

Prior Authorization Update: Bempedoic Acid

Date of Review: December 2023

Generic Name: bempedoic acid; bempedoic acid and ezetimibe

PDL Class: Other Dyslipidemia Drugs

End Date of Literature Search: 08/16/2023

Brand Name (Manufacturer): Nexletol; Nexlizet (Esperion Therapeutics)

Dossier Received: No

Purpose for Drug Evaluation:

- Evaluate new evidence for the effectiveness and safety of bempedoic acid for the prevention of cardiovascular (CV) mortality and CV events in patients with established atherosclerotic cardiovascular disease (ASCVD) and high-risk CV patients to evaluate if there is a need for a prior authorization (PA) update.

Plain Language Summary:

- This review looks at new evidence for using medications to treat high cholesterol, also called dyslipidemia. Dyslipidemia can lead to an increased risk of heart attack or stroke.
- Statin medications lower the cholesterol levels in the blood and prevent heart attacks in people with dyslipidemia. If a statin alone cannot lower their cholesterol levels to an acceptable range, then a second medication is often added.
- One cholesterol lowering medication that has been approved for use in combination with statin medication is bempedoic acid. This medication works to help your body eliminate cholesterol from the bloodstream and can lower cholesterol levels. However, previous studies have not studied if it prevents heart attacks, stroke, or death.
- In a recently published study, in patients who could not tolerate first line statin medications, bempedoic acid decreased heart attacks and surgeries to restore blood flow to the heart.
- Statins are considered first line therapy for patients at risk for heart attacks, strokes and death from high levels of cholesterol. However, bempedoic acid is an option in patients who have tried multiple statin medications and cannot take them due to side effects.
- Based on previous studies, the Oregon Health Authority has adopted a policy that requires patients to have a history of cardiovascular disease and be on statin therapy for Medicaid to pay for bempedoic acid. This is called prior authorization.

Research Questions:

1. Is there new evidence for bempedoic acid and bempedoic acid/ezetimibe in reducing CV outcomes in patients treated for the primary or secondary prevention of CV disease?
2. Is there new evidence for long-term safety of bempedoic acid and bempedoic acid/ezetimibe?
3. Are there specific subpopulations for which bempedoic acid may be specifically indicated, more effective, or associated with less harm?

Author:

Conclusions:

- There is moderate-quality evidence that bempedoic acid lowers risk of a composite of death from CV causes, nonfatal myocardial infarction (MI), nonfatal stroke, or coronary revascularization compared to placebo [11.7% versus 13.3%; absolute risk reduction (ARR) 1.6% / number needed to treat (NNT) 63; $p = 0.004$] in patients with a history of CV event or at high-risk for a CV event who cannot tolerate more than a low dose of a statin.¹ This was primarily driven by reductions in non-fatal CV events and coronary revascularization.¹
- There is moderate-quality evidence that bempedoic acid does not decrease CV death or all-cause mortality in statin intolerant patients compared to placebo.
- There is low-quality evidence based on a prespecified subgroup analysis that bempedoic acid lowers risk of a composite outcome of death from CV causes, nonfatal MI, nonfatal stroke, or coronary revascularization compared to placebo (5.3% vs. 7.6%; ARR 2.3%; NNT 43) in patients at high-risk for a CV event.²
- There is insufficient evidence evaluating clinical CV outcomes in patients on maximally tolerated statin therapy and limited data in low-risk individuals on therapy for primary prevention of CVD.
- There is insufficient evidence evaluating bempedoic acid in reducing CV outcomes in patients from racial and ethnic minority populations.

Recommendations:

- Continue to prioritize statin optimization in patients with clinical atherosclerotic cardiovascular disease (ASCVD) and those at high risk for CV disease. Bempedoic acid should not be considered an alternative to statin therapy.
- Update prior authorization criteria to include coverage for bempedoic acid for high-risk primary prevention in patients with documented statin intolerance already on ezetimibe.

