BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

MEDICATIONS WHICH CONTAIN SIMVASTATIN 80 MG:
Ezetimibe-Simvastatin
Simvastatin
VYTORIN (ezetimibe-simvastatin)
ZOCOR (simvastatin)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** A medication with 80 mg of simvastatin is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual is 18 years of age or older

2. Medication with 80 mg of simvastatin is prescribed according to FDA recommendations

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3. Evidence is provided by either the individual or prescriber of treatment with a medication with 80 mg of simvastatin for 12 months previously without evidence of muscle toxicity

4. Individual has been adherent with the medication throughout the 12 months

5. There are no significant interacting drugs such as itraconazole, ketoconazole, posaconazole, and voriconazole, erythromycin, clarithromycin, daptomycin, nelfinavir, ritonavir, darunavir/ritonavir), boceprevir, cobicistat-containing products, nefazodone, cyclosporine, danazol, gemfibrozil, grapefruit juice, etc.

Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** A medication with 80 mg of simvastatin is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual's condition has responded while on therapy with response defined as documented evidence of efficacy, disease stability and/or improvement

2. Individual has been adherent with the medication throughout the 12 months

3. Individual has not developed any FDA-label contraindications or other significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in FDA-approved package label
    b. Significant adverse effect such as:
        i. Myopathy
        ii. Immune-mediated necrotizing myopathy (IMNM)
        iii. Rhabdomyolysis
        iv. Hepatotoxicity

4. There are no significant interacting drugs such as itraconazole, ketoconazole, posaconazole, and voriconazole, erythromycin, clarithromycin, daptomycin, nelfinavir, ritonavir, darunavir/ritonavir, boceprevir, cobicistat-containing products, nefazodone, cyclosporine, danazol, gemfibrozil, grapefruit juice, etc.

Renewal duration: 12 months

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- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

Description:

In 2011, the Food and Drug Administration (FDA) issued a recommendation that use of medications which contain 80 mg of simvastatin—the highest approved dose—be sharply curtailed because of the risk of muscle injury.

FDA said this dose should only be used by individuals who have been taking it for 12 months or longer without ill effect. Another goal of the recommendation was to inform providers to not start individuals on 80 mg of simvastatin. These recommendations were prompted by a comprehensive review of clinical trial data and from the agency's Adverse Event Reporting System that tracks the safety of drugs once they are on the market.

All statins carry some risk of myopathy, characterized by unexplained muscle weakness or pain. Myopathy can be debilitating and the rare form of myopathy, known as rhabdomyolysis, can lead to kidney failure and death.

The risk is greater for individuals who take the 80 mg doses of simvastatin, especially in the first year of treatment. The muscle damage is often caused by interactions with other medications and some people are genetically predisposed towards simvastatin-related myopathy.

Simvastatin is sold under the brand name Zocor and as a single-ingredient generic drug. It is also sold in combination with Ezetimibe as Vytorin. Vytorin is now available as a generic product.

The maximum amount of simvastatin found in Vytorin is 80 mg. FDA has revised the drug labels for simvastatin (brand and generic) and Vytorin (brand and generic) to include the new restrictions for the 80 mg dose. The labels of simvastatin (brand and generic) and Vytorin (brand and generic) have all been changed to include dosing recommendations when these drugs are used with medicines that can increase the level of simvastatin, thus increasing the risk of myopathy.

For individuals taking 40 mg of simvastatin and who are not meeting their LDL cholesterol goal, FDA is advising providers to choose a different statin rather than raise the simvastatin dose to 80 mg.

Like all statins, simvastatin is used to lower low-density lipoprotein (LDL) cholesterol. The 80 mg dose of simvastatin has been shown to lower LDL cholesterol by an additional 6% over the 40 mg dose.

It is important that individuals should not stop their statin medication without consulting their provider. The benefits of the treatment far outweigh the risks, as the occurrence of rhabdomyolysis is considered extremely rare.

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Resources:

Zocor (simvastatin) product information, revised by Organon, LLC. 08-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 20, 2023.

Simvastatin product information, revised by Accord Healthcare, Inc 05-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 20, 2023.

Vytorin (simvastatin/ezetimibe) product information, revised by Organon, LLC. 06-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 20, 2023.

Simvastatin/ezetimibe product information, revised by Dr.Reddys Laboratories Inc. 10-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 20, 2023.

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