Statin Step Therapy and Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

FDA APPROVED INDICATIONS AND DOSAGE[1-12, 15, 16]
Single Ingredient Products

Agent(s)	Indication(s)
Altoprev® (lovastatin ER) Tablet	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. • Limitations of use: has not been studied in Fredrickson Types I, III, and V dyslipidemias.

Atorvaliq® (atorvastatin)
 	
Suspension
	• To reduce the risk of:
	  ○ Myocardial infarction (MI), stroke, revascularization procedures, and angina in adults with multiple risk factors for coronary heart disease (CHD) but without clinically evident CHD.
	  ○ MI and stroke in adults with type 2 diabetes mellitus with multiple risk factors for CHD but without clinically evident CHD.
	  ○ Non-fatal MI, fatal and non-fatal stroke, revascularization procedures, hospitalization for congestive heart failure, and angina in adults with clinically evident CHD.
	• As an adjunct to diet to reduce low-density lipoprotein (LDL-C) in:
	  ○ Adults with primary hyperlipidemia.
	  ○ Adults and pediatric patients aged 10 years and older with heterozygous familial hypercholesterolemia (HeFH).
	• As an adjunct to other LDL-C-lowering therapies to reduce LDL-C in adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia.
	• As an adjunct to diet for the treatment of adults with:
	  ○ Primary dysbetaliproteinemia
	  ○ Hypertriglyceridemia

Crestor®[a] (rosuvastatin) Tablet	Adjunctive therapy to diet for: • Adult patients with primary hyperlipidemia and mixed dyslipidemia to reduce elevated total-C, LDL-C, ApoB, nonHDL-C, and TG levels and to increase HDL-C

Agent(s)	Indication(s)
	• Pediatric 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, either alone or with other lipid-lowering treatments • Adult patients with hypertriglyceridemia • Adult patients with primary dysbeta-lipoproteinemia (Type III hyperlipoproteinemia) • Slowing the progression of atherosclerosis as part of a treatment strategy to lower total-C and LDL-C • Adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C, total-C, and ApoB • Risk reduction of MI, stroke, and arterial revascularization procedures in patients without clinically evident CHD, but with multiple risk factors • Limitations of use: Not studied in Fredrickson Type I and V dyslipidemias
Ezallor™ Sprinkle (rosuvastatin) Capsule	• Adult patients with hypertriglyceridemia as an adjunct to diet • Adult patients with primary dysbetalipoproteinemia (Type III hypercholesterolemia) as an adjunct to diet • Adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C, total-C, and ApoB • Limitations of use: Not studied in Fredrickson Type I and V dyslipidemias
Flolipid™, Simvastatin oral suspension Oral suspension	Adjunctive therapy to diet to: • Reduce the risk of total mortality by reducing CHD deaths and reduce the risk of non-fatal MI, 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 dysbetalipoproteinemia. • 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. • Limitations of use: Simvastatin has not been studied in Fredrickson Types I and V dyslipidemias.
Lescol XL®[a] (fluvastatin) Extended release tablet	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 postmenarchal 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

Agent(s)	Indication(s)
	• Slow the progression of atherosclerosis in patients with clinically evident CHD • Limitations of use: Not studied in conditions where the major abnormality is elevation of chylomicrons, VLDL, or IDL (i.e., hyperlipoproteinemia Types I, III, IV, or V)
Lipitor®[a] (atorvastatin) Tablet	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 dysbetalipoproteinemia • 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 • Limitations of use: has not been studied in Fredrickson Types I and V dyslipidemias.
Livalo®[a] (pitavastatin) Tablet	Adjunctive therapy to diet in: • Adult 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) • Pediatric patients aged 8 years and older with heterozygous familial hypercholesterolemia (HeFH) to reduce elevated TC, LDL-C, and ApoB. Limitations of use: The effect of Livalo on cardiovascular morbidity and mortality has not been determined.
Pravachol®[a] (pravastatin) Tablet	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 dysbetalipoproteinemia who are not responding to diet.

Agent(s)	Indication(s)
	• Treat children and adolescent patients ages 8 years and older with heterozygous familial hypercholesterolemia after failing an adequate trial of diet therapy • Limitations of use: Has not been studied in Fredrickson Types I and V dyslipidemias.
Zocor®[a] (simvastatin) Tablet	Adjunctive therapy to diet to: • Reduce the risk of total mortality by reducing CHD deaths and reduce the risk of non-fatal MI, 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 dysbetalipoproteinemia. • 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. • Limitations of use: Has not been studied in Fredrickson Types I and V dyslipidemias.
Zypitamag™ (pitavastatin) tablet	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) Limitations of use: The effect of Zypitamag on cardiovascular morbidity and mortality has not been determined.

a - Generic equivalent available

Combination Products

Drug	Indication
Ezetimibe/Atorvastatin	Adjunctive therapy to diet to: • Reduce elevated TC, 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 Limitations of use: • No incremental benefit of ezetimibe/atorvastatin on cardiovascular morbidity and mortality over and above that demonstrated for atorvastatin has been established.

