Clinical Policy: Ezetimibe and Simvastatin (Vytorin)

Reference Number: PA.CP.PMN.77
Effective Date: 02.01.17
Last Review Date: 07.18

Description
Ezetimibe/simvastatin (Vytorin®) contains ezetimibe, a selective inhibitor of intestinal cholesterol and related phytosterol absorption, and simvastatin, an HMG-CoA reductase inhibitor.

FDA Approved Indication(s)
Vytorin is indicated as adjunctive therapy to diet to:
- Reduce elevated total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B, triglycerides, and non-high-density lipoprotein cholesterol, and to increase high-density lipoprotein cholesterol in patients with primary (heterozygous familial and non-familial) hyperlipidemia or mixed hyperlipidemia
- Reduce elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH), as an adjunct to other lipid lowering treatments (e.g., LDL apheresis) or if such treatments are unavailable

Limitation(s) of use:
- No incremental benefit of Vytorin on cardiovascular morbidity and mortality over and above that demonstrated for simvastatin has been established.
- Vytorin has not been studied in Fredrickson Type I, III, IV, and V dyslipidemias.

Policy/Criteria
Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness that Vytorin is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Hypercholesterolemia (must meet all):
      1. Diagnosis of hypercholesterolemia/hyperlipidemia;
      2. Age ≥ 10 years;
      3. Failure of a high intensity statin per Appendix B for ≥ 3 consecutive months unless one of the following applies (a or b):
         a. Member has used a moderate intensity statin per Appendix B adherently for ≥ 3 consecutive months due to clinically significant adverse effects to high intensity statins;
         b. Member has used a low intensity statin per Appendix B adherently ≥ 3 consecutive months due to clinically significant adverse effects to high and moderate intensity statins;
      4. Adherence to statin therapy in the last 3 months as evidenced by pharmacy claims history;
5. Request does not exceed ezetimibe 10 mg/simvastatin 40 mg per day (1 tablet per day), or ezetimibe 10 mg/simvastatin 80 mg (1 tablet per day) for member on previous therapy with simvastatin 80 mg for at least one year.

**Approval duration:** 12 months

**B. Homozygous Familial Hypercholesterolemia, Heterozygous Familial Hypercholesterolemia, or Atherosclerotic Cardiovascular Disease (must meet all):**
1. Diagnosis of one of the following (a, b, or c):
   a. HoFH;
   b. Heterozygous familial hypercholesterolemia (HeFH);
   c. Atherosclerotic cardiovascular disease (ASCVD);
2. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
3. Age ≥ 10 years;
4. Member is unable to use high intensity statins per Appendix B due to clinically significant adverse effects;
5. Request does not exceed ezetimibe 10 mg/simvastatin 40 mg per day (1 tablet per day), or ezetimibe 10 mg/simvastatin 80 mg (1 tablet per day) for member on previous therapy with simvastatin 80 mg for at least one year.

**Approval duration:** 12 months

**C. Other diagnoses/indications**
1. Refer to PA.CP.PMN.53.

**II. Continued Therapy**

**A. All Indications in Section I (must meet all):**
1. Currently receiving medication via PA Health & Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed ezetimibe 10 mg/simvastatin 40 mg per day (1 tablet per day), or ezetimibe 10 mg/simvastatin 80 mg (1 tablet per day) for member on previous therapy with simvastatin 80 mg for at least one year.

