

bempedoic acid Products (Nexletol™, Nexlizet™)

Policy # 00714

Original Effective Date: 12/14/2020

Current Effective Date: 08/01/2026

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member’s contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider bempedoic acid products (Nexletol, Nexlizet)™‡ to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility will be considered for bempedoic acid products (Nexletol, Nexlizet) when the following criteria are met:

Initial Authorization: (Patient must meet I, II, III, and IV)

- I. Patient is 18 years of age or older; AND
- II. Patient is compliant with any medications required for therapy prior to receiving authorization for bempedoic acid products (Nexletol, Nexlizet); AND
- III. bempedoic acid products (Nexletol, Nexlizet) will be used along with a maximally tolerated statin (in those who are not considered statin intolerant [see below for statin intolerance]); AND
- IV. Patient must meet ONE of the following (A, B, C, D, E, or F):
 - A. Patient has a diagnosis of Familial Hypercholesterolemia (FH) WITHOUT clinical atherosclerotic cardiovascular disease, defined as a WHO (World Health Organization)/Dutch Lipid Clinic Network score of greater than 8; AND
 - i. Patient’s low density lipoprotein cholesterol (LDL-C) is not adequately controlled (i.e., not at the LDL-C treatment goal of less than 70 mg/dL for the patient’s clinical risk category) with a high intensity statin (rosuvastatin [Crestor®]‡ 20-40 mg, atorvastatin [Lipitor®]‡ 40-80 mg) PLUS ezetimibe (Zetia®)‡ 10 mg daily for at least 3 months; OR
*(Note that the 3-month timeframe and the addition of ezetimibe (Zetia) are additional company requirements and will be denied as not medically necessary** if not met)*

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- ii. Patient's LDL-C is not adequately controlled (i.e., not at the LDL-C treatment goal of less than 70 mg/dL for the patient's clinical risk category) with a maximally tolerated stable daily statin (of any potency) PLUS ezetimibe (Zetia) 10 mg daily for at least 3 months ONLY if proof is given that a high potency maximum daily dose statin was not well tolerated; OR
*(Note that the 3-month timeframe and the addition of ezetimibe (Zetia) are additional company requirements and will be denied as not medically necessary** if not met)*
- B. Patient has a diagnosis of FH WITHOUT clinical atherosclerotic cardiovascular disease, defined as a WHO/Dutch Lipid Clinic Network score of greater than 8; AND
 - i. Patient's LDL-C is not adequately controlled (i.e., not at the LDL-C treatment goal of less than 70 mg/dL for the patient's clinical risk category) due to statin intolerance; AND
 - ii. Patient must meet ALL of the following criteria to be considered statin intolerant:
 - 1. Patient was unable to tolerate at least 2 different statins. (The inability to tolerate one statin will be accepted if the patient experienced rhabdomyolysis or clinically significant myonecrosis secondary to a statin. Rhabdomyolysis/myonecrosis is considered to be a muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness ALONG WITH either: a.) acute renal failure or myoglobinuria AND elevated creatine kinase levels [i.e., greater than or equal to 10 times the upper limit of normal] OR b.) elevated creatine kinase levels [i.e., greater than or equal to 10 times the upper limit of normal] alone); AND
 - 2. Patient's intolerance was associated with confirmed, intolerable statin-related adverse effects (i.e., skeletal related muscle symptoms [myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness)]); AND
 - 3. Patient's symptoms or biomarker changes resolved or showed significant improvement on dose decrease or discontinuation; OR
- C. Patient has the presence of clinical atherosclerotic cardiovascular disease (either FH or non-FH) OR patient is at high risk for a clinical ASCVD event but without established clinical ASCVD (see Policy Guidelines); AND
 - i. Patient's LDL-C is not adequately controlled (i.e., not at the LDL-C treatment goal of less than 55 mg/dL for very high-risk individuals or less than 70 mg/dL for high-risk individuals) with a high intensity statin (rosuvastatin [Crestor] 20-40 mg, atorvastatin [Lipitor] 40-80 mg) PLUS ezetimibe (Zetia) 10 mg daily for at least 3 months; OR
*(Note: that the 3-month timeframe and the addition of ezetimibe [Zetia] are additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

