Drug Monograph

Drug Name: **Nexletol™ (bempedoic acid) Tablet**
Drug Class: **Lipotropics, Statins (HMG-CoA Reductase Inhibitors and Combination Agents**
Prepared For: MO HealthNet
Prepared By: Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms:	Nexletol is available as an oral tablet containing 180 mg bempedoic acid
Manufacturer:	Manufactured for: Esperion Therapeutics, Inc., Ann Arbor, MI 48108.
Summary of Findings:	The efficacy of Nexletol was evaluated in a 52-week randomized, double blind, placebo controlled, clinical trial which enrolled patients with a history of heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease. Eligible patients included those on a maximally tolerated dose of lipid lowering therapy or a statin in combination with other lipid-lowering therapies. Efficacy was evaluated at week 12 and the primary outcome measure of the study was the percent change from baseline to week 12 in LDL-C. When compared to placebo, the addition of Nexletol to existing pharmacotherapeutic regimens resulted in a mean percent change in LDL-C from baseline to week 12 of -18% (95% CI: -20%, -16%; p<0.001).

Status Recommendation:	☐ Clinical Edit ☐ Open Access	☐ PA Required ☒ PDL
Type of PA Criteria:	☐ Appropriate Indications ☐ No PA Required	☒ Non-Preferred ☐ Preferred

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [1,2]

Familial hypercholesterolemia is an autosomal dominant disorder whose prevalence ranges between 1 in 200 and 1 in 500 individuals. Resultant elevations of low-density lipoprotein cholesterol (LDL-C) increases an individual's risk of early-onset atherosclerosis and cardiovascular events. Statins are recommended as initial therapy per current guidelines and are to be initiated at a low dose in order to reduce LDL-C levels. Add on therapy is recommended for those patients who are unable to reach their LDL-C goal on a maximally tolerated statin dose. Non-statin therapies utilized in such instances include ezetimibe, bile acid sequestrants, and PCSK9.

Dosage Form [3]

Nexletol: available as an oral tablet containing 180 mg bempedoic acid

Manufacturer [3]

Manufactured for: Esperion Therapeutics, Inc., Ann Arbor, MI 48108.

Indication(s) [3]

Nexletol and Nexlizet are indicated as an adjunct 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. The effect of Nexletol and Nexlizet on cardiovascular morbidity and mortality has not been established.

Clinical Efficacy [3,4,5] (mechanism of action/pharmacology, comparative efficacy)

Bempedoic acid is an adenosine triphosphate-citrate lyase (ACL) inhibitor that lowers LDL-C by inhibiting cholesterol synthesis in the liver. ACL is an enzyme that is upstream of HMG-CoA reductase in the cholesterol biosynthesis pathway.

Pharmacokinetics:

Absorption	Time to peak: 3.5 hours
Metabolism	Acyl glucuronide Reversible conversion to ESP15228, an active metabolite
Excretion	Urine 70%, feces 30%
Half-life	21 ± 11 hours

Clinical Trials Experience

"Evaluation of Long-Term Safety and Tolerability of ETC-1002 in High-Risk Patients With Hyperlipidemia and High CV Risk (CLEAR Harmony)"

STUDY 1 DESIGN	Randomized, double-blind, placebo-controlled, multicenter 52 week clinical trial (n=2230)
INCLUSION CRITERIA	• Fasting LDL-C ≥ 70 mg/dL • High cardiovascular risk (diagnosis of HeFH or ASCVD) • Be on maximally tolerated lipid-modifying therapy
EXCLUSION CRITERIA	• Total fasting triglyceride ≥ 500 mg/dL • Renal dysfunction or nephrotic syndrome or history of nephritis • Body Mass Index (BMI) ≥ 50 kg/m^2 • Significant cardiovascular disease or cardiovascular event in the past 3 months
TREATMENT REGIMEN	Patients were randomized 2:1 to receive either Nexletol or placebo as add-on to maximally tolerated lipid lowering therapy (defined as a maximally tolerated statin dose alone or in combination with other lipid-lowering therapies)
RESULTS	The primary efficacy outcome measure was the percent change of LDL-C from baseline to week 12. An 18% difference between Nexletol and placebo was evidenced from baseline to week 12 (95% CI: -20%, -16%; p < 0.001).
SAFETY	Discussed in the Adverse Effects section below.

Contraindications (3,4)

- None

Warnings and Precautions (3,4)

- Hyperuricemia – patients should contact healthcare provider if symptoms of hyperuricemia occur. Prescribers are recommended to assess urine uric acid when necessary and monitor for signs/symptoms of hyperuricemia, and initiate treatment with urate-lowering drugs as appropriate
- Tendon rupture – Nexletol should be immediately discontinued if tendon rupture occurs. Joint pain, swelling and inflammation are indicators that discontinuation may be necessary.

Adverse Effects (3,4)

Most common, ≥ 2 %	Nexletol + Statin ± Other Lipid Lowering Therapies (n =2009) %	Placebo (n=999) %
Upper respiratory tract infection	4.5	4.0
Muscle spasms	3.6	2.3
Hyperuricemia	3.5	1.1
Back pain	3.3	2.2
Abdominal pain or discomfort	3.1	2.2
Bronchitis	3.0	2.5
Pain in extremity	3.0	1.7
Anemia	2.8	1.9
Elevated liver enzymes	2.1	0.8

Drug Interactions [3,4]

- Simvastatin: Nexletol may cause an increase in simvastatin concentration and increase the risk of simvastatin-related myopathy. Concomitant therapy with Nexletol and simvastatin greater than 20 mg should be avoided.
- Pravastatin: Nexletol may cause an increase in pravastatin concentration and increase the risk of pravastatin-related myopathy. Concomitant therapy with Nexletol and pravastatin greater than 40 mg should be avoided.

Dosage and Administration [3,4]

The recommended daily dose of Nexletol is 180 mg once daily with or without food. Nexletol is to be taken in combination with maximally tolerated statin therapy.

Cost

Generic Name	Brand Name	Manufacturer	Dose	Cost**/ Month
Bempedoic acid	Nexletol	Esperion Therapeutics, Inc.	180 mg (1 tablet) once daily	$330

** Wholesale Acquisition Cost

Conclusion

Nexletol (bempedoic acid) showed improved ability to decrease LDL-C versus placebo in adults with a history of heterozygous familial hypercholesterolemia or established cardiovascular disease who require additional lowering of LDL-C. Nexletol should be used in combination with maximally tolerated statin therapy and can be considered as a reasonable add-on option when the current therapy regimen is unable to bring the patient to goal. Given that Nexletol must be administered with statin therapy, the risk of tendon rupture remains, and patients should be monitored for signs/symptoms on a regular basis. Hyperuricemia is a unique adverse reaction that was seen with the addition of Nexletol and should be monitored for appropriately.

Recommendation

This drug is being considered for inclusion in the state specific Preferred Drug List (PDL) as non-preferred.

References

1) NEXLETOL™ (bempedoic acid) [package insert]. Ann Arbor, MI: Esperion Therapeutics, Inc.; February 2020.
2) McGowan MP, Dehkordi SH, et. al. Diagnosis and Treatment of Heterozygous Familial Hypercholesterolemia. Journal of the American Heart Association. 16 December 2019 [cited 27 August 2020]. 8(24).
3) American College of Cardiology. Familial Hypercholesterolemia: Early Diagnosis and Treatment is Key for Cardiovascular Prevention. https://www.acc.org/latest-in-cardiology/articles/2020/04/16/09/58/familial-hypercholesterolemia. Accessed 27 August 2020.

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