BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

5.40.27

Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Cardiovascular Agents	**Original Policy Date:**	March 27, 2020
Subject:	Nexletol Nexlizet	**Page:**	1 of 6

Last Review Date: June 16, 2022

Nexletol Nexlizet

Description

Nexletol (bempedoic acid), Nexlizet (bempedoic acid and ezetimibe)

Background
Nexletol (bempedoic acid) is an adenosine triphosphate-citrate lyase (ACL) inhibitor that lowers low-density lipoprotein cholesterol (LCL-C) by inhibition of cholesterol synthesis in the liver. ACL is an enzyme upstream of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase in the cholesterol biosynthesis pathway. Inhibition of ACL results in decreased cholesterol synthesis in the liver and lowers LDL-C in blood via upregulation of low-density lipoprotein receptors. Nexlizet is a combination of bempedoic acid and ezetimibe; ezetimibe reduces blood cholesterol by inhibiting the absorption of cholesterol by the small intestine (1-2).

Regulatory Status
FDA Indicated for: Nexletol and Nexlizet are adenosine triphosphate-citrate lyase (ACL) inhibitors 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 (1-2).

Limitations of Use:
The effect of Nexletol and Nexlizet on cardiovascular morbidity and mortality has not been determined (1-2).

Nexletol and Nexlizet may increase blood uric acid levels, which may lead to the development of gout. Patients should be advised to contact their healthcare provider if symptoms of hyperuricemia occur. Serum uric acid should be assessed when clinically indicated (1-2).

Nexletol and Nexlizet are also associated with an increased risk of tendon rupture or injury. Nexletol or Nexlizet should be discontinued immediately if the patient experiences rupture of a tendon. Discontinuation should be considered if the patient experiences joint pain, swelling, or inflammation. Alternative therapy should be considered in patients with a history of tendon disorders or tendon rupture (1-2).

Nexletol and Nexlizet have an increased risk of myopathy when used with simvastatin > 20 mg or pravastatin > 40 mg. Patients should be advised to avoid concomitant use of Nexletol and Nexlizet with simvastatin > 20 mg or pravastatin >40 mg (1-2).

The safety and effectiveness of Nexletol and Nexlizet in pediatric patients less than 18 years of age have not been established (1-2).

Related policies
Juxtapid, Praluent, Repatha

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Nexletol and Nexlizet may be considered **medically necessary** in patients 18 years of age or older for the treatment of heterozygous familial hypercholesterolemia (HeFH) or for patients that have atherosclerotic cardiovascular disease and if the conditions indicated below are met.

Nexletol and Nexlizet may be considered **investigational** in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Heterozygous familial hypercholesterolemia (HeFH)
    a. LDL-C level ≥ 100 mg/dL in the past 90 days

AND ONE of the following:

i. Confirmed diagnosis by LDL-R DNA Sequencing Test or APOB (hypercholesterolemia) Mutation Analysis
ii. Dutch Lipid Clinic Network Criteria score > 5
iii. Simon-Broome Diagnostic Criteria for definite familial hypercholesterolemia

2. Atherosclerotic cardiovascular disease (ASCVD)
   a. LDL-C level ≥ 70 mg/dL in the past 90 days

   AND ONE of the following:
   i. Documented history of **ONE** of the following atherosclerotic cardiovascular disease (ASCVD) or cardiovascular events:
      1) Acute coronary syndrome
      2) Myocardial infarction
      3) Stable or unstable angina
      4) Coronary or other arterial revascularization procedure (such as PTCA, CABG)
      5) Transient ischemic attack (TIA)
      6) Peripheral arterial disease presumed to be of atherosclerotic origin
      7) Findings from CT angiogram or catheterization consistent with clinical ASCVD
   ii. At high risk for atherosclerotic cardiovascular disease (ASCVD) or cardiovascular event based on 10- year risk score used by **ONE** of the following tools:
      1) ASCVD Pooled Cohort Risk Assessment—score greater than or equal to 7.5%
      2) Framingham Risk Score—score greater than or equal to 20%

AND ALL of the following for **ALL** diagnoses:

1. Patient will be assessed for response (ie., LDL-C reduction) and adherence to the prescribed lipid lowering regimen
2. Patient has had an inadequate treatment response to statin therapy **OR** patient has an intolerance to higher dose/higher intensity statin therapy
3. Used in combination with maximally tolerated statin therapy
4. Prescriber agrees to monitor uric acid levels for hyperuricemia
5. **Nexletol only: NO** dual therapy with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, Juxtapid, or Nexlizet

6. **Nexlizet only: NO** dual therapy with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, Juxtapid, or Nexletol

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Heterozygous familial hypercholesterolemia (HeFH)
2. Atherosclerotic cardiovascular disease (ASCVD)

AND ONE of the following:

a. Percentage reduction of LDL-C level is greater than or equal to (≥) 40%, compared to the level immediately prior to starting therapy with Nexletol/Nexlizet
b. Absolute LDL-C is less than 100mg/dL

AND ALL of the following:

a. Patient will be assessed for adherence to the prescribed lipid lowering regimen
b. Prescriber agrees to monitor uric acid levels for hyperuricemia
c. **Nexletol only: NO** dual therapy with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, Juxtapid, or Nexlizet
d. **Nexlizet only: NO** dual therapy with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, Juxtapid, or Nexletol

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Drug	Quantity
Nexletol	90 tablets per 90 days **OR**
Nexlizet	90 tablets per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Nexletol (bempedoic acid) is an adenosine triphosphate-citrate lyase (ACL) inhibitor that lowers low-density lipoprotein cholesterol (LCL-C) by inhibition of cholesterol synthesis in the liver. ACL is an enzyme upstream of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase in the cholesterol biosynthesis pathway. Inhibition of ACL results in decreased cholesterol synthesis in the liver and lowers LDL-C in blood via upregulation of low-density lipoprotein receptors. Nexlizet is a combination of bempedoic acid and ezetimibe; ezetimibe reduces blood cholesterol by inhibiting the absorption of cholesterol by the small intestine. The safety and effectiveness of Nexletol and Nexlizet in pediatric patients less than 18 years of age have not been established (1-2).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of Nexletol and Nexlizet while maintaining optimal therapeutic outcomes.

References

1. Nexletol [package insert]. Ann Arbor, MI: Epserion Therapeutics, Inc.; September 2021.
2. Nexlizet [package insert]. Ann Arbor, MI: Epserion Therapeutics, Inc.; September 2021.

Policy History

Date	Action
March 2020	Addition to PA
June 2020	Annual review. Added initiation requirement of “Patient has had an inadequate treatment response to statin therapy OR patient has an intolerance to higher dose/higher intensity statin therapy” per FEP
September 2020	Annual review. Revised regulatory status section regarding concomitant use with simvastatin or pravastatin and added requirement to monitor uric acid levels
September 2021	Annual review and reference update
June 2022	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2021 and is effective on July 1, 2021.