Cigna National Preferred Formulary Coverage Policy

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Coverage Policy Number NPF058

Step Therapy
Hydroxy-methylglutaryl-coenzyme A Reductase Inhibitors (HMG)

Table of Contents

Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

NPF Coverage Policy

Drugs Affected

- Lipitor® (atorvastatin tablets - generic)
- Lescol® (fluvastatin capsules - generic)
- Lescol® XL (fluvastatin extended-release tablets - generic)
- Mevacor® (lovastatin tablets - generic)
- Altoprev® (lovastatin extended-release tablets)
- Pravachol® (pravastatin tablets - generic)
- Crestor® (rosuvastatin tablets - generic)
- Zocor® (simvastatin tablets - generic)
- Caduet® (atorvastatin/amlodipine tablets - generic)
- Vytorin® (ezetimibe/simvastatin tablets - generic
- Livalo® (pitavastatin tablets)
- Flolipid® (simvastatin oral suspension)
- Zypitamag® (pitavastatin magnesium tablets)
- Ezallor™ (rosuvastatin capsules)

A step therapy program has been developed to encourage the use of one generic Step 1 HMG product prior to the approval of a Step 2 HMG product. If the step therapy rule is not met at the point of service, coverage will be determined by the step therapy criteria below. All approvals are provided for 12 months in duration.

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

Step 2 HMGs: Livalo, Flolipid, Lescol, Lescol XL, Altoprev, Pravachol, Zocor, Zypitamag, Lipitor, Crestor, Ezallor, Caduet, and Vytorin

Cigna covers Step 2 agents as medically necessary when the following criteria are met:

1. Authorization may be given for a Step 2 HMG if the individual has tried one Step 1 HMG.

2. Authorization may be given for Flolipid for individuals who cannot or have difficulty swallowing tablets or capsules.

Conditions Not Covered

Any other exception is considered not medically necessary.

Background

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, Livalo and Zypitamag.[1-13] Simvastatin is available combined with Zetia® (ezetimibe tablets) a selective intestinal inhibitor of cholesterol and related phytosterol absorption, as Vytorin®, which is available generically.[9] Atorvastatin is available as a combination with amlodipine, a dihydropyridine calcium channel blocker, as Caduet®, which is also available generically.[10] Flolipid® (simvastatin oral suspension) is the only HMG oral suspension available and it has the same indications as simvastatin tablets.[11]

Guidelines/Scientific Statements
In November 2013, the American College of Cardiology (ACC) and the American Heart Association (AHA) published guidelines on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular (CV) risk in adults.[14] The guideline emphasizes the appropriate intensity of statin therapy to reduce CV 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 therapy. The guideline also identifies four major groups who should be treated with an appropriate statin-intensive therapy. These groups include: 1) Individuals with clinical atherosclerotic CV disease (ASCVD), which includes patients with a past acute coronary syndrome (ACS), or history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack (TIA), or peripheral arterial disease presumed to be atherosclerotic origin; 2) Individuals with primary elevations of LDL-C ≥ 190 mg/dL; 3) Individuals 40 to 75 years of age with diabetes and LDL-C between 70 to 189 mg/dL (without CV disease); and 4) Individuals 40 to 75 years of age without clinical ASCVD or diabetes with LDL-C between 70 to 189 mg/dL and have an estimated 10-year ASCVD risk of 7.5% or higher. 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. There is substantially 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. An update was recently published.[15]

Table 1. High-, Moderate-, and Low-Intensity Statin Therapy.[14*]

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 Food and Drug Administration due to the increased risk of myopathy, including rhabdomyolysis; BID – Twice daily.

All of the HMGs have good capacity to lower elevated LDL-C. However, there is some variability among the products. Atorvastatin and rosuvastatin are considered "high-potency" HMGs because of their ability to reduce LDL-C by -60% and -63%, respectively, at maximal approved dosages. Ezetimibe plus simvastatin (Vytorin) also achieves comparable LDL-C reductions as atorvastatin and rosuvastatin with reductions of 60% at maximal dose. Table 2 cites the LDL-C reductions with HMGs, including ezetimibe plus simvastatin (Vytorin).[1-7,9] Livalo, which is not included in the table due to different dosage range, lowered LDL-C by -31%, -39%, and -44% at the 1 mg, 2 mg and 4 mg once daily (QD) doses, respectively.[8]

Table 2. Estimated Percent LDL-C Reduction of the HMGs According to Prescribing Information in Patients with Primary Hypercholesterolemia.[1-7,9]

Drug	5 mg/day	10 mg/day	20 mg/day	40 mg/day	60 mg/day	80 mg/day
Lovastatin	N/A	21%	27%	31%	N/A	42%[#]
Pravastatin	N/A	22%	32%	34%	N/A	37%
Simvastatin	26%	30%	38%	41%	N/A	47%
Atorvastatin	N/A	39%	43%	50%	N/A	60%
Fluvastatin	N/A	N/A	22%	25%	N/A	36%[#]
Fluvastatin extended-release	N/A	N/A	N/A	N/A	N/A	35%
Altoprev	N/A	24%	30%	36%	41%	N/A
Rosuvastatin	45%	52%	55%	63%	N/A	N/A
Ezetimibe plus simvastatin (Vytorin)[*]	N/A	45%	52%	55%	N/A	60%

LDL-C – Low-density lipoprotein cholesterol; HMGs – Hydroxy-methylglutaryl-coenzyme A reductase inhibitors; N/A – Not applicable or available; [#] Dosed as 40 mg twice daily; XL – Extended-Release; [*] Value in the table is based on the simvastatin dose. Note: Values rounded to the nearest whole number.

References

1. Mevacor® tablets [prescribing information]. Whitehouse Station, NJ: Actavis Pharma; March 2017.
2. Crestor® tablets [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals; November 2018.
3. Zocor® tablets [prescribing information]. Whitehouse Station, NJ: Merck & Co., Inc.; April 2020.
4. Lipitor® tablets [prescribing information]. New York, NY: Pfizer, Inc.; April 2019.

5. Lescol® capsules and Lescol® XL extended-release tablets [prescribing information]. East Hanover, NJ: Novartis; August 2017.
6. Altoprev® extended-release tablets [prescribing information]. Florham Park, NJ: Shionogi; February 2018.
7. Pravachol® tablets [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; July 2016.
8. Livalo® tablets [prescribing information]. Montgomery, AL: Kowa Pharmaceuticals; October 2019.
9. Vytorin® tablets [prescribing information]. North Wales, PA: Merck; October 2019.
10. Caduet® tablets [prescribing information]. New York, NY: Pfizer, Inc.; December 2019.
11. Flolipid® oral suspension [prescribing information]. Brooksville, FL: Salerno; July 2017.
12. Zypitamag® tablets [prescribing information]. Somerset, NJ: Medicure; February 2020.
13. Ezallor™ capsules [prescribing information]. Cranbury, NJ: Sun Pharmaceuticals; December 2018.
14. 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. Available at http://circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437738.63853.7a. Accessed on June 8, 2020.
15. 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 6, 2020.

Last Revision Details

Annual revision	No criteria changes.	06/10/2020

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