

STEP THERAPY POLICY

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

- Altoprev[®] (lovastatin extended-release tablets – Covis)
- 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 – Lilly/Kowa)
- Mevacor[®] (lovastatin tablets – generic)
- Pravachol[®] (pravastatin tablets – Bristol-Myers Squibb, generic)
- Roszet[®] (rosuvastatin and ezetimibe tablets – Althera Pharmaceuticals)
- Rosuvastatin and ezetimibe tablets – SCOV3 LLC
- Vytorin[®] (ezetimibe/simvastatin tablets – Organon, generic)
- Zocor[®] (simvastatin tablets – Organon, generic)
- Zypitomag[®] (pitavastatin magnesium tablets – Medisure)

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OVERVIEW

Available hydroxy-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (HMGs), excluding combination products, include lovastatin, simvastatin, atorvastatin, pravastatin, fluvastatin, fluvastatin extended-release, rosuvastatin, Altoprev, Ezallor Sprinkle, Livalo and Zypitomag.¹⁻¹⁶ 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 the only HMG oral suspension available and it has the same indications as simvastatin tablets.¹⁶ 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 adults¹⁷ with an update published in 2019.¹⁸ 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.^{17*}

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL-C on average by approximately $\geq 50\%$.	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.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

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

Step 2: Altoprev, 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 Flolipid or Ezallor Sprinkle.
3. No other exceptions are recommended.

REFERENCES

1. Lovastatin tablets [prescribing information]. Goa, India: Lupin/BluePoint; September 2021.
2. Crestor[®] tablets [prescribing information]. Wilmington, DE: AstraZeneca; July 2021.
3. Zypitamag[®] tablets [prescribing information]. Princeton, NJ: Medisure; September 2020.
4. Ezallor Sprinkle[™] capsules [prescribing information]. Cranbury, NJ: Sun; September 2020.
5. Zocor[®] tablets [prescribing information]. Jersey City, NJ: Organon; May 2022.

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6. Lipitor[®] tablets [prescribing information]. New York, NY: Pfizer, November 2020.
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; August 2020.
11. Livalo[®] tablets [prescribing information]. Montgomery, AL: Kowa; September 2020.
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. 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.
18. 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. Available at: <https://www.ahajournals.org/doi/pdf/10.1161/CIR.0000000000000625>. Accessed on June 24, 2022.