**Approval duration:** 12 months

**B. Other diagnoses/indications (must meet 1 or 2):**
1. Currently receiving medication via PA Health & Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
   
   **Approval duration:** Duration of request or 12 months (whichever is less); or

2. Refer to PA.CP.PMN.53.

**III. Diagnoses/Indications for which coverage is NOT authorized:**
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HoFH: homozygous familial hypercholesterolemia
LDL-C: low-density lipoprotein cholesterol
total-C: total cholesterol

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High-Intensity Statin Therapy</strong>&lt;br&gt;Daily dose shown to lower LDL-C, on average, by approximately ≥ 50%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>atorvastatin (Lipitor®)</td>
<td>40-80 mg PO QD</td>
<td>80 mg/day</td>
</tr>
<tr>
<td>rosuvastatin (Crestor®)</td>
<td>20-40 mg PO QD</td>
<td>40 mg/day</td>
</tr>
<tr>
<td><strong>Moderate-Intensity Statin Therapy</strong>&lt;br&gt;Daily dose shown to lower LDL-C, on average, by approximately 30% to &lt; 50%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>atorvastatin (Lipitor®)</td>
<td>10-20mg PO QD</td>
<td>80 mg/day</td>
</tr>
<tr>
<td>fluvastatin (Lescol XL®)</td>
<td>Regular release (generic only): 40 mg PO BID&lt;br&gt;Extended release: 80 mg PO QD</td>
<td>80 mg/day</td>
</tr>
<tr>
<td>lovastatin</td>
<td>40 mg PO QD</td>
<td>80 mg/day</td>
</tr>
<tr>
<td>Livalo® (pitavastatin)</td>
<td>2-4 mg PO QD</td>
<td>4 mg/day</td>
</tr>
<tr>
<td>pravastatin (Pravachol®)</td>
<td>40-80 mg PO QD</td>
<td>80 mg/day</td>
</tr>
<tr>
<td>rosuvastatin (Crestor®)</td>
<td>5-10 mg PO QD</td>
<td>40 mg/day</td>
</tr>
<tr>
<td>simvastatin (Zocor®)</td>
<td>20-40 mg PO QD</td>
<td>40 mg/day for most patients; 80 mg/day for patients already taking 80 mg/day chronically without evidence of myopathy</td>
</tr>
<tr>
<td><strong>Low-Intensity Statin Therapy</strong>&lt;br&gt;Daily dose shown to lower LDL-C, on average, by &lt; 30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>fluvastatin</td>
<td>20-40 mg PO QD</td>
<td>80 mg/day</td>
</tr>
<tr>
<td>lovastatin</td>
<td>20 mg PO QD</td>
<td>80 mg/day</td>
</tr>
<tr>
<td>Livalo® (pitavastatin)</td>
<td>1 mg PO QD</td>
<td>4 mg/day</td>
</tr>
<tr>
<td>pravastatin (Pravachol®)</td>
<td>10-20 mg PO QD</td>
<td>80 mg/day</td>
</tr>
<tr>
<td>simvastatin (Zocor®)</td>
<td>10 mg PO QD</td>
<td>40 mg/day for most patients; 80 mg/day for patients already taking 80 mg/day</td>
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<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
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<tr>
<td></td>
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<td>mg/day chronically without evidence of myopathy</td>
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Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
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<tbody>
<tr>
<td>Primary hyperlipidemia and HoFH</td>
<td>Usual: 10/10 mg/day to 10/40 mg/day</td>
<td>10/40 mg/day for most patients</td>
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<tr>
<td></td>
<td>Use of the 10/80-mg dose of Vytorin should be restricted to patients who have been taking Vytorin 10/80 mg chronically (e.g., for 12 months or more) without evidence of muscle toxicity.</td>
<td>10/80 mg/day for patients already taking simvastatin 80 mg/day chronically without evidence of myopathy</td>
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<td></td>
<td>Due to the increased risk of myopathy, including rhabdomyolysis, associated with the 10/80-mg dose of Vytorin, patients unable to achieve their LDL-C goal utilizing the 10/40-mg dose of Vytorin should not be titrated to the 10/80-mg dose, but should be placed on alternative LDL-C-lowering treatment(s) that provides greater LDL-C lowering.</td>
<td></td>
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VI. Product Availability

Tablets (ezetimibe mg/simvastatin mg): 10/10, 10/20, 10/40, 10/80

VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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