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- ii. Patient's LDL-C is not adequately controlled (i.e., not at the LDL-C treatment goal of less than 55 mg/dL for very high risk individuals or less than 70 mg/dL for high-risk individuals with a maximally tolerated stable daily statin (of any potency) PLUS ezetimibe (Zetia) 10 mg daily for at least 3 months ONLY if proof is given that a high potency maximum daily dose statin was not well tolerated; OR
*(Note that the 3-month timeframe and the addition of ezetimibe (Zetia) are additional company requirements and will be denied as not medically necessary** if not met)*
- D. Patient has the presence of clinical atherosclerotic cardiovascular disease (either FH or non-FH) OR patient is at high risk for a clinical ASCVD event but without established clinical ASCVD (see Policy Guidelines); AND
 - i. Patient's LDL-C is not adequately controlled (i.e., not at the LDL-C treatment goal of less than 55 mg/dL for very high risk individuals or less than 70 mg/dL for high-risk individuals) due to statin intolerance; AND
 - ii. Patient must meet ALL of the following criteria for statin intolerance:
 - 1. Patient was unable to tolerate at least 2 different statins. (The inability to tolerate one statin will be accepted if the patient experienced rhabdomyolysis or clinically significant myonecrosis secondary to a statin. Rhabdomyolysis/myonecrosis is considered to be a muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness ALONG WITH either: a.) acute renal failure or myoglobinuria AND elevated creatine kinase levels [i.e., greater than or equal to 10 times the upper limit of normal] OR b.) elevated creatine kinase levels [i.e., greater than or equal to 10 times the upper limit of normal] alone); AND
 - 2. Patient's intolerance was associated with confirmed, intolerable statin-related adverse effects (i.e., skeletal related muscle symptoms [myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness)]); AND
 - 3. Patient's symptoms or biomarker changes resolved or showed significant improvement on dose decrease or discontinuation; OR
- E. Patient has hypercholesterolemia (NOT associated with FH or clinical ASCVD); AND
 - i. Patient has a baseline (untreated) LDL-C greater than or equal to 190 mg/dL; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
 - ii. Patient's LDL-C is not adequately controlled (i.e., not at the LDL-C treatment goal of less than 100 mg/dL for the patient's clinical risk category) with a high-intensity statin (rosuvastatin [Crestor] 20-40 mg, atorvastatin [Lipitor] 40-80 mg) PLUS ezetimibe (Zetia) 10 mg daily for at least 3 months; OR
*(Note that the 3-month timeframe and the addition of ezetimibe (Zetia) are additional company requirements and will be denied as not medically necessary** if not met)*

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- iii. Patient's LDL-C is not adequately controlled (i.e., not at the LDL-C treatment goal of less than 100 mg/dL for the patient's clinical risk category) with a maximally tolerated stable daily statin (of any potency) PLUS ezetimibe (Zetia) 10 mg daily for at least 3 months ONLY if proof is given that a high-intensity statin was not well tolerated; OR
*(Note the 3-month timeframe and the addition of ezetimibe (Zetia) are additional company requirements and will be denied as not medically necessary** if not met)*
- F. Patient has hypercholesterolemia (not associated with FH or clinical ASCVD); AND
 - i. Patient has a baseline (untreated) LDL-C greater than or equal to 190 mg/dL; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
 - ii. Patient's LDL-C is not adequately controlled (i.e., not at the LDL-C treatment goal of less than 100 mg/dL for the patient's clinical risk category) due to statin intolerance; AND
 - iii. Patient must meet ALL of the following criteria for statin intolerance:
 - 1. Patient was unable to tolerate at least 2 different statins. (The inability to tolerate one statin will be accepted if the patient experienced rhabdomyolysis or clinically significant myonecrosis secondary to a statin. Rhabdomyolysis/myonecrosis is considered to be a muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness ALONG WITH either: a.) acute renal failure or myoglobinuria AND elevated creatine kinase levels [i.e., greater than or equal to 10 times the upper limit of normal] OR b.) elevated creatine kinase levels [i.e., greater than or equal to 10 times the upper limit of normal] alone); AND
 - 2. Patient's intolerance was associated with confirmed, intolerable statin-related adverse effects (i.e., skeletal related muscle symptoms [myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness)]); AND
 - 3. Patient's symptoms or biomarker changes resolved or showed significant improvement on dose decrease or discontinuation.

