of age, with Heterozygous Familial Hyperlipidemia	Not studied in conditions where the major abnormality is elevation of chylomicrons, VLDL or IDL (i.e., hyperlipoproteinemia types I, III, IV, or V).	10 mg to 80 mg daily in single or two divided doses
Pravachol® * (pravastatin) tablets	Adjunctive therapy to diet to: • Reduce the risk of MI, revascularization, and cardiovascular mortality in hypercholesterolemic patients without clinically evident CHD. • Reduce the risk of total mortality by reducing coronary death, MI, revascularization, stroke/TIA, and the progression of coronary atherosclerosis in patients with clinically evident CHD. • Reduce elevated Total-C, LDL-C, ApoB, and TG levels and to increase HDL-C in patients with primary hypercholesterolemia and mixed dyslipidemia. • Reduce elevated serum TG levels in patients with hypertriglyceridemia. • Treat patients with primary dysbeta-lipoproteinemia who are not responding to diet. • Treat children and adolescent patients ages 8 years and older with heterozygous familial hypercholesterolemia after failing an adequate trial of diet therapy	Not studied in Fredrickson Types I and V dyslipidemias.	10 mg to 80 mg once daily

Drug	Indication	Limitations of Use	Dosage
Zocor® * (simvastatin) tablets	Adjunctive therapy to diet to: • Reduce the risk of total mortality by reducing CHD deaths and reduce the risk of non-fatal myocardial infarction, stroke, and the need for revascularization procedures in patients at high risk of coronary events. • Reduce elevated total-C, LDL-C, Apo B, TG and increase HDL-C in patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia. • Reduce elevated TG in patients with hypertriglyceridemia and reduce TG and VLDL-C in patients with primary dysbeta-lipoproteinemia. • Reduce total-C and LDL-C in adult patients with homozygous familial hypercholesterolemia. • Reduce elevated total-C, LDL-C, and Apo B in boys and postmenarchal girls, 10 to 17 years of age with heterozygous familial hypercholesterolemia after failing an adequate trial of diet therapy.	Not studied in Fredrickson Types I and V dyslipidemias.	5 mg to 80 mg once daily
Zypitamag (pitavastatin) tablets	Patients with primary hyperlipidemia or mixed dyslipidemia as an adjunctive therapy to diet to reduce elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and to increase high-density lipoprotein cholesterol (HDL-C)	Doses of Zypitamag greater than 4 mg once daily were associated with an increased risk for severe myopathy in premarketing clinical studies. Do not exceed 4 mg once daily dosing of Zypitamag. The effect of Zypitamag on cardiovascular morbidity and mortality has not been determined. Zypitamag has not been studied in Fredrickson Type I, III, and V dyslipidemias.	1-4 mg once daily

* - Generic available
a – Generic anticipated

Combination Products

Drug	Indication	Limitations of Use	Dosage
Advicor (niacin ER/ lovastatin) tablets	Indicated for treatment when both niacin ER and lovastatin is appropriate: Niacin ER • Adjunct to diet for reduction of elevated TC, LDL-C, Apo B and TG levels, and to increase HDL-C in patients with primary hypercholesterolemia (heterozygous familial and nonfamilial) and mixed dyslipidemia • In patients with a history of myocardial infarction and hypercholesterolemia, niacin is indicated to reduce the risk of recurrent nonfatal myocardial infarction • Niacin is also indicated as adjunctive therapy for treatment of adult patients with very high serum triglyceride levels who present a risk of pancreatitis Lovastatin • Adjunct to diet for the reduction of elevated TC and LDL-C levels in patients with primary hypercholesterolemia • Primary prevention of cardiovascular events • Secondary prevention of cardiovascular events		500 mg / 20 mg to 1000 mg / 20 mg once or twice daily
Liptruzet (ezetimibe/ atorvastatin) tablets	Adjunctive therapy to diet to: • Reduce elevated total-C, LDL-C, Apo B, TG, and non-HDL-C, and to increase HDL-C in patients with primary (heterozygous familial and non-familial) hyperlipidemia or mixed hyperlipidemia. • Reduce elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH), as an adjunct to other lipid lowering treatments.	• No incremental benefit of ezetimibe/atorvastatin on cardiovascular morbidity and mortality over and above that demonstrated for atorvastatin has been established. • Ezetimibe/atorvastatin has not been studied in Fredrickson Type I, III, IV, and V dyslipidemias.	10 mg / 10 mg to 10 mg / 80 mg once daily

Drug	Indication	Limitations of Use	Dosage
Simcor (niacin ER/ simvastatin) tablets	• Reduce elevated Total–C, LDL-C, Apo B, non-HDL-C, TG, or to increase HDL-C in patients with primary hypercholesterolemia and mixed dyslipidemia when treatment with simvastatin monotherapy or niacin extended-release monotherapy is considered inadequate. • Reduce TG in patients with hypertriglyceridemia when treatment with simvastatin monotherapy or niacin extended-release monotherapy is considered inadequate.	• No incremental benefit of niacin ER/simvastatin on cardiovascular morbidity and mortality over and above that demonstrated for simvastatin monotherapy and niacin monotherapy has been established. • Niacin extended-release, one of the components of niacin ER/simvastatin, at doses of 1,500 – 2,000 mg/day, in combination with simvastatin, did not reduce the incidence of cardiovascular events more than simvastatin in a randomized controlled trial of patients with cardiovascular disease and mean baseline LDL-C levels of 74 mg per deciliter	1000 mg / 20 mg to 2000 mg / 40 mg once daily
Vytorin * (ezetimibe/ simvastatin) tablets	Adjunctive therapy to diet to: • Reduce elevated total-C, LDL-C, Apo B, TG, and non-HDL-C, and to increase HDL-C in patients with primary (heterozygous familial and non-familial) hyperlipidemia or mixed hyperlipidemia. • Reduce elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH), as an adjunct to other lipid lowering treatments	• No incremental benefit of ezetimibe/simvastatin on cardiovascular morbidity and mortality over and above that demonstrated for simvastatin has been established. • Ezetimibe/simvastatin has not been studied in Fredrickson Type I, III, IV, and V dyslipidemias	10 mg / 10 mg to 10 mg / 80 mg once daily