Summary of Prior Reviews

- There is moderate-quality evidence that bempedoic acid modestly lowers low-density lipoprotein cholesterol (LDL-C) compared to placebo (17% to 18% placebo-adjusted treatment difference from baseline at week 12) in patients with established CVD on maximally tolerated statin therapy who require additional LDL-C lowering (i.e. $LDL \geq 70$ mg/dL).
- There is low-quality evidence that the combination of bempedoic acid and ezetimibe lowers LDL-C compared to placebo, bempedoic acid monotherapy and ezetimibe monotherapy (treatment difference of -38.2%, -18.9% and -13.5%, respectively).
- There is insufficient evidence to determine the long-term effectiveness of bempedoic acid or combination bempedoic acid and ezetimibe on clinically meaningful outcomes, including CV mortality and major adverse cardiovascular events (MACE).
- There are several concerning safety signals seen in 52-week trials of bempedoic acid including tendon rupture, gout, nephrolithiasis, and new-onset benign prostatic hypertrophy (BPH). More data are needed to better quantify the risks associated with therapy. Additionally, bempedoic acid resulted in multiple changes to lab parameters during treatment, including increases in serum creatinine, liver transaminases, creatinine kinase and decreases in white blood cell (WBC) count, neutrophils and hemoglobin.

Background:

Based on high-quality and consistent evidence demonstrating ASCVD risk reduction, statins are recommended as first line pharmacological agents for primary and secondary prevention of cardiovascular disease (CVD).³ The 2018 American College of Cardiology (ACC) guidelines recommend non-statin therapy in specific settings.³ In high-risk CVD, the guideline recommends adding non-statins when LDL-C remains above 70 mg/dL despite maximally tolerated statin therapy.³ Among the potential non-statin therapies, the ACC guidelines recommend adding ezetimibe first, followed by a PCSK9 inhibitor if LDL-C levels remain above

70mg/dL.³ This recommendation is supported by evidence of CV risk reduction with ezetimibe and PCSK9 inhibitors when used in combination with statin therapy.³ There is a lack of data demonstrating CV risk reduction with other lipid lowering therapies, including fibrates and omega-3 fatty acids.³

Bempedoic acid was approved by the Food and Drug Administration (FDA) as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established ASCVD who require additional lowering of LDL-C.⁴ Approval was based on the results from the CLEAR – Harmony and CLEAR – Wisdom trials.⁴ Both trials resulted in a significant reduction in LDL-C from baseline at week 12 compared to placebo (treatment difference -18.1%; 95% CI -20 to -16.1% in CLEAR Harmony and -17.4%; 95% CI -21 to -13.9% in CLEAR Wisdom).^{5,6} Significant reductions in non-HDL cholesterol, total cholesterol, apolipoprotein B and high-sensitivity C-reactive protein were also observed.^{5,6} Since its approval, an additional study (CLEAR Outcomes) evaluated the impact of bempedoic acid on CV outcomes in patients who are unwilling or unable to take statin medications.¹

Prior to the reporting of the CLEAR – Outcomes trial, the ACC released an expert opinion on the use of non-statin therapies for the lowering of LDL-C.⁷ In the report, they recommend the addition of bempedoic acid if additional LDL-C lowering is indicated despite triple therapy with a maximally tolerated statin, ezetimibe, and PCSK9 inhibitor.⁷ For patients with statin intolerance, the report recommends PCSK9 inhibitors for lipid lowering. If patients with statin intolerance are unwilling to take an injectable medication, then bempedoic acid may be considered.

The National Lipid Association defines statin intolerance as one or more adverse effects associated with statin therapy that improves with dose reduction or discontinuation and a trial of at least 2 statin medications at the lowest approved daily dose.⁸ In addition, they define partial intolerance as an inability to tolerate the recommended dose while possibly being able to tolerate lower statin doses, a different statin, or alternative regimen.⁸ While up to 25% of patients who start on statin therapy discontinue due to adverse effects, a randomized controlled trial has shown that most symptoms caused by statin are nocebo.⁹ The author of this study recommend that clinicians do not interpret symptom intensity or timing as statin causation because the pattern is identical for placebo.⁹

Methods:

A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 1**, which includes dates, search terms and limits used. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

Systematic Reviews:

After review, 5 systematic reviews were excluded due to a surrogate outcome (i.e., LDL-C)¹⁰⁻¹² or poor quality (i.e., AMSTAR II assessment).^{13,14}

New Guidelines:

Two new guidelines have been published since 2021. Both were excluded for not including bempedoic acid or awaiting results from ongoing clinical trials.^{15,16} One expert opinion was identified but was excluded since it was not a high-quality clinical practice guideline.⁷

New Formulations or Indications:

No new formulations or indications identified.