Re-authorization: (Patient must meet I and II)

- I. Patient previously met the initial criteria and received an approval for bempedoic acid products (Nexletol, Nexlizet); AND
- II. Patient has achieved clinically significant LDL-C lowering AND is compliant with bempedoic acid products (Nexletol, Nexlizet).
*(Note that the re-authorization criteria are additional company requirements and will be denied as not medically necessary** if not met)*

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of bempedoic acid products (Nexletol, Nexlizet) when the member has not tried and failed the required pre-requisite medications for a timeframe of at least 3 months to be **not medically necessary**.**

Based on review of available data, the Company considers the use of bempedoic acid products (Nexletol, Nexlizet) when the re-authorization criteria are NOT met to be **not medically necessary**.**

Based on review of available data, the Company considers the use of bempedoic acid products (Nexletol, Nexlizet) when ezetimibe (Zetia) has NOT been added to the patient's statin regimen to be **not medically necessary**.**

Based on review of available data, the Company considers the use of bempedoic acid products (Nexletol, Nexlizet) when the patient does not have a baseline (untreated) LDL-C greater than or equal to 190 mg/dL to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of bempedoic acid products (Nexletol, Nexlizet) when patient selection criteria are not met (except those listed above as **not medically necessary****) to be **investigational**.*

Policy Guidelines

The 2026 ACC/AHA/Multisociety Guideline on the Management of Dyslipidemia retires and replaces the 2018 ACC/AHA Guideline on the Management of Blood Cholesterol. A key difference from the 2018 guideline is the return of defined LDL-C treatment goals. The 2018 guideline emphasized statin intensity, percentage LDL-C reduction, and LDL-C thresholds for considering additional therapy, rather than assigning specific LDL-C goals by risk category. In contrast, the 2026 guideline provides a more goal-directed, lifelong, risk-based approach to lipid evaluation and treatment, with lower LDL-C goals for patients at higher ASCVD risk. Key updates also include expanded guidance across primary, secondary, and primordial prevention; routine lipid screening; lifestyle optimization; and earlier intensification of lipid-lowering therapy when LDL-C remains above goal.

The updated guidance supports lower LDL-C treatment goals based on ASCVD risk. In general, an LDL-C goal of less than 55 mg/dL is recommended for very high-risk patients, including those with clinical ASCVD at very high risk or marked subclinical atherosclerosis. An LDL-C goal of less than 70 mg/dL is recommended for high-risk patients, including those with clinical ASCVD not at very high risk, certain higher-risk primary prevention patients, and patients with subclinical atherosclerosis based on coronary artery calcium burden. For primary prevention patients with an LDL-C greater than or equal to 190 mg/dL, a goal of less than 100 mg/dL is generally recommended, although a lower goal of less than 70 mg/dL may be appropriate when additional risk factors are present. The NLA graphic below provides additional detail on risk stratification and LDL-C goal selection.

