NEXLIZET® (bempedoic acid and ezetimibe) tablets

NEXLETOL® (bempedoic acid) tablets

Pill images are not actual size.

Common criteria for submission of a NEXLIZET or NEXLETOL Prior Authorization (PA) Form[1-6]

INFORMATION CATEGORY / CLINICAL DETAILS		DOCUMENTATION EXAMPLES
Primary diagnosis ☐ **Atherosclerotic cardiovascular disease (ASCVD)** *The conditions and procedures associated with ASCVD include: stroke, ministroke/TIA, ACS, heart attack/MI, revascularization, angina, PAD.* **and/or** ☐ **Heterozygous familial hypercholesterolemia (HeFH)** *HeFH is an autosomal dominant disease characterized by markedly elevated plasma concentrations of LDL, typically with LDL-C levels >190 mg/dL (untreated).* *The Dutch Lipid Clinic Network Criteria is one diagnostic tool to help determine whether a patient has a definite, probable, possible, or unlikely diagnosis (considers cholesterol levels, family history, clinical history, physical examination, and DNA analysis).* *This is for your information only. Diagnosis of FH should be determined by the clinical judgment of a healthcare professional. ESPERION does not endorse any particular criteria for diagnosis of FH.*		**ICD-10-CM codes* (conditions of atherosclerotic origin):** ***Transient cerebral ischemic attacks and related syndromes:*** • **G45:** Transient cerebral ischemic attacks and related syndromes ***Ischemic heart diseases:*** • **I20:** Angina pectoris • **I20.0:** Unstable angina • **I20.8:** Other forms of angina pectoris • **I20.9:** Angina pectoris, unspecified • **I21:** Acute myocardial infarction • **I22:** Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction • **I23:** Certain current complications following ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction (within the 28 day period) • **I24:** Other acute ischemic heart diseases • **I25:** Chronic ischemic heart disease ***Cerebrovascular diseases:*** • **I63.0:** Cerebral infarction due to thrombosis of precerebral arteries • **I65:** Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction • **I66:** Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction ***Diseases of arteries, arterioles and capillaries:*** • **I70.0:** Atherosclerosis of aorta • **I70.1:** Atherosclerosis of renal artery • **I70.2:** Atherosclerosis of native arteries of the extremities • **I70.3:** Atherosclerosis of unspecified type of bypass graft(s) of the extremities • **I73:** Other peripheral vascular diseases • **I73.8:** Other specified peripheral vascular diseases • **I73.9:** Peripheral vascular disease, unspecified ***Disorders of lipoprotein metabolism and other lipidemias:*** • **E78:** Disorders of lipoprotein metabolism and other lipidemias • **E78.00:** Pure hypercholesterolemia, unspecified • **E78.01:** Familial hypercholesterolemia • **E78.2:** Mixed hyperlipidemia • **E78.4:** Other hyperlipidemia • **E78.5:** Hyperlipidemia, unspecified ***Family history of other specific disorders:*** • **Z83.42:** Family history of familial hypercholesterolemia
Diagnostic findings	☐ Baseline LDL-C levels	• Recent lipid panel • Documentation that the patient has one of the following LDL-C values: - LDL-C remains ≥70 mg/dL despite maximally tolerated statins (for patients with ASCVD) - LDL-C ≥190 mg/dL (for patients with HeFH prior to treatment)
History of other lipid-lowering therapy	☐ Statin ☐ Ezetimibe ☐ Other	**Confirmation that patient is currently on maximally tolerated statin therapy** (it should be noted that a maximally tolerated statin may be a low dose of a statin or no statin at all) • Duration of other lipid-lowering therapies (eg, for at least 12 weeks in the past 6 months) • Some plans may require additional information about ezetimibe, such as: - If the patient has received at least 12 consecutive weeks of ezetimibe therapy as an adjunct to maximally tolerated statin therapy, or - If the patient has a history of contraindication with, or intolerance to, ezetimibe
Lifestyle modifications	☐ Diet ☐ Exercise	

*Please see the following page for important information regarding ICD-10-CM codes.

TIA=transient ischemic attack; ACS=acute coronary syndrome; MI=myocardial infarction; PAD=peripheral artery disease; FH=familial hypercholesterolemia; LDL-C=low-density lipoprotein cholesterol; LDL-R=low-density lipoprotein receptor; PCSK9=proprotein convertase subtilisin/kexin type 9; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification.

Be sure to review carefully, as each payer may have unique requirements.

A Letter of Medical Necessity may be helpful when submitting your PA request.

INDICATION

NEXLETOL and NEXLIZET are indicated as adjuncts to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C.

Limitations of Use: The effect of NEXLETOL and NEXLIZET on cardiovascular morbidity and mortality has not been determined.

IMPORTANT SAFETY INFORMATION

Contraindications: NEXLETOL has no contraindications. NEXLIZET is contraindicated in patients with a known hypersensitivity to ezetimibe tablets. Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria have been reported with ezetimibe.

Please see additional Important Safety Information on the following page and full Prescribing Information for NEXLIZET and NEXLETOL.

About this Prior Authorization Checklist and ICD-10-CM codes

The information contained in this Checklist is of a general nature and is for educational purposes only. It is intended solely as a resource to assist the staff in physicians' offices and hospitals with certain reimbursement-related questions. ESPERION makes no representation about the information provided, as reimbursement information, including applicable policies and laws, are subject to change. The information in this Checklist is not conclusive or exhaustive and is not intended to replace the guidance of a qualified, professional advisor. ESPERION does not recommend or endorse the use of any particular diagnosis code, and makes no determination regarding if or how reimbursement may be available. The use of this information does not guarantee payment or that any payment received will equal a certain amount.

