MEDICAL MUTUAL®

Drug Policy

Policy:	ACL Inhibitors Nexletol (bempedoic acid) Nexlizet (bempedoic acid/ezetimibe)	Annual Review Date: 03/17/2022 Last Revised Date: 03/17/2022

OVERVIEW

Nexletol is an adenosine triphosphate-citrate lyase (ACL) inhibitor 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. Nexlizet contains the active ingredient present in Nexletol in combination with ezetimibe, a cholesterol absorption inhibitor, and is 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 effects of Nexletol and Nexlizet on cardiovascular morbidity and mortality have not been determined.

POLICY STATEMENT

This policy involves the use of Nexletol and Nexlizet. Prior authorization is recommended for pharmacy benefit coverage of Nexletol and Nexlizet. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Nexletol and Nexlizet as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Nexletol and Nexlizet be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Nexletol and Nexlizet is recommended in those who meet the following criteria:

1. <u>Heterozygous Familial Hypercholesterolemia (HeFH)</u>
Criteria. *Patient must meet the following criteria*

A. The patient is 18 years of age or older; AND
B. Nexletol or Nexlizet will be used in combination with a maximally tolerated statin (if patient is using simvastatin, dose should not exceed 20 mg/day; if patient is using pravastatin, dose should not exceed 40 mg/day) [documentation required]; AND
C. The patient will continue to follow an appropriate diet; AND

D. Nexletol or Nexlizet will be prescribed by or in consultation with a cardiologist, an endocrinologist, or a physician who specializes in the treatment of cardiovascular (CV) risk management and/or lipid disorders; AND

E. The patient has a diagnosis of "definite" HeFH as evidenced by the following:

- **a.** The patient has an LDL-C level of 190 mg/dL or greater after treatment with antihyperlipidemic agents, but prior to treatment with Nexletol or Nexlizet [documentation required]; AND
- **b.** The patient meets at least one of the following [documentation required]:
  - **i.** The patient has clinical manifestations of HeFH (e.g. tendon xanthomas, cutaneous xanthomas, arcus cornea, tuberous xanthomas, or xanthelasma); OR
  - **ii.** DNA-based evidence of an LDL-receptor (LDLR) mutation, familial defective apo B-100, an LDL-receptor adaptor protein 1 (LDLRAP1) gene mutation; OR
  - **iii.** The prescriber used the Simon Broome criteria and the patient meets the threshold for "definite" familial hypercholesterolemia; OR
  - **iv.** The prescriber used the Dutch Lipid Network diagnostic criteria and the patient's score is greater than 8 (indicating "definite" familial hypercholesterolemia); AND

F. The patient meets one of the following:

- **a.** If the request is for Nexletol: the patient has tried one high-intensity statin therapy (i.e. atorvastatin 40 mg or greater daily, rosuvastatin 20 mg or greater daily) for 3 or more continuous months [documentation required] AND the patent was adherent with therapy [documentation required] AND the patient's LDL-C remains at or above 70 mg/dL [documentation required]; OR
- **b.** If the request is for Nexlizet: the patient has tried one high-intensity statin therapy (i.e. atorvastatin 40 mg or greater daily, rosuvastatin 20 mg or greater daily) IN COMBINATION WITH ezetimibe (as single-entities or as a combination product) for 3 or more continuous months [documentation required] AND the patent was adherent with both therapies [documentation required] AND the patient's LDL-C remains at or above 70 mg/dL [documentation required]; OR
- **c.** The patient has been determined to be statin intolerant by meeting one of the following:
  - **i.** The patient experienced statin-related rhabdomyolysis (statin-induced muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness, elevated creatine kinase [CK] levels [e.g. 10 times the upper limit of normal or greater], and/or myoglobinuria [myoglobin present in urine]) [documentation required]; OR
  - **ii.** The patient experienced skeletal-related muscle symptoms (e.g. myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) AND meets both of the following:
    1. The skeletal-related muscle symptoms (e.g. myopathy or myalgia) occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products) [documentation required]; AND
    2. When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products), the skeletal-related muscle symptoms (e.g. myopathy or myalgia) resolved upon discontinuation of each respective statin therapy (atorvastatin AND rosuvastatin) [documentation required]

