CLEAR OUTCOMES: PRIMARY PREVENTION SUBGROUP

A PRESPECIFIED, EXPLORATORY ANALYSIS OF BEMPEDOIC ACID IN PATIENTS AT HIGH RISK FOR CVD

INDICATION[1]

Bempedoic acid (NEXLETOL®) is indicated:

- To reduce the risk of myocardial infarction and coronary revascularization in adults who are unable to take recommended statin therapy (including those not taking a statin) and with:
  - established cardiovascular disease (CVD), or
  - at high risk for a CVD event, but without established CVD.
- As an adjunct to diet, in combination with other LDL-C lowering therapies, or alone when concomitant LDL-C lowering therapy is not possible, to reduce LDL-C in adults with primary hyperlipidemia, including HeFH.

Please see accompanying full Prescribing Information.

CLEAR Outcomes: Overall Population Study Design & Methodology[2,3]

Patients **without established CVD** were considered at high risk for CVD based on meeting at least one of the following criteria:

- Type 1 or 2 diabetes in women >65 or men >60 years of age
- Reynolds Risk score >30% **OR** SCORE risk >7.5% over 10 years
- Any previous coronary artery calcium score of > 400 AU

Patients **with established CVD** had documented history of at least one of the following:

- coronary artery disease
- symptomatic peripheral arterial disease
- cerebrovascular atherosclerotic disease

CLEAR Outcomes: Overall Population Primary Composite Endpoint[3]

In the total CLEAR Outcomes population, which included both primary (30%) and secondary (70%) patients, the composite primary endpoint of the study (MACE-4) occurred in 819 patients (11.7%) in the bempedoic acid group vs. 927 patients (13.3%) in the placebo group; HR 0.87 (95% CI 0.79, 0.96), P=0.004

Summary of Safety[1]

NEXLETOL is contraindicated in patients with a prior serious hypersensitivity reaction to bempedoic acid or any of the excipients. Serious hypersensitivity reactions, such as angioedema, have occurred.

Hyperuricemia: NEXLETOL may increase blood uric acid levels, which may lead to gout. Hyperuricemia may occur early in treatment and persist throughout treatment, returning to baseline following discontinuation of treatment. 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: NEXLETOL is associated with an increased risk of tendon rupture or injury. Tendon rupture may occur more frequently in patients with previous tendon rupture, fluoroquinolone use, corticosteroid use, and over 60 years of age. Discontinue NEXLETOL at the first sign of tendon rupture. Consider alternative therapy in patients who have a history of tendon disorders or tendon rupture.

The most common adverse reactions in the primary hyperlipidemia trials of NEXLETOL in ≥2% of patients and greater than placebo were upper respiratory tract infection, muscle spasms, hyperuricemia, back pain, abdominal pain or discomfort, bronchitis, pain in extremity, anemia, and elevated liver enzymes.

The most common adverse reactions in the cardiovascular outcomes trial for NEXLETOL at an incidence of ≥2% and 0.5% greater than placebo were hyperuricemia, renal impairment, anemia, elevated liver enzymes, muscle spasms, gout, and cholelithiasis.

References: 1. NEXLETOL® (bempedoic acid) US Full Prescribing Information. Esperion Therapeutics, Inc. **2.** Nicholls SJ, et al. *Am Heart J.* 2021;235:104-112. **3.** Nissen SE, et al. *N Engl J Med*. 2023;388(15):1353-1364. **4.** Nissen SE, et. al. *JAMA*. 2023 Jul 11;330(2):131-140. **5.** Suppl to Nissen SE, et. al. *JAMA*. 2023 Jul 11;330(2):131-140. **6.** Data on file. 1002-043. Esperion Therapeutics Inc.

Abbreviations: AE = adverse event; AU = Agatston units; LDL-C=low density lipoprotein; CVD = cardiovascular disease; HCP = health care provider; HeFH= heterozygous familial hypercholesterolemia; MACE=major adverse cardiovascular event; MACE-4: CV death, nonfatal MI, nonfatal stroke, coronary revascularization; MI= myocardial infarction; PCSK9 = proprotein convertase subtilisin/kexin type 9; QD = daily

Primary Prevention Subgroup Analysis[4]

Select Baseline Demographics[4]

