

Drug Policy

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| Policy: | Nexlizet™ (bempedoic acid and ezetimibe tablets - Esperion) | Annual Review Date: 03/16/2023 |
| | | Last Revised Date: 06/15/2023 |

OVERVIEW

Nexlizet contains bempedoic acid, an adenosine triphosphate-citrate lyase inhibitor, and ezetimibe, a cholesterol absorption inhibitor. It is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with the following:¹

- Established **atherosclerotic cardiovascular disease (ASCVD)** for those who require additional lowering of low-density lipoprotein cholesterol (LDL-C).
- **Heterozygous familial hypercholesterolemia (HeFH)** for those who require additional lowering of LDL-C.

The effects of Nexlizet on cardiovascular (CV) morbidity and mortality have not been established.¹ The safety and effectiveness have not been established in pediatric patients.

POLICY STATEMENT

This policy involves the use of Nexlizet. Prior authorization is recommended for pharmacy benefit coverage of 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 Nexlizet as well as the monitoring required for adverse events and long-term efficacy, initial approval requires 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 Nexlizet is recommended in those who meet the following criteria:

FDA-Approved Indications

- 1. Atherosclerotic Cardiovascular Disease.** Approve for 1 year if the patient meets all of the following (A or B):
 - A) Initial Therapy.** Approve if the patient meets all of the following (i, ii, and iii):
 - i.** Patient is ≥ 18 years of age; AND
 - ii.** Patient has had one of the following conditions or diagnoses (a, b, c, d or e):

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- a) A previous myocardial infarction or a history of an acute coronary syndrome; OR
- b) Angina (stable or unstable); OR
- c) A past history of stroke or transient ischemic attack; OR
- d) Peripheral arterial disease; OR
- e) Patient has undergone a coronary or other arterial revascularization procedure in the past; AND
Note: Examples include coronary artery bypass graft surgery, percutaneous coronary intervention, angioplasty, and coronary stent procedures.

iii. Patient meets one of the following criteria (a or b):

- a) Patient meets both of the following [(1) and (2)]:
 - (1) Patient has tried one high-intensity statin therapy (i.e., atorvastatin \geq 40 mg daily; rosuvastatin \geq 20 mg daily [as a single-entity or as a combination product]) for \geq 8 continuous weeks; AND
 - (2) Low-density lipoprotein cholesterol level after therapy regimen remains \geq 70 mg/dL; OR
- b) Patient has been determined to be statin intolerant by meeting one of the following criteria [(1) or (2)]:

(1) Patient experienced statin-related rhabdomyolysis; OR

Note: Statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a \geq 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR

(2) Patient meets all of the following [(a), (b), and (c)]:

(a) Patient experienced skeletal-related muscle symptoms; AND

Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness).

(b) The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); AND

(c) When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); OR

Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

B) Patient Currently Receiving Nexlizet. Approve if according to the prescriber, the patient has experienced a response to therapy.

Note: Examples of a response to therapy include decreasing low-density lipoprotein cholesterol (LDL-C), total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels. Also, if the patient is currently receiving the requested therapy but has not previously received approval of Nexlizet for this specific indication through the Coverage Review Department, review under criteria for Initial Therapy. If the patient is restarting therapy with Nexlizet, Initial Therapy criteria must be met.

2. **Heterozygous Familial Hypercholesterolemia (HeFH).** Approve for 1 year if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve if the patient meets all of the following (i, ii, or iii):

- i. Patient is \geq 18 years of age; AND
- ii. Patient meets one of the following criteria (a, b, or c):

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- a) Patient has an untreated low-density lipoprotein cholesterol (LDL-C) level ≥ 190 mg/dL (prior to treatment with antihyperlipidemic agents); OR
 - b) Patient has genetic confirmation of heterozygous familial hypercholesterolemia by mutations in the low-density lipoprotein receptor, apolipoprotein B, proprotein convertase subtilisin kexin type 9 or low-density lipoprotein receptor adaptor protein 1 gene; OR
 - c) Patient has been diagnosed with heterozygous familial hypercholesterolemia by meeting one of the following diagnostic criteria thresholds [(1) or (2)]:
 - (1) Prescriber confirms that the Dutch Lipid Network criteria score was > 5 ; OR
 - (2) Prescriber confirms that Simone Broome criteria met the threshold for “definite” or “possible (or probable)” familial hypercholesterolemia; AND
- iii. Patient meets one of the following (a or b):
- a) Patient meets both of the following [(1) and (2)]:
 - (1) Patient has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin ≥ 20 mg daily [as a single-entity or as a combination product]) for ≥ 8 continuous weeks; AND
 - (2) LDL-C level after this treatment regimen remains ≥ 70 mg/dL; OR
 - b) Patient has been determined to be statin intolerant by meeting one of the following [(1) or (2)]:
 - (1) Patient experienced statin-related rhabdomyolysis; OR
Note: Statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR
 - (2) Patient meets all of the following [(a), (b), and (c)]:
 - (a) Patient experienced skeletal-related muscle symptoms; AND
Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness).
 - (b) The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); AND
 - (c) When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); OR
Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.
- B) Patient Currently Receiving Nexlizet. Approve if according to the prescriber, the patient has experienced a response to therapy.
Note: Examples of a response to therapy include decreasing low-density lipoprotein cholesterol (LDL-C), total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels. Also, if the patient is currently receiving the requested therapy but has not previously received approval of Nexlizet for this specific indication through the Coverage Review Department, review under criteria for Initial Therapy. If the patient is restarting therapy with Nexlizet, Initial Therapy criteria must be met.

