Bempedoic Acid Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
2/1/2024	10/1/2020

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Nexletol® (bempedoic acid) Tablet	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. Limitation of Use: The effect of bempedoic acid on cardiovascular morbidity and mortality has not been determined.		1
Nexlizet® (bempedoic acid/ezetimibe) Tablet	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. Limitation of Use: The effect of bempedoic acid on cardiovascular morbidity and mortality has not been determined.		2

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Familial hypercholesterolemia	Familial hypercholesterolemia (FH) is a common yet underdiagnosed autosomal dominant disorder that affects 1 in 220 individuals globally. An individual who is heterozygous for FH (HeFH) has a 50% chance of passing the gene to his or her children. FH is characterized by lifelong elevation of low-density lipoprotein cholesterol (LDL-C) and, if untreated, leads to early-onset atherosclerosis and increased risk of cardiovascular events. Affected men and women who are untreated have a 30% to 50% risk of a fatal or nonfatal cardiac event by ages 50 and 60 years, respectively. FH is generally a silent disease. Given the broad range of causes of hypercholesterolemia and early-onset coronary artery disease (CAD), it is not surprising that FH is not always in the differential diagnosis for healthcare professionals when confronted with a patient presenting with early CAD. Although diagnosis can be made on the basis of clinical features, genetic testing may offer additional insight regarding cardiac risk and diagnosis. There are no internationally agreed-upon criteria for the diagnosis of FH, so useful diagnostic criteria have been developed. Two of the criteria, the UK Simon Broome system and the Dutch Lipid Clinic Network criteria incorporate genetic tests into their algorithm. (3)
Heterozygous familial hypercholesterolemia (HeFH)	The Simon Broome Register criteria and Dutch Lipid Clinic Network criteria have been developed to aid in diagnosing HeFH.(5) Definitive diagnosis of HeFH according to Simon Broome diagnostic criteria requires the patient has one of the following:(3,5,10) A total cholesterol level greater than 6.7 mmol/L (260 mg/dL) or low-density lipoprotein cholesterol (LDL-C) level greater than 4.0 mmol/L (155 mg/dL) in a child younger than 16 years of age, or, a total cholesterol greater than 7.5 mmol/L (290 mg/dL) or LDL-C greater than 4.9 mmol/L (190 mg/dL) in an adult (levels either pre-treatment or highest on treatment) PLUS tendon xanthomas in the patient, or in first-

degree relative (parent, sibling or child), or in second-degree relative (e.g., grandparent, uncle or aunt)
OR
DNA-based evidence of an LDL receptor (LDLR) mutation, familial defective Apo B-100, proprotein convertase subtilisin/kexin type 9 (PCSK9), or low-density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene mutation

The Dutch Lipid Clinic Network criteria assign points based on cholesterol levels, family history of hyperlipidemia or cardiovascular disease, clinical presentation, and/or presence of identified genetic mutation affecting plasma LDL-C.(5,7) A definitive diagnosis of HeFH can be made in patients with greater than 8 points. A probable diagnosis of HeFH can be made in patients with a score of 6-8 points.

Dutch Lipid Clinic Network criteria for diagnosis of heterozygous familial hypercholesterolemia.(7)

Group 1: Family history	**Points**
• First-degree relative with known premature (less than 55 years, men; ;less than 60 years, women) coronary heart disease (CHD)	1
• First-degree relative with known LDL cholesterol greater than 95th percentile by age and gender for country	1
• First-degree relative with tendon xanthoma and/or corneal arcus	2
• Children less than 18 years with LDL cholesterol greater than 95th percentile by age and gender for country	2
Group 2: Clinical history	**Points**
• Subject has premature (less than 55 years, men; less than 60 years, women) CHD	2
• Subject has premature (less than 55 years, men; less than 60 years, women) cerebral or peripheral vascular disease	1
Group 3: Physical examination	**Points**
• Tendon xanthoma	6
• Corneal arcus in a person less than 45 years	4
Group 4: Biochemical results (LDL-C)	**Points**
• Greater than 8.5 mmol/L (greater than 325 mg/dL)	8
• 6.5–8.4 mmol/L (251–325 mg/dL)	5
• 5.0–6.4 mmol/L (191–250 mg/dL)	3
• 4.0–4.9 mmol/L (155–190 mg/dL)	1
Group 5: Molecular genetic testing (DNA analysis)	**Points**
• Causative mutation shown in the LDLR, APOB, or PCSK9 genes	8
Use and Interpretation	

	Assign only one score, the highest applicable, per group then add the points from each group to achieve the total score Definitive FH diagnosis: Greater than 8 points Probable FH diagnosis: 6 to 8 points Possible FH diagnosis: 3 to 5 points Unlikely FH diagnosis: 0 to 2 points
Atherosclerotic Cardiovascular Disease (ASCVD) - Secondary Prevention	The AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline considers having at least one of the following as clinical ASCVD:(9,11) • Acute coronary syndrome (ACS) • History of myocardial infarction (MI) • Stable or unstable angina • Coronary heart disease (CHD) or other arterial revascularization • Stroke • Transient ischemic attack (TIA) • Peripheral artery disease (PAD) including aortic aneurysm
Safety	Nexletol has no contraindication or box warnings.(1) Nexlizet has no box warnings, but has the following contraindication:(2) • Known hypersensitivity to ezetimibe tablets

