NEXLETOL® (bempedoic acid) tablets

NEXLIZET™ (bempedoic acid and ezetimibe) tablets

Oral, once-daily, nonstatin LDL-C lowering therapies[1,2]

SIGNIFICANT ADDITIONAL LDL-C REDUCTION REGARDLESS OF PATIENTS' MAXIMALLY TOLERATED STATIN DOSE[1-5]

NEXLETOL

18% MEAN LDL-C REDUCTION VS PLACEBO

LDL-C changes from baseline (LS mean) in CLEAR Harmony: NEXLETOL: -17% (n=1,488); placebo: +2% (n=742); *P*<0.001.

NEXLIZET

38% MEAN LDL-C REDUCTION VS PLACEBO

LDL-C changes from baseline (LS mean) in 053 Trial: NEXLIZET: -36% (n=86); placebo: +2% (n=41); *P*<0.001. LDL-C changes from baseline (LS mean) for other drugs in the trial: NEXLETOL: -17% (n=88); ezetimibe: -23% (n=86).

BEMPEDOIC ACID, A COMPONENT OF NEXLETOL AND NEXLIZET, IS THE FIRST AND ONLY ACL INHIBITOR, WITH A MECHANISM OF ACTION COMPLEMENTARY TO STATINS[1,2,6]

BEMPEDOIC ACID SHOWED AN INCIDENCE OF SKELETAL MUSCLE ADVERSE REACTIONS COMPARABLE TO PLACEBO[1]

SIMPLE, ORAL, ONCE-DAILY TABLETS, TAKEN WITH OR WITHOUT FOOD, WITH NO NEED TO TITRATE[1,2]

- Concomitant use of simvastatin or pravastatin with NEXLETOL, or of simvastatin, pravastatin, cyclosporine, fibrates, or cholestyramine with NEXLIZET, may require adjustments for these medications

CLEAR Harmony (Study 1) was a 52-week, randomized, double-blind, Phase 3 trial in 2,230 patients randomized 2:1 to receive NEXLETOL (n=1,488) or placebo (n=742). CLEAR Harmony included patients aged ≥18 years with fasting LDL-C ≥70 mg/dL, and high-risk patients with ASCVD and/or HeFH. NEXLETOL was added to whatever patient's maximally tolerated statin dose was, either alone or with other lipid-lowering therapies. Primary endpoint was general safety, which included adverse reactions, clinical safety laboratories, physical examinations, vital signs, and electrocardiogram. Secondary endpoint was % change from baseline to Week 12 in LDL-C.[3,7]

053 Trial (Study 1) was a 12-week, randomized, double-blind, Phase 3 trial in 301 patients randomized 2:2:2:1 to receive NEXLIZET (n=86), NEXLETOL (n=88), ezetimibe (n=86), or placebo (n=41). 053 Trial included patients aged ≥18 years with fasting LDL-C ≥100 mg/dL if they had ASCVD and/or HeFH, or ≥130 mg/dL if they had multiple cardiovascular risk factors. Therapies were added to whatever patient's maximally tolerated statin dose was (including no statin at all), either alone or with other lipid-lowering therapies. Primary endpoint was % change from baseline to Week 12 in LDL-C. Secondary endpoint was % change from baseline to Week 12 in hsCRP, non-HDL-C, total C, apolipoprotein B, HDL-C, and TGs.[2,5]

LDL-C=low-density lipoprotein cholesterol; LS=least squares; ACL=adenosine triphosphate citrate lyase; ASCVD=atherosclerotic cardiovascular disease; HeFH=heterozygous familial hypercholesterolemia; hsCRP=high-sensitivity C-reactive protein; non-HDL-C=non-high-density lipoprotein cholesterol; total C=total cholesterol; TGs=triglycerides.

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 reverse side and full Prescribing Information for NEXLETOL and NEXLIZET in pocket.

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 NEXLETOL and NEXLIZET in pocket.

References: 1. NEXLETOL. Prescribing information. ESPERION Therapeutics, Inc.; 2020. **2.** NEXLIZET. Prescribing information. ESPERION Therapeutics, Inc.; 2020. **3.** Data on file. CSR 1002-040. October 2018. **4.** Data on file. CSR 1002-047. January 2019. **5.** Data on file. CSR 1002-053. January 2019. **6.** Saeed A, Ballantyne CM. Bempedoic acid (ETC-1002): a current review. *Cardiol Clin.* 2018;36(2):257-264. **7.** Ray KK, Bays HE, Catapano AL, et al. Safety and efficacy of bempedoic acid to reduce LDL cholesterol. *N Engl J Med*. 2019;380(11):1022-1032.

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ESPERION