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Very High-Risk Individuals	
Major ASCVD Events ☐ ACS (< last 12 months) ☐ MI history (other than ACS above) ☐ Ischemic stroke history ☐ Symptomatic PAD*	Risk Assessment 2+ Major ASCVD Events or 1 Major ASCVD Event & 2+ High-Risk Conditions
High-Risk Conditions ☐ Age ≥ 65 years ☐ Diabetes mellitus ☐ Hypertension ☐ Smoker (current) ☐ LDL-C ≥ 100 mg/dL despite maximally tolerated statin & ezetimibe ☐ CHF history ☐ Heterozygous FH (LDL-C ≥ 190 mg/dL) ☐ CKD (eGFR 15-59 mL/min/1.73m²) ☐ Prior coronary artery bypass surgery^ ☐ Prior percutaneous coronary intervention^	
LDL-C Objective < 55 mg/dL	
*History of claudication with ABI <0.85 or previous revascularization or amputation ^Outside of the major ASCVD event(s)	
High-Risk Individuals	
Patients with 1+ of the Following: ☐ Type 2 diabetes mellitus ☐ Familial Hypercholesterolemia, without a prior event ☐ CAC score > 100 AU or ≥ 75th percentile of the CAC score distribution for a particular age and sex ☐ Clinical ASCVD without other high-risk features ☐ Primary prevention patient with an estimated 10-year event risk of ≥ 20% in a pooled cohort risk calculation	LDL-C Objective < 70 mg/dL
Patients with 1+ of the Following: ☐ No clinical ASCVD and baseline LDL-C ≥ 190 mg/dL ☐ Calculated 10-year ASCVD risk of 7.5-19.9% by AHA/ACC pooled cohort equation	LDL-C Objective < 100 mg/dL
Optimal LDL-C for healthy adults	< 100 mg/dL

The above chart comes from National Lipid Association 2025. Available at: [https://www.lipid.org/sites/default/files/files/LDL%20Management%20Simplified%20\(6_30_2020_5%20v2\).pdf](https://www.lipid.org/sites/default/files/files/LDL%20Management%20Simplified%20(6_30_2020_5%20v2).pdf)

Clinical ASCVD (includes one or more of the following):

- I. Myocardial infarction or other acute coronary syndrome
- II. Angina (stable or unstable)
- III. Coronary or other revascularization procedure
- IV. Transient ischemic attack
- V. Ischemic stroke
- VI. Atherosclerotic peripheral arterial disease (ABI of < 0.90)
- VII. Other documented atherosclerotic diseases such as
 - A. Clinically significant coronary atherosclerosis diagnosed by coronary angiography, stress test, stress echocardiography, or myocardial perfusion imaging
 - B. Renal atherosclerosis
 - C. Aortic aneurysm secondary to atherosclerosis
 - D. Carotid plaque (greater than or equal to 50% stenosis)

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Primary hyperlipidemia is defined as an elevated LDL-C that is not due to a secondary cause. For the purpose of this policy, this condition is not associated with established cardiovascular disease, heterozygous familial hypercholesterolemia (HeFH), or homozygous familial hypercholesterolemia (HoFH). It may also be referred to as combined hyperlipidemia, hypercholesterolemia (pure, primary), dyslipidemia, or increased/elevated LDL-C levels.

Background/Overview

Nexletol is an adenosine triphosphate-citrate lyase (ACL) inhibitor indicated to reduce the risk of MI and coronary revascularization in adults who are unable to take recommended statin therapy (including those not taking a statin) with established cardiovascular disease (CVD) or those at high risk for a CVD event but without established cardiovascular disease. Nexletol is also indicated 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. Nexlizet carries the same indication, but also contains an additional ingredient, ezetimibe, which is a cholesterol absorption inhibitor. Both products are dosed daily without regard to meals.

Hypercholesterolemia/Treatment Guidelines

Approximately 30% of the United States population has elevated LDL-C (low density lipoprotein cholesterol). There is also a subset of hypercholesterolemia, known as familial hypercholesterolemia, which can affect nearly 1 in 300 individuals. Familial hypercholesterolemia can further be broken down into homozygous and heterozygous forms of familial hypercholesterolemia. The homozygous form is by far the rarest with an estimated incidence of 1 in 1,000,000 individuals. The gold standard for the treatment of elevated LDL-C levels is a statin given along with ezetimibe (Zetia) to provide the greatest amount of LDL-C lowering. Statin products also have proven cardiovascular outcomes.