Initial Approval/ Extended Approval.

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A) Initial Approval: 1 year

B) Extended Approval: 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Nexlizet is not recommended in the following situations:

1. 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.

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APPENDIX A

Simon Broome Register Diagnostic Criteria.⁹

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| Definite Familial Hypercholesterolemia |
| Raised cholesterol |
| --Total cholesterol greater than 6.7 mmol/L (260 mg/dL) or LDL-C > 4.0 mmol/L (155 mg/dL) in a child < 16 years; OR |
| --Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in an adult (aged > 16 years); |
| AND |
| --Tendon xanthomas in the patient or in a first (parent, sibling, or child) or second-degree relative (grandparent, aunt, or uncle); |
| OR |
| DNA-based evidence of LDL-receptor, familial defective APOB, or PCSK9 mutation. |
| Possible (or Probable) Familial Hypercholesterolemia |
| Raised cholesterol |
| --Total cholesterol greater than 6.7 mmol/L (260 mg/dL) or LDL-C > 4.0 mmol/L (155 mg/dL) in a child < 16 years; OR |
| --Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in an adult (aged > 16 years); |
| AND |
| Family history of premature myocardial infarction younger than 50 years of age in second-degree relative or younger than 60 years of age in first-degree relative; |
| OR |
| Raised cholesterol |
| --Total cholesterol greater than 6.7 mmol/L (260 mg/dL) or LDL-C > 4.0 mmol/L (155 mg/dL) in a child < 16 years; OR |
| --Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in an adult (aged > 16 years); |
| AND |
| Family history of raised cholesterol > 7.5 mmol (290 mg/dL) in adult first-degree or second-degree relative or > 6.7 mmol/L (260 mg/dL) in child or sibling aged < 16 years. |

LDL-C – Low-density lipoprotein cholesterol; LDL – Low-density lipoprotein; APOB – Apolipoprotein B; PCSK9 – Proprotein convertase subtilisin kexin type 9.

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APPENDIX B.

Dutch Lipid Network Criteria.⁸

| Criteria | Score |
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| Family History | |
| First-degree relative with known premature coronary and/or vascular disease (men < 55 years, women < 60 years) | 1 |
| First degree relative with known LDL-C > 95 th percentile for age and sex | 1 |
| First-degree relative with tendon xanthomata and/or arcus cornealis, OR | 2 |
| Children aged < 18 years with LDL-C > 95 th percentile for age and sex | 2 |
| Clinical History | |
| Patient with premature CAD (age as above) | 2 |
| Patient with premature cerebral or peripheral vascular disease (age as above) | 1 |
| Physical Examination | |
| Tendon xanthomas | 6 |
| Arcus cornealis at age < 45 years | 4 |
| LDL-C | |
| LDL-C ≥ 8.5 mmol/L (330 mg/dL) | 8 |
| LDL-C 6.5 to 8.4 mmol/L (250 to 329 mg/dL) | 5 |
| LDL-C 5.0 to 6.4 mmol/L (190 to 249 mg/dL) | 3 |
| LDL-C 4.0 to 4.9 mg/dL (155 to 189 mg/dL) | 1 |
| DNA analysis | |
| Functional mutation LDLR, APOB or PCSK9 gene | 8 |
| Stratification | |
| Definite familial hypercholesterolemia | > 8 |
| Probable familial hypercholesterolemia | 6 to 8 |
| Possible familial hypercholesterolemia | 3 to 5 |
| Unlikely familial hypercholesterolemia | < 3 |

LDL-C – Low-density lipoprotein cholesterol; CAD – Coronary artery disease; LDLR – Low-density lipoprotein receptor; APOB – Apolipoprotein B; PCSK9 – Proprotein convertase subtilisin kexin type 9.