STEP THERAPY CRITERIA

BRAND NAME*
(generic)

EZALLOR
(rosuvastatin capsules)

LIVALO
(pitavastatin calcium)

NIKITA
(pitavastatin sodium)

(rosuvastatin 5 mg and 10 mg only) (generic only)

ZYPITAMAG
(pitavastatin magnesium)

Status: CVS Caremark Criteria
Type: Initial Step Therapy; Post Step Therapy Prior Authorization ***Ref # 2530-F***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Ezallor
Hypertriglyceridemia
Ezallor is indicated as adjunctive therapy to diet for the treatment of adult patients with hypertriglyceridemia.

Primary Dysbetalipoproteinemia (Type III Hyperlipoproteinemia)
Ezallor is indicated as an adjunct to diet for the treatment of adult patients with primary dysbetalipoproteinemia (Type III Hyperlipoproteinemia).

Adult Patients with Homozygous Familial Hypercholesterolemia
Ezallor is indicated as adjunctive therapy to other lipid-lowering treatments (e.g., LDL apheresis) or alone if such treatments are unavailable to reduce LDL-C, Total-C, and ApoB in adult patients with homozygous familial hypercholesterolemia.

Limitations of Use
Ezallor has not been studied in Fredrickson Type I and V dyslipidemias.

Livalo
Drug therapy should be one component of multiple-risk-factor intervention in individuals who require modifications of their lipid profile. Lipid-altering agents should be used in addition to a diet restricted in saturated fat and cholesterol only when the response to diet and other nonpharmacological measures has been inadequate.

Primary Hyperlipidemia and Mixed Dyslipidemia
Livalo (pitavastatin) is indicated as 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 HDL-C in adult patients with primary hyperlipidemia and dyslipidemia.

Limitations of Use
Doses of Livalo (pitavastatin) 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 (pitavastatin).

The effect of Livalo (pitavastatin) on cardiovascular morbidity and mortality has not been determined.

Livalo (pitavastatin) has not been studied in Fredrickson Type I, III, and V dyslipidemias.

Nikita
Drug therapy should be one component of multiple-risk-factor intervention in individuals who require modifications of their lipid profile. Lipid-altering agents should be used in addition to a diet restricted in saturated fat and cholesterol only when the response to diet and other nonpharmacological measures has been inadequate.

Primary Hyperlipidemia and Mixed Dyslipidemia
Nikita (pitavastatin) is indicated 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 HDL-C in adult patients with primary hyperlipidemia or mixed dyslipidemia.

Limitations of Use
Doses of Nikita (pitavastatin) 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 Nikita (pitavastatin).

The effect of Nikita (pitavastatin) on cardiovascular morbidity and mortality has not been determined.

Nikita (pitavastatin) has not been studied in Fredrickson Type I, III, and V dyslipidemias.

Rosuvastatin
Hyperlipidemia and Mixed Dyslipidemia
Rosuvastatin is indicated as adjunctive therapy to diet to reduce elevated Total-C, LDL-C, ApoB, nonHDL-C, and triglycerides and to increase HDL-C in adult patients with primary hyperlipidemia or mixed dyslipidemia. Lipid-altering agents should be used in addition to a diet restricted in saturated fat and cholesterol when response to diet and nonpharmacological interventions alone has been inadequate.

Pediatric Patients with Familial Hypercholesterolemia
Rosuvastatin is indicated as adjunct to diet to:

- Reduce Total-C, LDL-C and ApoB levels in children and adolescents 8 to 17 years of age with heterozygous familial hypercholesterolemia if after an adequate trial of diet therapy the following findings are present: LDC-C > 190 mg/dL, or > 160 mg/dL along with a positive family history of premature cardiovascular disease (CVD) or two or more other CVD risk factors.
- Reduce LDL-C, Total-C, nonHDL-C and ApoB in children and adolescents 7 to 17 years of age with homozygous familial hypercholesterolemia, either alone or with other lipid-lowering treatments (e.g., LDL apheresis).

Hypertriglyceridemia
Rosuvastatin is indicated as adjunctive therapy to diet for the treatment of adult patients with hypertriglyceridemia.

Primary Dysbetalipoproteinemia (Type III Hyperlipoproteinemia)
Rosuvastatin is indicated as an adjunct to diet for the treatment of adult patients with primary dysbetalipoproteinemia (Type III Hyperlipoproteinemia).

Adult Patients with Homozygous Familial Hypercholesterolemia
Rosuvastatin is indicated as adjunctive therapy to other lipid-lowering treatments (e.g., LDL apheresis) or alone if such treatments are unavailable to reduce LDL-C, Total-C, and ApoB in adult patients with homozygous familial hypercholesterolemia.