Drug	Indication
	Ezetimibe/atorvastatin has not been studied in Fredrickson Type I, III, IV, and V dyslipidemias
Roszet™, Ezetimibe/rosuvastatin Tablet	Adjunctive therapy to diet in patients with primary non-familial hyperlipidemia to reduce low-density lipoprotein cholesterol (LDL-C) Alone or as an adjunct to other LDL-C lowering therapies in patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C
Vytorin®[a] (ezetimibe/simvastatin) Tablet	Adjunctive therapy to diet to: • Reduce elevated TC, 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 Limitations of use: • 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

a – Generic equivalent available

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Among lipid-lowering drugs, statins are the cornerstone of LDL-C lowering therapy, in addition to healthy lifestyle interventions. Statins are recommended as first-line treatment to prevent 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]. Both high intensity and medium intensity statin therapy reduce primary and secondary ASCVD events.[13]

Safety

All statin and statin combinations are contraindicated in active liver disease, pregnancy, and lactation. Livalo and Zypitamag are also contraindicated with the concomitant use of cyclosporine. Altoprev, Flolipid, Vytorin, and Zocor are contraindicated with concomitant administration of strong CTP3A4 inhibitors. Flolipid, Vytorin, and Zocor are also contraindicated with the concomitant use of gemfibrozil, cyclosporine, or danazol, while Altoprev is contraindicated with the concomitant use of erythromycin.[1-11]

For additional clinical information see Prime Therapeutics Formulary Chapters 5.9C: HMG-CoA Reductase Inhibitors and 5.9D HMG-CoA Reductase Inhibitor Combinations, and Prime Therapeutics Formulary Monograph: Livalo (pitavastatin).

REFERENCES

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4. Flolipid prescribing information. Rosemont Pharmaceuticals. June 2020.
5. Lescol XL Prescribing Information. Novartis. September 2020.
6. Lipitor Prescribing Information. Pfizer. December 2020.
7. Livalo prescribing information. Kowa Pharmaceuticals America, Inc./Lilly USA LLC. May 2019.
8. Pravastatin Prescribing Information. Accord Healthcare Inc. November 2020.
9. Zocor Prescribing Information. Merck & Co. December 2020.
10. Vytorin prescribing information. Merck & Co, Inc.. September 2020.
11. Zypitamag Prescribing Information. Medicure. September 2020.
12. Roszet Prescribing Information. Althera Pharmaceuticals LLC. March 2021.
13. Fluvastatin prescribing information. Teva Pharmaceuticals USA, Inc. August 2020
14. ACC/AHA Task Force on Clinical Practice Guidelines. "2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/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. https://www.ahajournals.org/doi/epub/10.1161/CIR.0000000000000625
15. Ezetimibe and atorvastatin tablet Prescribing Information. Althera Phamaceuticals, LLC. September 2022.
16. Atorvaliq prescribing information. CMP Pharma, Inc. February 2023

Statin Step Therapy

TARGET AGENT(S)	PREREQUISITE AGENT(S)
Altoprev® (lovastatin extended release) **Atorvaliq®** (atorvastatin suspension) **Crestor®** (rosuvastatin)[a] **Ezetimibe/atorvastatin** **Ezetimibe/rosuvastatin** **Ezallor™ Sprinkle** (rosuvastatin) **Flolipid™** (simvastatin oral suspension) **Lescol XL®** (fluvastatin extended release)[a] **Lipitor®** (atorvastatin)[a] **Livalo®** (pitavastatin)[a] **Pravachol®** (pravastatin)[a] **Roszet™** (ezetimibe/rosuvastatin) **Simvastatin oral suspension 20 mg/5ml** **Vytorin®** (ezetimibe/simvastatin)[a] **Zocor®** (simvastatin)[a] **Zypitamag** (pitavastatin)	Any generic statin or stain combination

a - available as a generic

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Target Agent will be approved when ONE of the following is met:

1. The patient's medication history includes use of ONE prerequisite agent
   OR
2. The patient has an intolerance or hypersensitivity to a prerequisite agent
   OR
3. The patient has an FDA labeled contraindication to ALL prerequisite agents
   OR
4. BOTH of the following:
   A. The prescriber has stated that the patient has tried ONE prerequisite agent
      AND
   B. The prerequisite agent was discontinued due to lack of effectiveness or an adverse event

   OR
5. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   A. A statement by the prescriber that the patient is currently taking the requested agent
      AND
   B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
      AND
   C. The prescriber states that a change in therapy is expected to be ineffective or cause harm

   OR
6. The prescriber has provided documentation that ALL prerequisite agents cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: 12 months

NOTE: If Quantity Limit applies, please refer to Quantity Limit criteria.