Author: Kendal Pucik, PharmD Candidate & Megan Herink, PharmD

No new FDA Safety Alerts identified.

A total of 8 citations were manually reviewed from the initial literature search. After further review, 7 citations were excluded because of wrong study design (i.e. simulation model, rationale and design of a trial)^{17,18}, drug (i.e. alirocumab)¹⁹, or outcome studied (i.e. LDL-C, patient characteristics, glycemic changes from baseline).²⁰⁻²³ The single trial which evaluated bempedoic acid is summarized below in **Table 1**.

[illegible]

				Death from CV causes 1. 269 (3.8%) 2. 257 (3.7%) HR: 1.04 (95% CI 0.88-1.24)	NS			
Abbreviations: ACS = acute coronary syndrome; ARR = absolute risk reduction; ASCVD = atherosclerotic cardiovascular disease; CI = confidence interval; CV = cardiovascular event; DB = double blind; GFR = glomerular filtration rate; HbA1c = hemoglobin A1c; HR = hazard ratio; HTN = hypertension; ITT = intention to treat; LDL-C = low density lipoprotein cholesterol; MI = myocardial infarction; mITT = modified intention to treat; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; NR = not reported; NS = non-significant; NYHA = New York Heart Association; PC = placebo-controlled; PCSK9 = proprotein convertase subtilisin-kexin type 9; RCT = randomized controlled-trial; ULN = upper limit normal								

Clinical Efficacy:

The CLEAR–Outcomes trial was the first clinical trial designed to evaluate the effects of bempedoic acid on CV outcomes.¹ This trial was double-blind, placebo-controlled study with statin-intolerant patients randomized to receive either bempedoic acid 180 mg or placebo once daily.¹ Investigators defined statin intolerance as patient-reported intolerance due to an adverse event that started or increased during statin therapy or improved when statin therapy was discontinued, resulting in an inability to tolerate 2 or more statins at any dose or 1 statin at any dose and an unwellness or inability to attempt a second statin medication.¹ Also, patients were allowed to continue statin therapy if the dose they currently received was defined as very low dose statin therapy.¹ The primary endpoint was a composite of death from CV causes, nonfatal MI, nonfatal stroke, or coronary revascularization.¹

Overall risk of bias of the study was low. However, extensive exclusion criteria limits applicability to complex patients seen in clinical practice. While this trial included both primary and secondary prevention patients, 70% had ASCVD, limiting generalizability to patients on therapy for primary prevention. Almost all participants were white (91%) and it is difficult to apply results to other high-risk subgroups, including Black patients which included only 3% of the population. Furthermore, the study included a 4-week run-in period with single-blind placebo. Patients who were unable to tolerate therapy due to adverse effects or with adherence less than 80 percent were not eligible for randomization.¹ Of the 22084 patients who were screened, 7187 were excluded prior to randomization, leading to a 32.5% of screening failures.¹ This limits the study population to individuals less likely to experience side effects. Lastly, this study used a definition of statin intolerance that does not match the definition employed in clinical practice. This difference creates a concern for clinical applicability.