2. <u>Hyperlipidemia in Patients with Established Atherosclerotic Cardiovascular Disease (ASCVD)</u>
Criteria. *Patient must meet the following criteria*

A. The patient is 18 years of age or older; AND

B. Nexletol or Nexlizet will be used in combination with a maximally tolerated statin (if patient is using simvastatin, dose should not exceed 20 mg/day; if patient is using pravastatin, dose should not exceed 40 mg/day) [documentation required]; AND
C. The patient will continue to follow an appropriate diet; AND
D. Nexletol or Nexlizet will be prescribed by or in consultation with a cardiologist, and endocrinologist, or a physician who specializes in the treatment of cardiovascular (CV) risk management and/or lipid disorders; AND
E. The patient has one of the following conditions or diagnoses [documentation required]:
- **a.** Prior myocardial infarction (MI) or history of an acute coronary syndrome (ACS); OR
- **b.** Angina (stable or unstable); OR
- **c.** History of stroke or transient ischemic attack (TIA); OR
- **d.** Peripheral arterial disease (PAD); OR
- **e.** Coronary artery disease (CAD); OR
- **f.** The patient has undergone a coronary or other arterial revascularization procedure in the past (e.g. coronary artery bypass graft [CABG], percutaneous coronary intervention [PCI], etc.); AND

F. The patient meets one of the following:
- **a.** If the request is for Nexletol: the patient has tried one high-intensity statin therapy (i.e. atorvastatin 40 mg or greater daily, rosuvastatin 20 mg or greater daily) for 3 or more continuous months [documentation required] AND the patent was adherent with therapy [documentation required] AND the patient's LDL-C remains at or above 70 mg/dL [documentation required]; OR
- **b.** If the request is for Nexlizet: the patient has tried one high-intensity statin therapy (i.e. atorvastatin 40 mg or greater daily, rosuvastatin 20 mg or greater daily) IN COMBINATION WITH ezetimibe (as single-entities or as a combination product) for 3 or more continuous months [documentation required] AND the patent was adherent with both therapies [documentation required] AND the patient's LDL-C remains at or above 70 mg/dL [documentation required]; OR
- **c.** The patient has been determined to be statin intolerant by meeting one of the following:
  - **i.** The patient experienced statin-related rhabdomyolysis (statin-induced muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness, elevated creatine kinase [CK] levels [e.g. 10 times the upper limit of normal or greater], and/or myoglobinuria [myoglobin present in urine]) [documentation required]; OR
  - **ii.** The patient experienced skeletal-related muscle symptoms (e.g. myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) AND meets both of the following:
    1. The skeletal-related muscle symptoms (e.g. myopathy or myalgia) occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products) [documentation required]; AND
    2. When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products), the skeletal-related muscle symptoms (e.g. myopathy or myalgia) resolved upon discontinuation of each respective statin therapy (atorvastatin AND rosuvastatin) [documentation required]

Initial Approval/ Extended Approval.
A) *Initial Approval:* 3 months

B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Nexletol and Nexlizet have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Concomitant use of a PCSK9 Inhibitor (i.e. Praluent or Repatha).** Use of Nexletol or Nexlizet in combination with a PCSK9 inhibitor has not been adequately studied.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Nexletol [prescribing information]. Ann Arbor, MI: Esperion Therapeutics, Inc.; September 2021.
2. Nexlizet [prescribing information]. Ann Arbor, MI: Esperion Therapeutics, Inc.; September 2021.
3. Bempedoic acid. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 11 June 2021. Accessed on 17 March 2022.
4. Bempedoic acid. In: Lexi-Drugs. Lexicomp. Wolters Kluwer Clinical Drug Information, Inc.; Riverwoods, IL. Available at: http://www.online.lexi.com. Last updated 15 March 2022. Accessed on 17 March 2022.