Slowing of the Progression of Atherosclerosis

Rosuvastatin is indicated as adjunctive therapy to diet to slow the progression of atherosclerosis in adult patients as part of a treatment strategy to lower Total-C and LDL-C to target levels.

Primary Prevention of Cardiovascular Disease
In individuals without clinically evident coronary heart disease but with an increased risk of cardiovascular disease based on age ≥ 50 years old in men and ≥ 60 years old in women, hsCRP ≥ 2 mg/L, and the presence of at least one additional cardiovascular disease risk factor such as hypertension, low HDL-C, smoking, or a family history of premature coronary heart disease, rosuvastatin is indicated to:

- Reduce the risk of stroke
- Reduce the risk of myocardial infarction
- Reduce the risk of arterial revascularization procedures

Limitations of Use
Rosuvastatin has not been studied in Fredrickson Type I and V dyslipidemias.

Zypitamag
Drug therapy should be one component of multiple-risk-factor intervention in individuals who require modifications of their lipid profile. Lipid-altering agents should be used in addition to a diet restricted in saturated fat and cholesterol only when the response to diet and other nonpharmacological measures has been inadequate.

Primary Hyperlipidemia and Mixed Dyslipidemia
Zypitamag (pitavastatin) is indicated 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 HDL-C in adult patients with primary hyperlipidemia or mixed dyslipidemia.

Limitations of Use
Doses of Zypitamag (pitavastatin) 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 (pitavastatin).

The effect of Zypitamag (pitavastatin) on cardiovascular morbidity and mortality has not been determined.

Zypitamag (pitavastatin) has not been studied in Fredrickson Type I, III, and V dyslipidemias.

INITIAL STEP THERAPY for Ezallor, Rosuvastatin 5 mg and 10 mg (generic only)
If the patient is less than 10 years of age OR has filled a prescription for at least a 30-day supply of atorvastatin or simvastatin within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

INITIAL STEP THERAPY for Livalo, Nikita, Zypitamag
If the patient has filled a prescription for at least a 30-day supply of atorvastatin or simvastatin within the past 180 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has experienced an inadequate treatment response, intolerance, or contraindication to atorvastatin OR simvastatin
  OR
- The request is for a rosuvastatin product **AND**
- The requested drug is being prescribed for the treatment of homozygous familial hypercholesterolemia in a patient less than 18 years of age

RATIONALE

This criteria was developed to align with the Marketplace Exchange formulary.

For Ezallor (rosuvastatin) and generic rosuvastatin 5 mg and 10 mg, if the patient has filled a prescription for at least a 30-day supply of atorvastatin or simvastatin within the past 180 days under a prescription benefit administered by CVS Caremark, then Ezallor (rosuvastatin) or generic rosuvastatin 5 mg or 10 mg will be paid under that prescription benefit. Additionally, since rosuvastatin is indicated in children as young as 7 years of age whereas atorvastatin and simvastatin are only indicated in children as young as 10 years of age, patients less than 10 years of age will not be required to have a trial of simvastatin or atorvastatin.[1-10]

For Livalo, Nikita, and Zypitamag, if the patient has filled a prescription for at least a 30-day supply of atorvastatin or simvastatin within the past 180 days under a prescription benefit administered by CVS Caremark, then Livalo, Nikita, or Zypitamag will be paid under that prescription benefit.

If the patient does not meet the initial step therapy criteria, then prior authorization is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Rosuvastatin is indicated for the treatment of hyperlipidemia and mixed dyslipidemia, hypertriglyceridemia, primary dysbetalipoproteinemia (Type III hyperlipoproteinemia), adult patients with homozygous familial hypercholesterolemia, slowing of the progression of atherosclerosis, primary prevention of cardiovascular disease, and pediatric patients with familial hypercholesterolemia. Ezallor (rosuvastatin) is indicated for hypertriglyceridemia, primary dysbetalipoproteinemia (Type III hyperlipoproteinemia), and adult patients with homozygous familial hypercholesterolemia. Specifically, rosuvastatin is indicated for the treatment of homozygous familial hypercholesterolemia in children and adolescents 7 to 17 years of age and for the treatment of heterozygous familial hypercholesterolemia in children and adolescents 8 to 17 years of age.[2, 6, 9, 10] Livalo, Nikita, and Zypitamag are indicated for primary hyperlipidemia and mixed dyslipidemia.[4, 5, 8-10]

Rosuvastatin is the only statin indicated for the treatment of pediatric patients with homozygous familial hypercholesterolemia.[1-10] For this reason, patients less than 18 years of age will not be required to have a trial of any other statins for homozygous familial hypercholesterolemia. For those patients with heterozygous familial hypercholesterolemia there are more treatment options available, but most are not indicated in children under 10 years of age. Therefore, prior authorization criteria will not apply to patients less than 10 years of age who are requesting a rosuvastatin product.

