Oscar Clinical Guideline: ezetimibe (Zetia) (PG073, Ver. 7)

ezetimibe (Zetia)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Ezetimibe (Zetia), FDA approved in 2002, reduces blood cholesterol by inhibiting the absorption of cholesterol by the small intestine. Ezetimibe (Zetia) is FDA-indicated:

- In combination with a statin, or alone when additional low-density lipoprotein cholesterol (LDL-C) lowering therapy is not possible, as an adjunct to diet to reduce elevated LDL-C in adults with primary hyperlipidemia, heterozygous familial hypercholesterolemia (HeFH).
- In combination with a statin as an adjunct to diet to reduce elevated LDL-C in pediatrics 10 years of age and older with HeFH.
- In combination with fenofibrate as an adjunct to diet to reduce elevated LDL-C in adults with mixed hyperlipidemia.
- In combination with a statin, and other LDL-C lowering therapies, to reduce elevated LDL-C levels in adults and in pediatrics 10 years of age and older with homozygous familial hypercholesterolemia (HoFH).
- As an adjunct to diet for the reduction of elevated sitosterol and campesterol levels in adults and patients 9 years of age and older with homozygous familial sitosterolemia.

American College of Cardiology (ACC)/American Heart Association (AHA) guidelines prioritize statin therapy as the primary intervention for blood cholesterol level management, with an objective of reducing atherosclerotic cardiovascular disease risk (ASCVD). Statins, recognized for their potent LDL-C

(low-density lipoprotein cholesterol) lowering effects, are considered first-line treatment for the prevention of coronary disease in high-risk individuals. However, non-statin cholesterol-lowering therapy like ezetimibe may be used in high-risk individuals who show a less-than-anticipated response to statins, who cannot tolerate a less-than-recommended intensity of a statin, or who are completely statin intolerant.

Ezetimibe, either as a monotherapy or in combination with an HMG CoA reductase inhibitor (statins), serves as an adjunct to diet for reducing elevated total cholesterol (TC), LDL-C, apolipoprotein B (Apo B), and non-high-density lipoprotein cholesterol (HDL-C) in individuals with primary hyperlipidemia (heterozygous familial and non-familial). For homozygous familial hypercholesterolemia, ezetimibe can be co-administered with atorvastatin or simvastatin to reduce elevated TC and LDL-C, especially in situations where other lipid-lowering treatments are unavailable. In cases of homozygous familial sitosterolemia, ezetimibe may be provided in addition to diet to reduce elevated sitosterol and campesterol levels.

Primary recommendation for clinical ASCVD involves the use of statin therapy. However, if not viable, moderate-intensity statin therapy can be initiated. In cases where LDL-C levels remain ≥ 70mg/dL on maximally tolerated statin, the addition of ezetimibe may be considered. For very high-risk individuals with multiple high-risk clinical factors, ezetimibe can be added to maximally tolerated statin therapy (See Appendix). Thus, coverage is extended to patients who have experienced an inadequate treatment response, intolerance, or contraindication to a statin or statin combination product.

The ACC/AHA guidelines should be routinely reviewed for the most updated recommendations. More information is available on the ACC website at https://www.acc.org/Guidelines#/.

Definitions

"Cholesterol" is a waxy, fat-like substance produced by the body, which is integral to cellular structure and function.

"Clinical atherosclerotic cardiovascular disease (ASCVD)" refers to a group of conditions characterized by plaque buildup within the arterial walls. This can result in reduced blood flow and lead to cardiovascular events such as angina (chest pain), myocardial infarction (heart attack), and stroke.

"Homozygous familial hypercholesterolemia (HoFH)" is a rare, genetically inherited disorder, with genes inherited from both parents, that leads to extremely elevated cholesterol levels. This can predispose individuals to premature cardiovascular disease, often manifesting as early as adolescence.

"Homozygous sitosterolemia" is a rare, genetically inherited disorder where both parents contribute genes leading to altered sterol lipid metabolism from plant-based foods, causing elevated levels of plant

sterols in the blood and tissues. Dietary therapy is often insufficient to control this disease due to the ubiquity of plant sterols in food.

"Lipids" refer to various types of fats present in the body, which play crucial roles in hormone production, vitamin D synthesis, and digestive processes.

"Low-density lipoprotein (LDL-C)" is a type of lipid-carrying particle that transports fats around the body. Elevated levels of LDL-C, also known as "bad cholesterol," can contribute to the development of atherosclerosis.

"Statins" are a class of medications used primarily to lower cholesterol and triglyceride levels. They work by inhibiting an enzyme (HMG-CoA reductase) involved in the body's cholesterol synthesis. Examples include atorvastatin, lovastatin, simvastatin, and rosuvastatin.

Medical Necessity Criteria for Authorization

The Plan considers ezetimibe medically necessary when BOTH of the following criteria are met:

1. The member is 9 years of age or older; *AND*
2. The member is already prescribed, unable to use, or has tried and failed ONE (1) of the following:
    a. Atorvastatin; *or*
    b. Fluvastatin; *or*
    c. Lovastatin; *or*
    d. Pravastatin; *or*
    e. Rosuvastatin; *or*
    f. Simvastatin.

If the above prior authorization criteria are met, ezetimibe will be approved for up to 36 months.

References

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Clinical Guideline Revision / History Information

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Appendix:

Ezetimibe has been studied as adjunct therapy to statins in those with established ASCVD in the IMPROVE-IT study. In a double-blind randomized trial of 18,144 participants 50 years of age and older who had been hospitalized for an acute coronary syndrome (i.e., an acute myocardial infarction, with or without ST-segment elevation on electrocardiography, or high-risk unstable angina) with baseline LDL-C

of 50-100 mg/dl, were randomized to receive either ezetimibe 10 mg or placebo in addition to 40 mg of simvastatin. After a median of 6 years of follow-up, the following was found:

- Study participants in the ezetimibe-simvastatin group experienced a 24% greater LDL-C reduction compared to those in the placebo-simvastatin group (mean difference of 16.7 mg/dl) at 1 year. All cholesterol levels and inflammatory markers (total cholesterol, Apo B, high-sensitivity C-reactive protein, non-HDL cholesterol, triglycerides) were significantly lower in the ezetimibe-simvastatin group compared to the placebo-simvastatin group.
- The primary endpoint of the composite of cardiovascular death, nonfatal myocardial infarction, unstable angina requiring hospitalization, coronary revascularization (≥30 days after randomization) or non-fatal stroke was significantly different at 7 years, occurring in 32.7% and 34.7% in the ezetimibe-simvastatin group versus the placebo-simvastatin group, respectively, (Absolute risk reduction [ARR] 2%, HR 0.936; 95% CI, 0.89-0.99; p=0.016; number needed to treat [NNT]=50).