IMPORTANT SAFETY INFORMATION (cont.)

Warnings and Precautions: *Hyperuricemia:* Bempedoic acid, a component of NEXLETOL and NEXLIZET, may increase blood uric acid levels. Hyperuricemia may occur early in treatment and persist throughout treatment, and may lead to the development of gout, especially in patients with a history of gout. Assess uric acid levels periodically as clinically indicated. Monitor for signs and symptoms of hyperuricemia, and initiate treatment with urate-lowering drugs as appropriate.
Tendon Rupture: Bempedoic acid is associated with an increased risk of tendon rupture or injury. In clinical trials, tendon rupture occurred in 0.5% of patients treated with bempedoic acid versus 0% of patients treated with placebo, and involved the rotator cuff (the shoulder), biceps tendon, or Achilles tendon. Tendon rupture occurred within weeks to months of starting bempedoic acid. Tendon rupture may occur more frequently in patients over 60 years of age, patients taking corticosteroid or fluoroquinolone drugs, patients with renal failure, and patients with previous tendon disorders. Discontinue NEXLETOL or NEXLIZET at the first sign of tendon rupture. Avoid NEXLETOL and NEXLIZET in patients who have a history of tendon disorders or tendon rupture.

Adverse Reactions: In NEXLETOL clinical trials, the most commonly reported adverse reactions were upper respiratory tract infection, muscle spasms, hyperuricemia, back pain, abdominal pain or discomfort, bronchitis, pain in extremity, anemia, and elevated liver enzymes. Reactions reported less frequently, but still more often than with placebo, included benign prostatic hyperplasia and atrial fibrillation.
In the NEXLIZET clinical trial, the most commonly reported adverse reactions observed with NEXLIZET, but not observed in clinical trials of bempedoic acid or ezetimibe, a component of NEXLIZET, and occurring more frequently than with placebo, were urinary tract infection, nasopharyngitis, and constipation.
Adverse reactions reported in clinical trials of ezetimibe, and occurring at an incidence greater than with placebo, included upper respiratory tract infection, diarrhea, arthralgia, sinusitis, pain in extremity, fatigue, and influenza. Other adverse reactions reported in postmarketing use of ezetimibe included hypersensitivity reactions, including anaphylaxis, angioedema, rash, and urticaria; erythema multiforme; myalgia; elevated creatine phosphokinase; myopathy/rhabdomyolysis; elevations in liver transaminases; hepatitis; abdominal pain; thrombocytopenia; pancreatitis; nausea; dizziness; paresthesia; depression; headache; cholelithiasis; cholecystitis.

Drug Interactions: *Simvastatin and Pravastatin:* Concomitant use with bempedoic acid results in increased concentrations and increased risk of simvastatin or pravastatin-related myopathy. Use of either NEXLETOL or NEXLIZET with greater than 20 mg of simvastatin or 40 mg of pravastatin should be avoided.
Cyclosporine: Caution should be exercised when using NEXLIZET and cyclosporine concomitantly due to increased exposure to both ezetimibe and cyclosporine. Monitor cyclosporine concentrations in patients receiving NEXLIZET and cyclosporine. In patients treated with cyclosporine, the potential effects of the increased exposure to ezetimibe from concomitant use should be carefully weighed against the benefits of alterations in lipid levels provided by NEXLIZET.
Fibrates: Coadministration of NEXLIZET with fibrates other than fenofibrate is not recommended. Fenofibrate and ezetimibe may increase cholesterol excretion into the bile, leading to cholelithiasis. If cholelithiasis is suspected in a patient receiving NEXLIZET and fenofibrate, gallbladder studies are indicated and alternative lipid-lowering therapy should be considered.
Cholestyramine: Concomitant use of NEXLIZET and cholestyramine decreases ezetimibe concentration. This may result in a reduction of efficacy. Administer NEXLIZET either at least 2 hours before, or at least 4 hours after, bile acid sequestrants.

Lactation and Pregnancy: It is not recommended that NEXLETOL or NEXLIZET be taken during breastfeeding. Discontinue NEXLETOL or NEXLIZET when pregnancy is recognized, unless the benefits of therapy outweigh the potential risks to the fetus. Based on the mechanism of action of bempedoic acid, NEXLETOL and NEXLIZET may cause fetal harm.

Please see full Prescribing Information for NEXLIZET and NEXLETOL.

References: 1. Prior Authorization/Medical Necessity. UnitedHealthcare. October 2020. **2.** American Diabetes Association. 8. Cardiovascular disease and risk management. *Diabetes Care.* 2016;39(suppl 1):S60-S71. **3.** Gidding SS, Champagne MA, de Ferranti SD, et al. The agenda for familial hypercholesterolemia: a scientific statement from the American Heart Association. *Circulation.* 2015;132(22):2167-2192. **4.** Pećin I, Hartgers ML, Hovingh GK, Dent R, Reiner Ž. Prevention of cardiovascular disease in patients with familial hypercholesterolaemia: the role of PCSK9 inhibitors. *Eur J Prev Cardiol.* 2017;24(13):1383-1401. **5.** Austin MA, Hutter CM, Zimmern RL, Humphries SE. Genetic causes of monogenic heterozygous familial hypercholesterolemia: a HuGE prevalence review. *Am J Epidemiol.* 2004;160(5):407-420. **6.** Prior Authorization: Hyperlipidemia – Nexletol™ (bempedoic acid tablets). Cigna. January 2021.

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