30% Overall Population at high risk for CVD

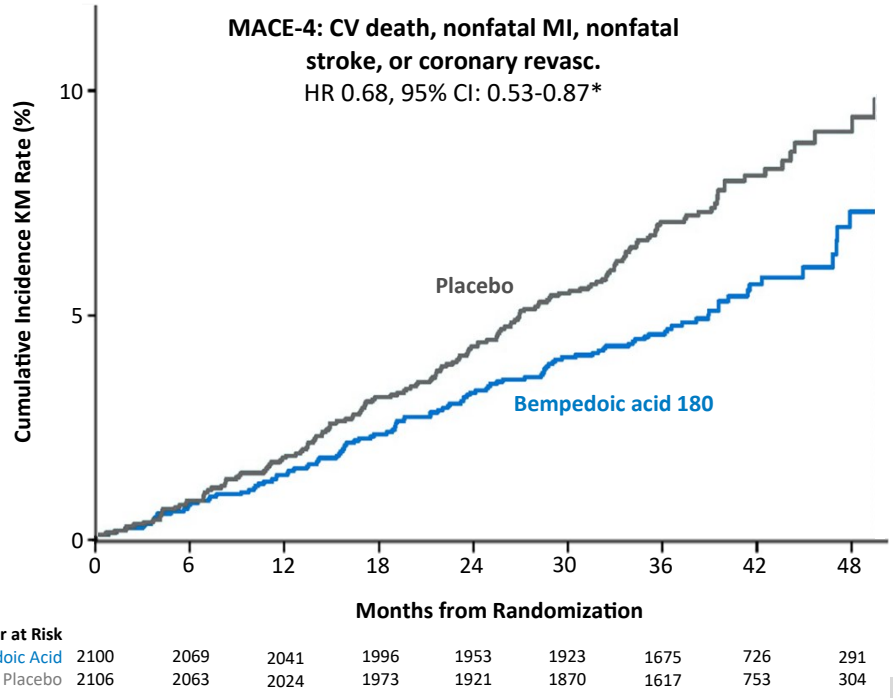
LDL-C 142 mg/dL

59% Women

66% Diabetes

*Numbers presented represent patients enrolled in both bempedoic acid and placebo groups

Primary Composite Endpoint[4]

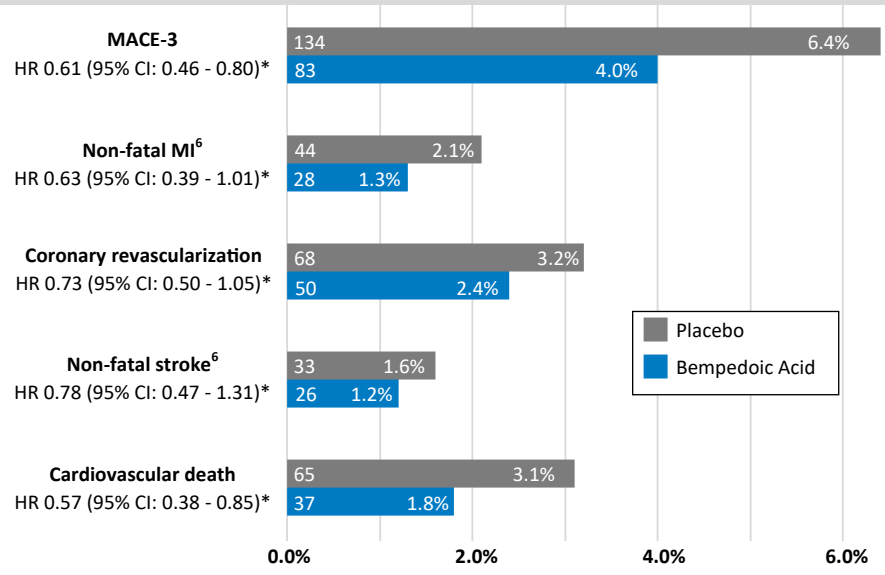


Number at Risk

Bempedoic Acid	2100	2069	2041	1996	1953	1923	1675	726	291
Placebo	2106	2063	2024	1973	1921	1870	1617	753	304

Note: This Kaplan Meier (KM) Curve presents the time to first occurrence for each of the components of MACE-4.

MACE-3 and Components of Primary Composite Endpoint[5,6]



Limitations[4]

- This is a secondary analysis of a subpopulation in a larger randomized trial, such analyses can result in false-positive findings due to testing of multiple subgroups and may represent a play of chance
- The sample size represented a fraction of the total enrolled population and the number of events was smaller resulting in wider confidence intervals
- The inclusion of patients who reported inability to tolerate statins resulted in a high mean baseline LDL-C level. The effects of cholesterol lowering on cardiovascular events in populations with lower pretreatment LDL-C was not studied.
- The trial selected patients using specific criteria for a high level of risk of a first cardiac event. Whether outcomes would be similar in patients identified using other criteria for an increased risk remains uncertain.

Summary of Safety[1]

Concomitant use of NEXLETOL with greater than 20 mg of simvastatin or 40 mg of pravastatin should be avoided due to the potential for increased risk of simvastatin- or pravastatin-related myopathy.

Discontinue NEXLETOL when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus. Because of the potential for serious adverse reactions in a breast-fed infant, breastfeeding is not recommended during treatment with NEXLETOL.

Report pregnancies to Esperion Therapeutics, Inc. Adverse Event reporting line at 1-833-377-7633.

Nissen SE, et al. Clear Outcomes: Primary Prevention Subgroup

Nissen SE, et al. CLEAR Outcomes

NEXLETOL® Prescribing Information

Contact Us: EsperionMedical.com

*All results are hypothesis generating and are descriptive in nature instead of confirmatory. Multiplicity is not adjusted/corrected.
Abbreviations: MACE-3: CV death, nonfatal MI, nonfatal stroke