Genetic testing is available to determine whether or not an individual has familial hypercholesterolemia, however clinical signs/symptoms are often a more practical method of diagnosing this condition. Clinical studies have used the WHO/Dutch Lipid Clinic Network Familial Hypercholesterolemia diagnostic criteria to determine if an individual had familial hypercholesterolemia. A score of >8 is representative of “definite” familial hypercholesterolemia.

The criteria are located in the following chart:

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WHO (World Health Organization)/Dutch Lipid Clinic Network Familial Hypercholesterolemia Criteria

	Points
Criteria	
Family history	
First-degree relative with known premature* coronary and vascular disease, OR	1
First-degree relative with known LDL-C level above the 95th percentile	
First-degree relative with tendinous xanthomata and/or arcus cornealis, OR	2
Children aged less than 18 years with LDL-C level above the 95th percentile	
Clinical history	
Patient with premature* coronary artery disease	2
Patient with premature* cerebral or peripheral vascular disease	1
Physical examination	
Tendinous xanthomata	6
Arcus cornealis prior to age 45 years	4
Cholesterol levels mg/dL (mmol/liter)	
LDL-C $\geq$ 330 mg/dL ($\geq$ 8.5)	8
LDL-C 250 – 329 mg/dL (6.5–8.4)	5
LDL-C 190 – 249 mg/dL (5.0–6.4)	3
LDL-C 155 – 189 mg/dL (4.0–4.9)	1
DNA analysis	
Functional mutation in the <i>LDLR</i> , <i>apo B</i> or <i>PCSK9</i> gene	8
Diagnosis (diagnosis is based on the total number of points obtained)	
Definite Familial Hypercholesterolemia	>8
Probable Familial Hypercholesterolemia	6 – 8
Possible Familial Hypercholesterolemia	3 – 5
Unlikely Familial Hypercholesterolemia	<3

Premature = < 55 years in men; < 60 years in women

The 95th percentile in the “WHO/Dutch Lipid Clinic Network Familial Hypercholesterolemia Criteria” chart refers to the following LDL cholesterol values:

Men				Women			
Age (yr)	5th Percentile (LDL-C, mg/dL)	75th Percentile (LDL-C, mg/dL)	95th percentile (LDL-C, mg/dL)	Age (yr)	5th Percentile (LDL-C, mg/dL)	75th Percentile (LDL-C, mg/dL)	95th Percentile (LDL-C, mg/dL)
0–19	65	105	130	0–19	65	110	140
20–24	65	120	145	20–24	55	120	160
25–29	70	140	165	25–34	70	125	160

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Men				Women			
Age (yr)	5th Percentile (LDL-C, mg/dL)	75th Percentile (LDL-C, mg/dL)	95th percentile (LDL-C, mg/dL)	Age (yr)	5th Percentile (LDL-C, mg/dL)	75th Percentile (LDL-C, mg/dL)	95th Percentile (LDL-C, mg/dL)
30–34	80	145	185	35–39	75	140	170
35–39	80	155	190	40–44	75	145	175
40–44	85	155	185	45–49	80	150	185
45–69	90	165	205	50–54	90	160	200
70 +	90	165	185	55 +	95	170	215

The above chart comes from Lipid Research Clinic Data 1983. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK351/table/A968/?report=objectonly>

The following link for the ATP III- A distribution of LDL Cholesterol in the US Adult Population also provides percentile values. It is located at: <http://circ.ahajournals.org/content/106/25/3237/T2.expansion.html>.