For the primary prevention of atherosclerotic cardiovascular disease (ASCVD), the 2018 American College of Cardiology/American Heart Association (ACC)/(AHA) Guideline on the Management of Blood Cholesterol states that drug therapy is needed only in selected patients with moderately high low-density lipoprotein cholesterol (LDL-C) levels (≥160 mg/dL [≥4.1 mmol/L]) or patients with very high LDL-C levels (190 mg/dL [4.9 mmol/L]). Selection of patients for statin therapy is a multistep process. The first step to determine individual risk of clinical ASCVD is to categorize patients into 4 categories of risk, from high to low. The categories with highest overall risk (secondary prevention and primary LDL-C levels ≥190 mg/dL [≥4.9 mmol/L]) require prompt treatment to lower ASCVD risk. Adults 40 to 75 years of age with diabetes mellitus merit initiation of a moderate-intensity statin without using risk calculation; however, it is reasonable to use a risk calculation to further stratify risk. The fourth category includes adults 40 to 75 years of age whose 10-year ASCVD risk is estimated by the risk calculation. Factors to consider are risk calculation scoring, presence or absence of other risk-enhancing factors, potential benefit of intensified lifestyle therapy, likelihood of statin-associated side effects or drug–drug interactions, and patient choice.[11]

Among lipid-lowering drugs, statins are the cornerstone of therapy, in addition to healthy lifestyle interventions. The intensity of statin therapy is divided into 3 categories: high-intensity, moderate-intensity, and low-intensity. High-intensity statin therapy typically lowers LDL-C levels by ≥50%, moderate-intensity statin therapy by 30% to 49%, and low-intensity statin therapy by <30%. The magnitude of LDL-C lowering will vary in clinical practice.[11] The guidelines do not recommend one drug over the other, but instead point to the intensity groups to initiate therapy.

High-, Moderate-, and Low-Intensity Statin Therapy[11]

High Intensity Statins	Moderate Intensity Statins	Low Intensity Statins
Atorvastatin 40 mg, 80 mg	Atorvastatin 10 mg, 20 mg	
Rosuvastatin 20 mg, 40 mg	Rosuvastatin 5 mg, 10 mg	
	Simvastatin 20 mg, 40 mg	Simvastatin 10 mg
	Pravastatin 40 mg, 80 mg	Pravastatin 10-20 mg
	Lovastatin 40 mg, 80 mg	Lovastatin 20-40 mg
	Fluvastatin XL 80 mg	
	Fluvastatin 40 mg BID	
	Pitavastatin 1-4 mg	

REFERENCES

1. Atorvastatin [package insert]. Iselin, NJ: Biocon Pharma Inc.; October 2018.
2. Crestor [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2018.
3. Ezallor [package insert]. Cranbury, NJ: Sun Pharmaceuticals Industries, Inc.; December 2018.
4. Livalo [package insert]. Montgomery, AL; Kowa Pharmaceuticals America, Inc.; November 2016.
5. Nikita [package insert]. Baltimore, MD; Lupin Pharmaceuticals, Inc.; August 2017.
6. Rosuvastatin [package insert]. Weston, FL: Apotex Corp; September 2018.
7. Simvastatin [package insert]. East Windsor, NJ: Aurobindo Pharma USA, Inc.; October 2018.
8. Zypitamag [package insert]. Princeton, NJ; Medicure; August 2018.
9. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed December 2018.
10. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed December 2018.
11. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol. *Circulation* 2018;000:e000-e000.

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CRITERIA FOR APPROVAL

1	Has the patient experienced an inadequate treatment response, intolerance, or contraindication to atorvastatin OR simvastatin? [If yes, then no further questions.]	Yes	No
2	Is this request for a rosuvastatin product?	Yes	No
3	Is the requested drug being prescribed for the treatment of homozygous familial hypercholesterolemia in a patient less than 18 years of age?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 36 months	Go to 2	
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried atorvastatin or simvastatin and it either did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance, or contraindication to atorvastatin or simvastatin.]
3.	Approve, 36 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: -You have tried atorvastatin or simvastatin and it either did not work for you or you cannot use it -You are using a rosuvastatin product for homozygous familial hypercholesterolemia and are less than 18 years of age Your request has been denied based on the information we have. [Short Description: No approvable diagnosis; no inadequate response, intolerance or contraindication to atorvastatin or simvastatin.]