STEP THERAPY POLICY

POLICY: Hydroxy-Methylglutaryl-Coenzyme A Reductase Inhibitors Step Therapy Policy

- Altoprev® (lovastatin extended-release tablets – Covis)
- Atorvaliq® (atorvastatin oral suspension – CMP)
- Atorvastatin and ezetimibe tablets (generic only)
- Caduet® (atorvastatin/amlodipine tablets – Pfizer, generic)
- Crestor® (rosuvastatin tablets – AstraZeneca, generic)
- Ezallor Sprinkle™ (rosuvastatin capsules – Sun)
- Flolipid® (simvastatin oral suspension – Salerno/Rosemont)
- Lescol® (fluvastatin capsules – Novartis, generic)
- Lescol® XL (fluvastatin extended-release tablets – Novartis, generic)
- Lipitor® (atorvastatin tablets – Pfizer, generic)
- Livalo® (pitavastatin tablets – Lily/Kowa, generic)
- Mevacor® (lovastatin tablets – generic only)
- Pravachol® (pravastatin tablets – Bristol-Myers Squibb, generic)
- Roszet® (rosuvastatin and ezetimibe tablets – Althera)
- Rosuvastatin and ezetimibe tablets – SCOV3 LLC
- Vytorin® (ezetimibe/simvastatin tablets – Organon, generic)
- Zocor® (simvastatin tablets – Organon, generic)
- Zypitamag® (pitavastatin magnesium tablets – Medicure)

REVIEW DATE: 06/14/2023; selected revision 11/08/2023

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Available hydroxy-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (HMGs), excluding combination products, include lovastatin, simvastatin,

atorvastatin, pravastatin, fluvastatin, fluvastatin extended-release, pitavastatin, rosuvastatin, Altoprev, Ezallor Sprinkle, and Zypitamag.[1-16] All of the HMGs are indicated as an **adjunct to diet for patients with primary hypercholesterolemia and/or mixed dyslipidemia** (to impact lipid parameters such as to reduce elevated total cholesterol [total-C] and low-density lipoproprotein cholesterol [LDL-C]). Several agents have additional indications, including those related to improvement in cardiovascular (CV) outcomes. Simvastatin is available as a combination with ezetimibe, a selective intestinal inhibitor of cholesterol and related phytosterol absorption, as Vytorin, which is available generically.[12] Rosuvastatin is combined with ezetimibe in products as well.[14,15] Atorvastatin is available as a combination with amlodipine, a dihydropyridine calcium channel blocker, as Caduet, which is also available generically.[13] Flolipid (simvastatin oral suspension) is available and it has the same indications as simvastatin tablets.[16] Atorvaliq is an oral suspension that has the same indications as atorvastatin tablets.[17] Ezallor Sprinkle has administration options for patients who cannot swallow an intact capsule whole.[4] The contents can be opened and sprinkled over soft food (e.g., applesauce, pudding). Also, Ezallor Sprinkle capsules can be opened and administered by a nasogastric tube.

Guidelines

In November 2013, the American College of Cardiology and the American Heart Association published guidelines on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease (ASCVD) risk in adults[18] with an update published in 2019.[19] The guideline emphasizes the appropriate intensity of statin therapy to reduce cardiovascular risk. No statin is preferred, but instead, statins with related doses are categorized as "high-intensity" (lowers low-density lipoprotein cholesterol [LDL-C] by approximately ≥ 50%), moderate-intensity (lowers LDL-C by approximately 30% to < 50%), and low-intensity (lowers LDL-C by < 30%). Only atorvastatin and rosuvastatin are categorized as acceptable "high-intensity" statin therapies. According to the guidelines, clinical trial evidence clearly shows that ASCVD events are reduced by using the maximum-tolerated statin intensity in groups shown to benefit (e.g., those at risk). There is relatively less evidence for non-statin medications in reducing ASCVD risk. Table 1 categorizes the different statin regimens as high-, moderate-, and low-intensity. Refer to the guideline for the most appropriate intensity for the individual patient.

Table 1. High-, Moderate-, and Low-Intensity Statin Therapy.[18,19]*

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL-C on average by approximately ≥ 50%.	Daily dose lowers LDL-C on average by approximately 30% to 50%.	Daily dose lowers LDL-C on average by < 30%.
Atorvastatin (40 mg†) to 80 mg Rosuvastatin 20 mg (40 mg)	Atorvastatin 10 mg (20 mg) Rosuvastatin (5 mg) 10 mg Simvastatin 20 mg to 40 mg‡ Pravastatin 40 mg (80 mg) Lovastatin 40 mg Fluvastatin extended-release 80 mg Fluvastatin 40 mg BID Livalo 2 mg to 4 mg	Simvastatin 10 mg Pravastatin 10 mg to 20 mg Lovastatin 20 mg Fluvastatin 20 mg to 40 mg Livalo 1 mg