Primary Hypercholesterolemia/Clinical Atherosclerotic Cardiovascular Disease

Primary hyperlipidemia is defined as an elevated LDL-C that is not due to a secondary cause. Given that there is no long-term cardiovascular evidence in subjects with non-familial hypercholesterolemia who do NOT have ASCVD, other proven products (e.g., statins) should be used until further evidence is provided. Note that Nexletol has cardiovascular outcomes data in patients with, or at high risk for atherosclerotic cardiovascular disease who are statin intolerant. This policy already provides coverage for these members, so no changes to coverage criteria are warranted.

Clinical ASCVD is defined as those with ACS or history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke or transient ischemic attack, or peripheral artery disease (PAD) presumed to be of atherosclerotic origin. Subclinical atherosclerosis is defined in this document as significant atherosclerotic plaque observed in an asymptomatic patient on any of the following diagnostic studies: coronary artery calcification noted on computed tomography (CT) studies, including calcium scoring, cardiac CT coronary angiography, chest CT for ruling out pulmonary embolism, chest CT for lung cancer screening, or diagnostic chest CT; carotid plaque noted on carotid ultrasound or angiography; or abnormal ankle-brachial index or plaque noted on peripheral arterial angiography. For clarity, calcium scoring alone is not indicative of ASCVD.

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Statin Intolerance

Statins have been associated with muscle-related adverse effects such as myalgia (e.g., muscle aches, soreness, stiffness, or tenderness), myopathy (muscle weakness), and/or myositis (muscle inflammation). Although the incidence is variable, muscle adverse effects are reported in around 5% of patients receiving statins, but may be due to other causes (e.g., excessive exercise, other medical conditions [hypothyroidism], non-statin medications). It is advisable to assess for drug interactions as well as to check vitamin D levels and thyroid function status. Rhabdomyolysis, which is uncommon with statin therapy, is a severe muscle-related adverse effect that results in muscle breakdown associated with muscle-related symptoms (e.g., muscle pain, weakness, tenderness) along with acute renal failure and elevated creatine kinase [CK] levels (myonecrosis). In patients with statin-related muscle adverse events, symptoms may not re-occur if the patient switches to a different statin therapy. Pravastatin and fluvastatin appear to have much less intrinsic muscle toxicity than other statins and could be considered for those who had statin related intolerable muscle symptoms.

In 2014, the NLA Statin Intolerance Panel published an update. It was stated that most statin intolerance is due to myalgia. The strongest evidence at present for statin intolerance in a population is that myalgia appears but then remits with withdrawal but reoccurs with re-challenge. The incidence of statin intolerance is widely variable. The Panel states that statins are among the safest medications available. The Panel does advise that due to statin benefits, it is safe to recommend a patient continue statin therapy even when some degree of statin intolerance is present, if the patient can reasonably tolerate the statin. A pivotal trial with Praluent called ODYSSEY ALTERNATIVE defined statin intolerance as the inability to take at least two different statins due to muscle-related adverse effects, of which one statin was administered at the lowest approved starting dose. Data also suggest that many patients who are re-challenged with statin therapy after an adverse event may be able to tolerate statin therapy long-term. Of note, in the ODYSSEY ALTERNATIVE trial with Praluent, 69.8% of patients who were considered statin intolerant were treated with atorvastatin 20 mg daily and completed the double-blind 24-week portion of the trial. This suggests that re-challenge with a statin in those purported to be statin intolerant is reasonable and may lead to successful use of a statin therapy.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Nexletol and Nexlizet are both 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) with established CVD or high risk for a CVD event but without established CVD and as an adjunct to diet, in combination with other low-density lipoprotein cholesterol (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 heterozygous familial hypercholesterolemia (HeFH).

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Nexletol

Primary Hyperlipidemia Trials in Adults

The efficacy of Nexletol was investigated in two multicenter, randomized, double-blind, placebo-controlled trials that enrolled 3,009 adult patients with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who were on maximally tolerated statin therapy. Demographics and baseline disease characteristics were balanced between the treatment arms in all trials. In both trials, the maximum LDL-C lowering effects occurred at Week 4.