Participants in the bempedoic acid arm had a significant reduction in the primary CV outcome (11.7% versus 13.3%; ARR = 1.6%; NNT = 63; p = 0.004) over a median of 3.4 years.¹ This was primarily driven by a reduction in fatal or nonfatal MI (3.7% versus 4.8%; ARR = 1.1%; NNT = 91; p = 0.002) and coronary revascularization (6.2% versus 4.8%; ARR = 1.42%; NNT= 72; p = 0.001).¹ There was no significant reduction in CV death or all-cause mortality. In addition, participants experienced significant reductions in LDL at 6 months (-21.1 versus -0.8).¹ Of note, 22.9% of participants were on a baseline statin, 11.5% were on ezetimibe, 0.7% were on bile acid sequestrants, 5.3% were on fibrates, 0.5% were on PCSK9 inhibitors, and 0.5% were on a niacin derivative.¹

This study focused on patients who were intolerant to statin medications. There is insufficient evidence evaluating CV benefit in patients with ASCVD on maximally tolerated statin therapy and in a broader low risk primary prevention population. In CLEAR-Outcomes, 30% of participants enrolled in the study did not have a history of a CV event and were included in the high-risk primary prevention cohort (n=4206).² To meet high-risk criteria, participants had to have an LDL-C of 100 mg/dl higher with a Reynolds Risk score > 30% or a SCORE Risk score > 7.5% over 10 years, or coronary artery calcium score > 400 Agatston units, or presence of type 1 or type 2 DM in women older than 65 years or men older than 60 years.² The Reynolds Risk score is a risk assessment used in the United States (US).²⁴ It differs from ASCVD assessments in that it excludes individuals with diabetes but does include high-sensitivity C-reactive protein.²⁴ The SCORE Risk assessment is a common tool used in European countries to predict 10-year risk of cardiovascular death.²⁴ A published subgroup analysis of primary prevention

participants found a significant reduction in the CV composite endpoint with bempedoic acid compared to placebo (5.3% vs. 7.6%; HR 0.70; 95% CI 0.55-0.89; NNT 43).² There was also a reduction seen in MI (1.4% vs. 2.2%; HR 0.61; 95% CI 0.39-0.98), CV death (81.8% vs. 3.1%; HR 0.61; 95% CI 0.39 to 0.98), and all-cause mortality (3.6% vs. 5.2%; HR 0.73; 95% CI 0.54 to 0.98).² However, these findings of a subgroup analysis should not be used to make strong conclusion due to the increased risk of false-positive results. In the primary prevention subgroup, 66% of participant had diabetes and 42% met the high-risk clinical score enrollment criteria.²

Clinical Safety:

There were not significantly more discontinuations due to adverse events in the bempedoic acid group compared to placebo (10.8% vs. 10.4%).¹ Higher discontinuation rates were seen in previous clinical trials (10.9% versus 7.5%), however the CLEAR Harmony trial did not have a run-in period unlike the CLEAR-Outcomes trial.^{1,5,6} The presence or lack of a run-in period could be a potential reason for differences in discontinuations due to adverse events. Similar to previous trials, more patients on bempedoic acid experienced hyperuricemia (10.9% vs. 5.6%), gout (3.1% vs. 2.1%), increased alanine aminotransferase (1.2% vs. 0.8%), and increased aspartate aminotransferase (1.1% vs. 0.6%) compared to placebo.¹ Adverse events occurring at rates greater than 2 percent and at higher rates compared to placebo are included in **Table 2.**¹

Table 2. Adverse Events Occurring in More than 2% of Patients and at Higher Rates than Placebo

	Bempedoic Acid (N=7001)	Placebo (N=6964)
Hypoglycemia	304 (4.3%)	267 (3.8%)
Elevated hepatic enzyme level	317 (4.5%)	209 (3.0%)
Renal Impairment	802 (11.5%)	599 (8.6%)
Hyperuricemia	763 (10.9%)	393 (5.6%)
Gout	215 (3.1%)	143 (2.1%)
Cholelithiasis	152 (2.2%)	81 (1.2%)

References:

1. Nissen SE, Lincoff AM, Brennan D, et al. Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients. *N Engl J Med*. 2023;388(15):1353-1364.
2. Nissen SE MV, Nicholls SJ, Brennan D, Laffin L, Ridker P, Ray KK, Mason D, Kastelein JJP, Cho L, Libby P, Li N, Foody J, Louie MJ, Lincoff AM. Bempedoic Acid for Primary Prevention of Cardiovascular Events in Statin-Intolerant Patients. *JAMA*. 2023 Jul 11;330(2):131-140. doi: 10.1001/jama.2023.9696. PMID: 37354546; PMCID: PMC10336623.
3. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2019;73(24):e285-e350.
4. 2020 BApiET.
5. Goldberg AC, Leiter LA, Stroes ESG, et al. Effect of Bempedoic Acid vs Placebo Added to Maximally Tolerated Statins on Low-Density Lipoprotein Cholesterol in Patients at High Risk for Cardiovascular Disease: The CLEAR Wisdom Randomized Clinical Trial. *JAMA*. 2019;322(18):1780-1788.
6. Ray KK, Bays HE, Catapano AL, et al. Safety and Efficacy of Bempedoic Acid to Reduce LDL Cholesterol. *N Engl J Med*. 2019;380(11):1022-1032.
7. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. *Journal of the American College of Cardiology*. 2022;80(14):1366-1418.
8. Gaine SP PJ, Dixon DL, Kulkarni A. NLA 2022 definition of statin intolerance. American College of Cardiology. Accessed September 7, 2023. <https://www.acc.org/Latest-in-Cardiology/Articles/2022/08/08/12/27/NLA-2022-Definition-of-Statin-Intolerance>. .
9. Howard JP, Wood FA, Finegold JA, et al. Side Effect Patterns in a Crossover Trial of Statin, Placebo, and No Treatment. *J Am Coll Cardiol*. 2021;78(12):1210-1222.
10. Toth PP, Bray S, Villa G, et al. Network Meta-Analysis of Randomized Trials Evaluating the Comparative Efficacy of Lipid-Lowering Therapies Added to Maximally Tolerated Statins for the Reduction of Low-Density Lipoprotein Cholesterol. *J Am Heart Assoc*. 2022;11(18):e025551.
11. Burnett H FK, Cichewicz A, et al. Comparative efficacy of non-statin lipid-lowering therapies in patients with hypercholesterolemia at increased cardiovascular risk: a network meta-analysis. *Curr Med Res Opin*. . 2022;38(5):777-784. doi:10.1080/03007995.2022.2049164, 10.1080/03007995.2022.2049164.
12. Dai L, Zuo Y, You Q, Zeng H, Cao S. Efficacy and safety of bempedoic acid in patients with hypercholesterolemia: A systematic review and meta-analysis of randomized controlled trials. *Eur J Prev Cardiol*. 2021;28(8):825-833.
13. Bhagavathula AS, Al Matrooshi NO, Clark CCT, Rahmani J. Authors' Reply to 'Comment on: Bempedoic Acid and Ezetimibe for the Treatment of Hypercholesterolemia: A Systematic Review and Meta-Analysis of Randomized Phase II/III Trials'. *Clin Drug Investig*. 2021;41(5):495-496.
14. Lin Y, Parco C, Karathanos A, et al. Clinical efficacy and safety outcomes of bempedoic acid for LDL-C lowering therapy in patients at high cardiovascular risk: a systematic review and meta-analysis. *BMJ Open*. 2022;12(2):e048893.
15. In: *Cardiovascular disease: risk assessment and reduction, including lipid modification*. London2023.

