Clinical Policy: Ezetimibe (Zetia)

Reference Number: PA.CP.PMN.78
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

Description
Ezetimibe (Zetia®) is an inhibitor of intestinal cholesterol (and related phytosterol) absorption.

FDA approved indication
Zetia is indicated as an adjunct to diet to

- Reduce elevated total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with primary hyperlipidemia, alone or in combination with an HMG-CoA reductase inhibitor (statin)
- Reduce elevated total-C, LDL-C, Apo B, and non-HDL-C in patients with mixed hyperlipidemia in combination with fenofibrate
- Reduce elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH), in combination with atorvastatin or simvastatin
- Reduce elevated sitosterol and campesterol in patients with homozygous sitosterolemia (phytosterolemia)

Limitations of use:

- The effect of Zetia on cardiovascular morbidity and mortality has not been determined.
- Zetia has not been studied in Fredrickson Type I, III, IV, and V dyslipidemias.

Policy/Criteria
** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria **

It is the policy of Pennsylvania Health and Wellness® that Zetia is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hypercholesterolemia (must meet all)**:**

1. Diagnosis of hypercholesterolemia/hyperlipidemia;
2. Failure of a high intensity statin per Appendix B for ≥ 3 consecutive months unless one of the following applies (a, b, or c):
   a. Member has received 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 received a low intensity statin per Appendix B adherently ≥ 3 consecutive months due to clinically significant adverse effects to high and moderate intensity statins;
   c. Statin therapy is contraindicated per Appendix C;

3. Adherence to statin therapy in the last 3 months as evidenced by pharmacy claims history;
4. Request does not exceed 10 mg per day (1 tablet per day).

Approval duration: 12 months

B. Sitosterolemia (must meet all):
1. Diagnosis of homozygous sitosterolemia (phytosterolemia);
2. Request does not exceed 10 mg per day (1 tablet per day).

Approval duration: 12 months

C. Homozygous Familial Hypercholesterolemia, Heterozygous Familial Hypercholesterolemia, or Atherosclerotic Cardiovascular Disease (must meet all):
1. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
2. Diagnosis of one of the following (a, b, or c):
   a. Homozygous familial hypercholesterolemia (HoFH);
   b. Heterozygous familial hypercholesterolemia (HeFH);
   c. Atherosclerotic cardiovascular disease (ASCVD);
3. Request does not exceed 10 mg per day (1 tablet per day).

Approval duration: 12 months

D. Other diagnoses/indications – Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. Continued Therapy

A. All Indications (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit, or member has previously met initial approval criteria or the Continuity of Care policy applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 10 mg per day (1 tablet per day).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or Continuity of Care policy applies; or
2. Refer to PA.CP.PMN.53 if requested indication is NOT listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

Approval duration: 12 months or duration of request (whichever is less)

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 policy – PA.CP.PMN.53 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation Key
Apo B: apolipoprotein B
ASCVD: atherosclerotic cardiovascular disease
FDA: Food and Drug Administration
HeFH: heterozygous familial hypercholesterolemia
HoFH: homozygous familial hypercholesterolemia LDL-C: low-density lipoprotein cholesterol non-HDL-C: non-high-density lipoprotein cholesterol total-C: total cholesterol

Appendix B: High-, Moderate-, and Low-Intensity Statin Therapy

- High-Intensity Statin Therapy
  Daily dose shown to lower LDL-C, on average, by approximately ≥50% o Atorvastatin 40-80 mg o Rosuvastatin 20-40 mg
- Moderate-Intensity Statin Therapy
  Daily dose shown to lower LDL-C, on average, by approximately 30% to < 50%
  o Atorvastatin 10-20mg o Fluvastatin XL 80 mg o Fluvastatin 40 mg twice daily
  o Lovastatin 40 mg o Pitavastatin 2-4 mg o Pravastatin 40-80 mg o Rosuvastatin 5-10 mg o Simvastatin 20-40 mg
- Low-Intensity Statin Therapy
  Daily dose shown to lower LDL-C, on average, by < 30% o Fluvastatin 20-40 mg o Lovastatin 20 mg o Pitavastatin 1 mg o Pravastatin 10-20 mg
  o Simvastatin 10 mg

Appendix C: Statin Contraindications

- Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy);

- Laboratory-confirmed acute liver injury or rhabdomyolysis resulting from statin treatment;
- Pregnancy, actively trying to become pregnant, or nursing;
- Immune-mediated hypersensitivity to the HMG-CoA reductase inhibitor drug class (statins) as evidenced by an allergic reaction occurring with at least TWO different statins.

V. Dosage and Administration

- The recommended dose of Zetia is 10 mg orally once daily.
- Zetia can be administered with or without food.
- Dosing of Zetia should occur either ≥ 2 hours before or ≥ 4 hours after administration of a bile acid sequestrant.

VI. Product Availability Tablets:
10 mg.

VIII. References

1. Zetia Prescribing Information. Whitehouse Station, NJ: Merck Sharp & Dohme Corp.; August 2013. Available at: https://dailymed.nlm.nih.gov/dailymed/. Accessed November 14, 2017.
2. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol 2016;68:92–125.
3. Jellinger PS, Handelsman Y, Rosenblit PD, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease. Endocr Pract. 2017 Apr;23(Suppl 2):1-87.
4. Third Report of the National Cholesterol Educational Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). https://www.nhlbi.nih.gov/files/docs/guidelines/atp3xsum.pdf. Accessed December 1, 2016.
5. Stone NJ, et al. 2013 ACC/AHA guideline 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. November 2013. DOI: 10.1161/01.cir.0000437738.63853.7a
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: http://www.clinicalpharmacology-ip.com/.

Reviews, Revisions, and Approvals	Date	Approval Date
References reviewed and updated.	02/18	