Study 1 was a multicenter, randomized, double-blind, placebo-controlled 52-week trial that evaluated safety and efficacy of bempedoic acid in patients with HeFH and/or ASCVD. Efficacy of Nexletol was evaluated at Week 12. The trial included 2,230 patients randomized 2:1 to receive either Nexletol (n = 1488) or placebo (n = 742) as add-on to a maximally tolerated lipid lowering therapy. Maximally tolerated lipid lowering therapy was defined as a maximally tolerated statin dose alone or in combination with other lipid-lowering therapies. Patients were stratified by presence of HeFH and by baseline statin intensity. Patients on simvastatin 40 mg per day or higher and patients taking PCSK9 inhibitors were excluded from the trial.

The primary efficacy outcome measure of the study was the percent change from baseline to Week 12 in LDL-C. The difference between Nexletol and placebo in mean percent change in LDL-C from baseline to Week 12 was -18% (95% CI: -20%, -16%; p < 0.001).

Study 2 was a multi-center, randomized, double-blind, placebo-controlled, 52-week trial in patients with HeFH and/or ASCVD. Efficacy of Nexletol was evaluated at Week 12. The trial included 779 patients randomized 2:1 to receive either Nexletol (n = 522) or placebo (n = 257) as add-on to a maximally tolerated lipid lowering therapy. Maximally tolerated lipid lowering therapy was defined as a maximally tolerated statin dose alone or in combination with other lipid-lowering therapies. Patients were stratified by presence of HeFH and baseline statin intensity. Patients on simvastatin 40 mg/day or higher were excluded from the trial.

The primary efficacy outcome measure of the study was the percent change from baseline to Week 12 in LDL-C. The difference between Nexletol and placebo in mean percent change in LDL-C from baseline to Week 12 was -17 % (95% CI: -21%, -14%; p < 0.001).

Cardiovascular Outcomes Trial in Adults with CVD or at High Risk for CVD

Trial 3 was a randomized, double-blind, placebo-controlled, event-driven trial in 13,970 adult patients with established CVD (70%) or at high risk for a CVD event but without CVD (30%) who were not receiving recommended statin dosages. Patients with established CVD had documented

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history of coronary artery disease, symptomatic peripheral arterial disease, and/or cerebrovascular atherosclerotic disease. Patients without established CVD were considered at high risk for CVD based on meeting at least one of the following criteria:

- Diabetes mellitus (type 1 or type 2) in females over 65 years of age or males over 60 years of age;
- A Reynolds Risk score > 30% or a SCORE Risk score > 7.5% over 10 years. Reynolds risk score and SCORE risk score evaluate a 10-year risk of having a cardiovascular (CV) event. The Reynolds risk score is based on the following risk factors: sex, age, smoking status, systolic blood pressure, total cholesterol, HDL cholesterol, high sensitivity C-reactive protein (hsCRP), and familial history of CVD events. LDL-C is an additional risk factor considered in SCORE risk score; OR
- A coronary artery calcium score > 400 Agatston units at any time in the past.

Patients were randomized 1:1 to receive either oral Nexletol 180 mg per day (n = 6,992) or placebo (n = 6,978), alone or as an add on to other background lipid-lowering therapies. Background therapy could include less than low-intensity statin dosages.

The risk for the primary composite endpoint (MACE-4: time to first occurrence of CV death, nonfatal myocardial infarction, nonfatal stroke, or coronary revascularization; p = 0.0037) and the key secondary composite endpoint (MACE-3: time to first occurrence of CV death, nonfatal myocardial infarction, or nonfatal stroke; p = 0.0058) was significantly reduced in Nexletol treated patients compared to placebo-treated patients. The difference between the Nexletol and placebo groups in mean percent change in LDL-C from baseline to Month 6 was -20% (95% CI: -21%, -19%).