* Used in the randomized controlled trials reviewed by the expert panel. Of note, individual responses to statin therapy varied in the randomized controlled trials and should be expected to vary in clinical practice. There might be a biologic basis for a less-than-average response; LDL-C – Low-density lipoprotein cholesterol; † Evidence from one randomized controlled trial only and down titration is recommended if the patient is unable to tolerate atorvastatin 80 mg; ‡ Although simvastatin 80 mg was assessed in randomized controlled trials, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis; BID – Twice daily.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Note: When compliance with the Affordable Care Act, Health Resources and Services Administration Guidelines, and Public Health Services Act section 2713 is required and the conditions for coverage listed under the Criteria are not met, approval is granted when the requested single-entity drug is used for the primary prevention of cardiovascular disease (CVD) in an adult aged 40 to 75 years who has one or more CVD risk factors (i.e., dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year CVD event risk of 10% or greater and who does NOT have a history of (or signs or symptoms of) CVD and, according to the prescriber, the alternative Step 1 Products would not be as medically appropriate for the patient as the requested single-entity drug.

Hydroxy-Methylglutaryl-Coenzyme A Reductase Inhibitors product(s) is(are) covered as medically necessary when the following step therapy criteria is(are) met. Any other exception is considered not medically necessary.

Step 1: atorvastatin, atorvastatin/amlodipine, ezetimibe/simvastatin, fluvastatin, fluvastatin extended-release, lovastatin, pravastatin, pitavastatin, rosuvastatin, simvastatin

Step 2: Altoprev, Atorvaliq, Caduet, Crestor, Ezallor Sprinkle, Flolipid, Lescol, Lescol XL, Lipitor, Livalo, Pravachol, ezetimibe and rosuvastatin (brand product), ezetimibe and atorvastatin (generic product), Roszet, Vytorin, Zocor, Zypitamag

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. If the patient cannot swallow or has difficulty swallowing tablets or capsules, approve Atorvaliq, Flolipid, or Ezallor Sprinkle.

REFERENCES

1. Lovastatin tablets [prescribing information]. Baltimore, MD/Goa, India: Lupin/BluePoint; September 2021.
2. Crestor® tablets [prescribing information]. Wilmington, DE: AstraZeneca; January 2023.
3. Zypitamag® tablets [prescribing information]. Princeton, NJ: Medicure; September 2020.
4. Ezallor Sprinkle™ capsules [prescribing information]. Cranbury, NJ: Sun; September 2020.
5. Zocor® tablets [prescribing information]. Jersey City, NJ: Organon; March 2023.
6. Lipitor® tablets [prescribing information]. New York, NY: Pfizer, December 2022.
7. Lescol® capsules and Lescol® XL extended-release tablets [prescribing information]. East Hanover, NJ: Novartis; August 2017.
8. Lescol® XL extended-release tablets [prescribing information]. East Hanover, NJ: Novartis; September 2020.
9. Altoprev® extended-release tablets [prescribing information]. Zug, Switzerland: Covis; September 2020.
10. Pravachol® tablets [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; May 2022.
11. Livalo® tablets [prescribing information]. Montgomery, AL: Kowa; November 2022.
12. Vytorin® tablets [prescribing information]. Jersey City, NJ: Organon; June 2021.
13. Caduet® tablets [prescribing information]. New York, NY: Pfizer; January 2021.
14. Roszet® tablets [prescribing information]. Morristown, NJ: Althera; March 2021.
15. Rosuvastatin and ezetimibe tablets [prescribing information]. Wilmington, DE: SCOV3 LLC; August 2021.
16. Flolipid® oral suspension [prescribing information]. Brooksville, FL: Salerno/Rosemont; September 2020.
17. Atorvaliq® oral suspension [prescribing information]. Farmville, NC: CMP; February 2023.
18. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA guidance on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice guidelines. *Circulation*. 2014;129(25 Suppl 2):S1-45.
19. Grundy SM, Stone NJ, Bailey AL, et al. ACC/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Ezallor Sprinkle:** Exceptions were added for Ezallor Sprinkle – if the patient cannot swallow or has difficulty swallowing tablets or capsules. It was also clarified that the name of Ezallor contains the descriptor of "Sprinkle."	06/29/2022
Selected Revision	**Atorvastatin and ezetimibe (generic product):** Added as a Step 2 Product.	02/01/2023
Selected Revision	**Atorvaliq:** Added as a Step 2 Product. Exceptions are made if the patient cannot swallow or has difficulty swallowing tablets or capsules.	03/22/2023
Annual Revision	**Policy Statement:** The following note was added to the Policy Statement. Note: When compliance with the Affordable Care Act, Health Resources and Services Administration Guidelines, and Public Health Service Act section 2713 is required and the conditions for coverage listed under the Criteria are not met, approval is granted when the requested drug is used for the primary prevention of cardiovascular disease (CVD) in an adult aged 40 to 75 years who has one or more CVD risk factors (i.e., dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year CVD event risk of 10% or greater and who does NOT have a history of (or signs or symptoms of) CVD and, according to the prescriber, the alternative	06/14/2023

	Step 1 Products would not be as medically appropriate for the patient as the requested drug.	
Selected Revision	**Pitavastatin (generic):** Added as a Step 1 Product. There were no other changes to the criteria.	11/08/2023