* - Generic available
a - Generic anticipated

POLICY

Prior Authorization Criteria for Approval

Brand Statins will be approved when ANY ONE of the following is met:

1. The patient's medication history includes use of a generic statin or statin combination in the past 90 days
   OR
2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the available generic statin or statin combination products

Length of approval: 12 months

RATIONALE

Statins are recommended as first line treatment to prevent nonfatal and fatal atherosclerotic cardiovascular disease events (ASCVD) [Clinical ASCVD is defined as acute coronary syndromes, or a history of myocardial infarction (MI), or stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin].[13,15-19] Statin therapy reduces ASCVD events across the spectrum of baseline LDL-C levels ≥70 mg/dL.[13] Guidelines do not differentiate between the drugs in this class. Most people who have intolerable to a statin will still be able to take a different statin or the same statin at a lower dose.[13,14,20]

REVISIONS	
01-01-2010	Policy added to the bcbsks.com web site.
05-20-2011	Added the following target drugs: Livalo® (pitavastatin)
	Description section updated
	In Policy section: Wording clarified from question format to statement format.
	Rationale section removed
	References section updated
08-30-2012	Removed "Target Drugs" list and added "FDA Approved Indications and Dosage" chart with Target Drugs listed.
	In Policy section: ▪ Removed the following criteria: 1. The patient has a medical diagnosis that puts patient at a high risk of major coronary event (defined as myocardial infarction, coronary atherosclerosis disease (CAD), stroke, congestive heart failure, diabetes, or a surgical procedure for a coronary stent placement, percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass graft (CABG), or intracoronary thrombolysis infusion) OR 3. The patient requires LDL lowering that cannot be achieved with available generic statins* *defined as greater than 40% LDL lowering, achievable with simvastatin 40 mg once daily or lovastatin 40 mg twice daily ▪ Revised Length of approval from "Indefinite" to "12 months".
	Added Rationale section

REVISIONS	
	References updated
01-01-2013	Policy Title updated from "Statin Step Therapy Prior Authorization Criteria" to "Statin Prior Authorization"
	In Description section: ▪ Updated description ▪ Added Target Drug Brand Statins list
	In Policy section: ▪ Added the word statin to item #1 to read "The patient's medication history includes use of a generic statin" - This update causes no change to the policy statement meaning.
07-01-2013	Policy posted July 12, 2013.
	Added under Prior Authorization Form link "Prime Therapeutics will review Prior Authorization requests."
	Administrative Update In Description section: ▪ Added Liptruzet (ezetimibe/atorvastatin tabs)
01-01-2014	In Header: ▪ Revised Title from "Statin Prior Authorization" to "Statin Therapy"
	Description section updated
	In Policy section: ▪ In Items 1 and 2 added "or statin combination" ▪ In item 1 added look-back information
	Rationale section updated
	Coding section added
	References updated
10-28-2014	Description section updated
	Rationale section updated
	Coding section removed as codes are not used for pharmacy benefit.
	References updated
10-01-2015	Published 09-16-2015. Effective 10-01-2015.
	Updated Description section to include: ▪ Reformatting of FDA Approved Indications and Dosage chart ▪ Added indication of "Excluded Drug in some member contracts"
	Rationale section updated
	References updated
09-01-2016	In Description section Updated keys in Target Drugs list and FDA Approved Indications and Dosage chart
	In Policy section: ▪ In Item 1 removed "(evidence of a paid claim within the past 90 days, or patient is new to the claim system within the past 120 days AND a statement by the physician that patient has taken a generic statin agent in the past 90 days)" and added "in the past 90 days" to read "The patient's medication history includes use of a generic statin or statin combination in the past 90 days"
	Rationale section updated
	References updated
05-15-2017	Policy published 06-09-2017. Policy retro-effective to 05-15-2017.
	In Description section: ▪ Noted generic availability of Vytorin.
10-15-2017	In Description section: ▪ In FDA Approved Indications an Dosage chart updated Crestor indications to separate pediatric and adult indications.
	Rationale section updated

REVISIONS	
	References updated
04-16-2018	Policy published 05-232018. Policy retro-effective to 04-16-2018.
	In Description section ▪ Added Zypitamag (pitavastatin) as a new single ingredient agent. ▪ Updated FDA Approved Indications and Dosage chart for single Ingredient Products adding Zypitamag.
	References updated
10-01-2018	In Description section: Summary of revisions: • Advicor, Liptruzet, and Simcor are discontinued • fluvastatin is only available generically ▪ Added the key "b" for discontinued agents

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22. Zypitamag Prescribing Information. Zydus. July 2017.