BlueCross BlueShield of Alabama

Zetia® (ezetimibe) Step Therapy Criteria Program Summary

Step Therapy will only apply to members that have a benefit including the Enhanced Step Therapy Package. This program is implemented with grandfathering.

OBJECTIVE

The intent of the Zetia (ezetimibe) Step Therapy (ST) program is to encourage the use of ezetimibe as adjunctive or add on therapy. Although ezetimibe is approved as monotherapy for the treatment of primary hypercholesterolemia, concomitant therapy with a statin has demonstrated effectiveness in improving serum lipid profiles beyond either treatment alone, and in clinical trials, greater effectiveness has been seen from a statin plus ezetimibe than from increased doses of statin monotherapy. The step therapy edit for ezetimibe requires recent or concomitant use of a statin agent, or a fenofibrate product in patients with mixed hyperlipidemia. The program allows continuation of Zetia therapy when there is documentation that the patient is receiving the requested agent.

TARGET AGENTS

Zetia (ezetimibe)[a]

a – generic available and targeted in program

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Zetia (ezetimibe) will be approved when ANY ONE of the following is met:

1. The patient has a diagnosis of homozygous sitosterolemia
   OR
2. The patient's diagnosis is mixed hyperlipidemia AND the patient's medication history includes use of a fenofibrate product in the past 90 days
   OR
3. The patient's medication history includes use of a statin or statin-niacin combination in the past 90 days
   OR
4. There is documentation that the patient is currently receiving Zetia (ezetimibe)
   OR
5. The prescriber states the patient is using Zetia (ezetimibe) AND is at risk if therapy is changed
   OR
6. The patient has a history of a documented intolerance, FDA labeled contraindication, or hypersensitivity to a statin or statin-niacin combination

Length of approval: 12 months

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.

FDA APPROVED INDICATIONS AND DOSAGE

FDA Indication[1]:
Ezetimibe is indicated:

- As adjunctive therapy to diet for the reduction of 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 (heterozygous familial and nonfamilial) hyperlipidemia, alone or in combination with a 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor (statin);
- As adjunctive therapy to diet for reduction of elevated total-C, LDL-C, Apo B, and non-HDL-C in patients with mixed hyperlipidemia in combination with a fenofibrate;
- For the reduction of elevated total-C and LDL in patients with homozygous familial hypercholesterolemia (HoFH), in combination with atorvastatin or simvastatin, as an adjunct to other lipid-lowering treatments (e.g. LDL apheresis) or if such treatments are unavailable;
- As adjunctive therapy to diet for reduction or elevated sitosterol and campesterol in patients with homozygous familial sitosterolemia.

Dosing[1]: The recommended dose of ezetimibe is one 10 mg tablet once daily. Ezetimibe may be administered with a statin or fenofibrate. Dosing of ezetimibe should occur either ≥2 hours before or ≥4 hours after administration of a bile acid sequestrant.

CLINICAL RATIONALE

The 2013 American College of Cardiology/American Heart Association (ACC/AHA) Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the ACC/AHA Task Force on Practice Guidelines states the following:[2]

- Adherence to lifestyle and statin therapy should be emphasized before the addition of a non-statin drug is considered.
- The panel could find no data supporting the routine use of non-statin drugs combined with statin therapy to reduce further ASCVD events. In addition, identification of any randomized controlled trials (RCTs) that assessed ASCVD outcomes in statin-intolerant patients was not found.
- Clinicians treating high risk patients (i.e., including those with ASCVD, those with LDL-C ≥ 190 mg/dL, and those individuals with DM) who have less than anticipated response to statins, who are unable to tolerate a less than recommended intensity of a statin, or who are completely statin intolerant may consider the addition of a non-statin cholesterol lowering therapy.
- Therapy based on atherosclerotic CV disease risk and potential for adverse effects is recommended rather than focusing on specific LDL-C or non-HDL goals.

The National Lipid Association (NLA) task force on statin safety note that ezetimibe may be considered in those with statin intolerance who have not achieved the LDL-C goal.[3,5]

The Standards in Diabetes (2017) recommends the addition of ezetimibe to moderate-intensity statin therapy has been shown to provide additional cardiovascular benefit compared with moderate-intensity statin therapy alone for patients with recent acute coronary syndrome and LDL cholesterol ≥50 mg/dL (1.3 mmol/L) and should be considered for these patients and also in patients with diabetes and history of ASCVD who cannot tolerate high-intensity statin therapy.[4]

According the American Heart Association (AHA), initial treatment for Familial Hypercholesterolemia should include a high intensity statin.[6] If the LDL-C is not at goal after 3 months of therapy with the high intensity statin and the patient has been adherent, AHA recommends the addition of ezetimibe. For patients who do not respond to this two drug

regimen within 3 months, AHA recommends addition of a PCKS9, a bile acid sequestrant, or niacin. Patients with HoFH who require additional therapy despite treatment with the three drug regimen, AHA recommends addition of Juxtapid or Kynamro and LDL apheresis.[6]

The 2016 American College of Cardiology (ACC) Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for Low-Density Lipoprotein Cholesterol (LDL-C) Lowering in the Management of Atherosclerotic Cardiovascular Diseaes (ASCVD) Risk recommends the consideration of adding ezetimibe 10 mg daily as the initial non-statin agent in combination therapy in patients with stable ASCVD and diabetes; patients with uncomplicated HeFH; patients without diabetes but with multiple ASCVD risk factors; and in patients with acute coronary syndromes.[7]

For additional clinical information see Prime Therapeutics Formulary Chapter 5.9F: Cholesterol Absorption Inhibitors.

REFERENCES

1. Zetia Prescribing Information. Merck/Schering-Plough Pharmaceuticals, Whitehouse Station, NJ 0889. February 2016.
2. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA Guideline for the Treatment of Blood Cholesterol to Reduce Atherosclerotic CV risk in adults: A report of the ACC/AHA taskforce on practice guidelines. Available at: http://circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437738.63853.7a..DC1.html Accessed February 5, 2014.
3. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia:Part 1 – full report. *J Clin Lipidology* 2015; 9: 129-169.
4. Standards of Medical Care in Diabetes 2017. Diabetes Care 2017; 40(Suppl. 1):S75–S87 | DOI: 10.2337/dc17-S012
5. Jacobson TA, Maki KC, Orringer CE, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 2. *J Clin Lipidology* 2015; 9: S1-S122.
6. Gidding S, Champagne M, Ferranti S, et al. The Agenda for Familial Hypercholesterolemia. A Scientific Statement From the American Heart Association. Circulation. 2015; 132:00-00
7. Journal of American College of Cardiology 2016; April: 1-42.