Nexlizet

The efficacy of Nexlizet was investigated in a single, multi-center, randomized, double-blind, placebo-controlled, parallel group trial that enrolled 301 patients with heterozygous familial hypercholesterolemia, established atherosclerotic cardiovascular disease, or multiple risk factors for cardiovascular disease on maximally tolerated statin therapy. The efficacy of Nexlizet in patients with multiple risk factors for cardiovascular disease has not been established.

Study 1 randomized patients 2:2:2:1 to receive either Nexlizet (180 mg of bempedoic acid and 10 mg of ezetimibe) (n = 86), bempedoic acid 180 mg (n = 88), ezetimibe 10 mg (n = 86), or placebo (n = 41) once daily as add-on to maximally tolerated statin therapy. Patients were stratified by cardiovascular risk and baseline statin intensity. Patients on simvastatin 40 mg per day or higher and patients taking non-statin lipid-lowering therapy (including fibrates, niacin, bile acid sequestrants, ezetimibe, and PCSK9 inhibitors) were excluded from the trial.

The primary efficacy outcome measure of the study was the percent change from baseline to Week 12 in LDL-C. The difference between Nexlizet and placebo in mean percent change in LDL-C from baseline to Week 12 was -38% (95% CI: -47%, -30%; p < 0.001). High-density lipoprotein (HDL) and triglycerides (TG) were examined as exploratory endpoints and were not included in the statistical hierarchy. The difference between Nexlizet and placebo in mean percent change from baseline to Week 12 was -5% for HDL and median percent change from baseline to Week 12 was -11% for TG. The maximum LDL-C lowering effect was observed at Week 4.

Policy # 00714

Original Effective Date: 12/14/2020

Current Effective Date: 08/01/2026

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bempedoic acid Products (NexletolTM, NexlizetTM)

Policy # 00714

Original Effective Date: 12/14/2020

Current Effective Date: 08/01/2026

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Policy History

Original Effective Date: 12/14/2020

Current Effective Date: 08/01/2026

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| 11/05/2020 | Medical Policy Committee review |
| 11/11/2020 | Medical Policy Implementation Committee approval. New policy. |
| 11/04/2021 | Medical Policy Committee review |
| 11/10/2021 | Medical Policy Implementation Committee approval. No change to coverage. |
| 11/03/2022 | Medical Policy Committee review |
| 11/09/2022 | Medical Policy Implementation Committee approval. No change to coverage. |
| 11/02/2023 | Medical Policy Committee review |
| 11/08/2023 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged. |
| 12/05/2024 | Medical Policy Committee review |
| 12/11/2024 | Medical Policy Implementation Committee approval. Updated policy to reflect new FDA labeled indication, to reduce the risk of MI and coronary revascularization in adults who are unable to take recommended statin therapy in patients who have established CVD or are at high risk for a CVD event, but do not have established CVD. Updated policy to reflect updated FDA labeled indication, to reduce LDL-C in adults with primary hyperlipidemia. Added the use of Nexlizet/Nexletol for NON-familial hypercholesterolemia WITHOUT the presence of clinical atherosclerotic cardiovascular disease as not medically necessary. |
| 08/07/2025 | Medical Policy Committee review |
| 08/13/2025 | Medical Policy Implementation Committee approval. Updated LDL-C goals based on current guidance from the NLA and 2022 ACC Expert Consensus Decision Pathway Statements. Updated criteria for the clinical ASCVD indication to include coverage for patients who are at risk of clinical ASCVD but who have not had an ASCVD event. Added policy guidelines section. Updated background information. |
| 07/21/2026 | Medical Policy Committee review |
| 07/22/2026 | Medical Policy Implementation Committee approval. Added new indication, hypercholesterolemia to the policy with criteria. Updated relevant information in the Policy Guidelines section to include updates from 2026 ACC guidelines. |

Next Scheduled Review Date: 07/2027

Policy # 00714

Original Effective Date: 12/14/2020

Current Effective Date: 08/01/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.