REFERENCES

Number	Reference
1	Nexletol prescribing information. Esperion Therapeutics, Inc. June 2022.
2	Nexlizet prescribing information. Esperion Therapeutics, Inc. September 2021.
3	McGowan MP, Dehkordi SH, Moriarty PM, et. al. "Diagnosis and Treatment of Heterozygous Familial Hypercholesterolemia". JAHA 8 (24) 2019. Available at: https://www.ahajournals.org/doi/10.1161/JAHA.119.013225
4	~~Identification and Management of Familial Hypercholesterolemia. Simon Broome Diagnostic criteria for index individuals and relatives. Available at: http://www.ncbi.nlm.nih.gov/books/NBK53810/~~ Reference no longer used.
5	National Collaborating Centre for Primary Care (UK). Identification and Management of Familial Hypercholesterolaemia (FH) [Internet]. London: Royal College of General Practitioners (UK); 2008 Aug. (NICE Clinical Guidelines, No. 71.) 3, Diagnosis. Available from: https://www.nice.org.uk/guidance/CG71.
6	~~World Health Organization. Familial Hypercholesterolaemia (FH): Report of a second WHO consultation. Geneva: World Health Organization; 1999. Available at: https://apps.who.int/iris/handle/10665/66346~~. Reference no longer used.
7	Nordestgaard BG, Chapman MJ, Humphries ST, et al; for the European Atherosclerosis Society Consensus Panel. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease. Eur Heart J. 2013. doi.10.1093/eurheartj/eht273. https://pubmed.ncbi.nlm.nih.gov/23956253/
8	~~Gidding S, Champagne M, Ferranti S, et al. The Agenda for Familial Hypercholesterolemia. A Scientific Statement From the American Heart Association. Circulation. 2015; 132:00-00 https://www.ahajournals.org/doi/10.1161/CIR.0000000000000297~~. Reference no longer used.

Number	Reference
9	2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol. Journal of the American College of Cardiology. https://www.ahajournals.org/doi/10.1161/CIR.0000000000000625
10	Henderson, R., O'Kane, M., McGilligan, V. et al. The genetics and screening of familial hypercholesterolaemia. *J Biomed Sci* **23**, 39 (2016). https://doi.org/10.1186/s12929-016-0256-1
11	Writing Committee, Birtcher, K., Allen, L., et al., 2022 ACC Expert Consensus Decision Pathway for Integrating Atherosclerotic Cardiovascular Disease and Multimorbidity Treatment: A Framework for Pragmatic, Patient-Centered Care: A Report of the American College of Cardiology Solution Set Oversight Committee. Journal of the American College of Cardiology. 81 (3) 2023. https://www.jacc.org/doi/10.1016/j.jacc.2022.08.754

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Nexletol	bempedoic acid tab	180 MG	M ; N ; O ; Y	N		
Nexlizet	bempedoic acid-ezetimibe tab	180-10 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Nexletol	Bempedoic Acid Tab 180 MG	180 MG	30	Tablets	30	DAYS			
Nexlizet	Bempedoic Acid-Ezetimibe Tab 180-10 MG	180-10 MG	30	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Nexletol	bempedoic acid tab	180 MG	Medicaid
Nexlizet	bempedoic acid-ezetimibe tab	180-10 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Nexletol	Bempedoic Acid Tab 180 MG	180 MG	Medicaid
Nexlizet	Bempedoic Acid-Ezetimibe Tab 180-10 MG	180-10 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ALL of the following are met: 1. ONE of the following: A. BOTH of the following: 1. The patient has ONE of the following: A. A diagnosis of heterozygous familial hypercholesterolemia (HeFH) confirmed by ONE of the following: 1. Genetic confirmation of one mutant allele at the LDLR, Apo-B, PCSK9, or ARH adaptor protein 1/LDLRAP1 gene locus **OR** 2. BOTH of the following: A. ONE of the following: 1. History of total cholesterol greater than 290 mg/dL (greater than 7.5 mmol/L) (pretreatment or highest level while on treatment) **OR** 2. History of LDL-C greater than 190 mg/dL (greater than 4.9 mmol/L) (pretreatment or highest level while on treatment) **AND** B. History of tendon xanthomas in ONE of the following: 1. The patient **OR** 2. The patient's first degree relative (i.e., parent, sibling, or child) **OR** 3. The patient's second degree relative (e.g., grandparent, uncle, or aunt) **OR** 3. The Patient has a Dutch Lipid Clinic Network Criteria score of greater than 5 **OR** B. A diagnosis of clinical atherosclerotic cardiovascular disease (ASCVD) defined as having ONE of the following: 1. Acute coronary syndrome 2. History of myocardial infarction 3. Stable or unstable angina 4. Coronary or other arterial revascularization 5. Stroke 6. Transient ischemic attack 7. Peripheral arterial disease, including aortic aneurysm, presumed to be of atherosclerotic origin 8. Coronary heart disease **AND** 2. ONE of the following: A. The patient is on maximally tolerated statin therapy **OR** B. The patient has an intolerance or hypersensitivity to statin therapy **OR** C. The patient has an FDA labeled contraindication to ALL statins **OR** B. The patient has another FDA approved indication for the requested agent and route of administration **OR** C. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

Module	Clinical Criteria for Approval
	Renewal Evaluation **Target Agent(s)** will be approved when ALL of the following criteria are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. If the patient has ASCVD or HeFH, then ONE of the following: A. The patient is on maximally tolerated statin therapy **OR** B. The patient has an intolerance or hypersensitivity to statin therapy **OR** C. The patient has an FDA labeled contraindication to ALL statins **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** CMS Approved Compendia **Length of approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Prior Authorization with Quantity Limit	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. ONE of the Following: A. The requested quantity (dose) does NOT exceed the program quantity limit **OR** B. ALL of the following: 1. The requested quantity (dose) exceeds the program quantity limit **AND** 2. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 3. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** C. ALL of the following: 1. The requested quantity (dose) exceeds the program quantity limit **AND** 2. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** 3. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of approval:** 12 months