CENTENE Corporation

Clinical Policy: Ezetimibe (Zetia)

Reference Number: CP.PMN.78
Effective Date: 02.01.17
Last Review Date: 02.18
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

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)

Limitation(s) 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 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 Centene Corporation® 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. Age ≥ 10 years;
3. 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, unless contraindicated;
4 Dose 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. Age ≥ 10 years;
3. Dose 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. Diagnosis of one of the following (a, b, or c):
   a. HoFH;
   b. Heterozygous familial hypercholesterolemia;
   c. Atherosclerotic cardiovascular disease;
2. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
3. Age ≥ 10 years;
4. Dose does not exceed 10 mg per day (1 tablet per day).

Approval duration: 12 months

D. Other diagnoses/indications
1. Refer to 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 Centene benefit or member has previously met initial approval criteria;
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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

Apo B: apolipoprotein B
FDA: Food and Drug Administration
HoFH: homozygous familial hypercholesterolemia
LDL-C: low-density lipoprotein cholesterol
non-HDL-C: non-high-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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
High-Intensity Statin Therapy *Daily dose shown to lower LDL-C, on average, by approximately ≥ 50%*		
atorvastatin (Lipitor®)	40-80 mg PO QD	80 mg/day
rosuvastatin (Crestor®)	20-40 mg PO QD	40 mg/day
Moderate-Intensity Statin Therapy *Daily dose shown to lower LDL-C, on average, by approximately 30% to < 50%*		
atorvastatin (Lipitor®)	10-20mg PO QD	80 mg/day
fluvastatin (Lescol XL®)	Regular release (generic only): 40 mg PO BID Extended release: 80 mg PO QD	80 mg/day
lovastatin	40 mg PO QD	80 mg/day
Livalo® (pitavastatin)	2-4 mg PO QD	4 mg/day
pravastatin (Pravachol®)	40-80 mg PO QD	80 mg/day
rosuvastatin (Crestor®)	5-10 mg PO QD	40 mg/day
simvastatin (Zocor®)	20-40 mg PO QD	40 mg/day for most patients; 80 mg/day for patients already taking 80 mg/day chronically without evidence of myopathy
Low-Intensity Statin Therapy *Daily dose shown to lower LDL-C, on average, by < 30%*		
fluvastatin	20-40 mg PO QD	80 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
lovastatin	20 mg PO QD	80 mg/day
Livalo® (pitavastatin)	1 mg PO QD	4 mg/day
pravastatin (Pravachol®)	10-20 mg PO QD	80 mg/day
simvastatin (Zocor®)	10 mg PO QD	40 mg/day for most patients; 80 mg/day for patients already taking 80 mg/day chronically without evidence of myopathy

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.

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

Indication	Dosing Regimen	Maximum Dose
Primary hyperlipidemia, HoFH, and homozygous sitosterolemia	10 mg PO once daily	10 mg/day

VI. Product Availability

Tablets: 10 mg

VII. Workflow Document

N/A

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	P&T Approval Date
New policy created Policy split from CP.PMN.06 ezetimibe (Zetia) and ezetimibe and simvastatin (Vytorin) (retired) Clinical changes made to criteria: New policy mandates the use of high intensity statin for 3 months and provides a pathway to approval for patients with familial hypercholesterolemia with involvement of a specialist.	01.17	02.17
1Q18 annual review: - No significant changes - Age added per safety guidance endorsed by Centene Medical Affairs. - Added “unless contraindicated” to requirement related to adherence to statin therapy - References reviewed and updated.	11.10.17	02.18

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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