16. Pearson GJ, Thanassoulis G, Anderson TJ, et al. 2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in Adults. *Can J Cardiol.* 2021;37(8):1129-1150.
17. McQueen RB, Baum SJ, Louie MJ, et al. Potential Cardiovascular Events Avoided with Bempedoic Acid Plus Ezetimibe Fixed-Dose Combination Compared with Ezetimibe Alone in Patients with Atherosclerotic Cardiovascular Disease Taking Maximally Tolerated Statins. *Am J Cardiovasc Drugs.* 2023;23(1):67-76.
18. Nicholls S, Lincoff AM, Bays HE, et al. Rationale and design of the CLEAR-outcomes trial: Evaluating the effect of bempedoic acid on cardiovascular events in patients with statin intolerance. *Am Heart J.* 2021;235:104-112.
19. Ostadal P, Steg PG, Poulouin Y, et al. Metabolic risk factors and effect of alirocumab on cardiovascular events after acute coronary syndrome: a post-hoc analysis of the ODYSSEY OUTCOMES randomised controlled trial. *Lancet Diabetes Endocrinol.* 2022;10(5):330-340.
20. Ridker PM, Lei L, Ray KK, Ballantyne CM, Bradwin G, Rifai N. Effects of bempedoic acid on CRP, IL-6, fibrinogen and lipoprotein(a) in patients with residual inflammatory risk: A secondary analysis of the CLEAR harmony trial. *J Clin Lipidol.* 2023;17(2):297-302.
21. Ballantyne CM, Bays HE, Louie MJ, Smart J, Zhang Y, Ray KK. Factors Associated With Enhanced Low-Density Lipoprotein Cholesterol Lowering With Bempedoic Acid. *J Am Heart Assoc.* 2022;11(15):e024531.
22. Ballantyne CM, Banach M, Bays HE, et al. Long-Term Safety and Efficacy of Bempedoic Acid in Patients With Atherosclerotic Cardiovascular Disease and/or Heterozygous Familial Hypercholesterolemia (from the CLEAR Harmony Open-Label Extension Study). *Am J Cardiol.* 2022;174:1-11.
23. Leiter LA, Banach M, Catapano AL, et al. Bempedoic acid in patients with type 2 diabetes mellitus, prediabetes, and normoglycaemia: A post hoc analysis of efficacy and glycaemic control using pooled data from phase 3 clinical trials. *Diabetes Obes Metab.* 2022;24(5):868-880.
24. 1. Quispe R FR, Cainzos-Achirica M, et al. Risk assessment for cardiovascular disease prevention: Comparing the American and European approaches. American College of Cardiology. November 21, 2019. Accessed September 15, 2023. <https://www.acc.org/Latest-in-Cardiology/Articles/2019/11/21/07/26/Risk-Assessment-for-Cardiovascular-Disease-Prevention>. .

Appendix 1: Medline Search Strategy

OVID Medline

1. bempedoic acid.af.

307
2. (coronary disease or coronary artery disease or dyslipidemia or dyslipidemias or myocardial infarction or stroke or cardiovascular disease or cardiovascular diseases).af.

1162143
3. 1 and 2

204
4. limit 3 to (english language and humans and yr="2021 -Current" and (clinical trial, all or controlled clinical trial or meta-analysis or randomized controlled trial or "systematic review"))

13

Appendix 2: Key Inclusion Criteria

Population	Individuals with cardiovascular disease or at high-risk for cardiovascular disease
Intervention	Bempedoic acid or bempedoic acid/ezetimibe
Comparator	Placebo or active control
Outcomes	Cardiovascular events, all-cause mortality, cardiovascular mortality
Timing	At least 12 weeks
Setting	Outpatient or inpatient after acute coronary syndrome

Bempedoic Acid

Goal(s):

- Promote use of bempedoic acid that is consistent with medical evidence.

Length of Authorization:

- Up to 12 months

Requires PA:

- Bempedoic Acid (Nexletol™)
- Bempedoic acid and ezetimibe (Nexlizet™)

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code; go to #2	
2. Does the patient have clinical atherosclerotic cardiovascular disease (ASCVD), defined as documented history of one or more ASCVD events (see below) OR a diagnosis of homozygous or heterozygous familial hypercholesterolemia (HeFH or HoFH) OR at high risk for CVD, including those with: <ul style="list-style-type: none">• Diabetes mellitusOR• 10-year ASCVD risk of 10% or greater? <u>Major ASCVD events</u> <ul style="list-style-type: none">• Recent ACS (within past 12 months)• History of MI (other than recent ACS from above)• History of ischemic stroke• Symptomatic peripheral artery disease• Coronary artery disease	Yes: Go to #3	No: Pass to RPh; deny for medical appropriateness

Approval Criteria

<p>3. Has the patient taken a daily high-intensity statin (see table below) for at least 3 months with a LDL-C still ≥ 70 mg/dl with ASCVD or ≥ 100 mg/dl with HeFH or HoFH or high-risk CVD?</p> <p>Prescriber to submit chart documentation of:</p> <ol style="list-style-type: none"> 1) Doses and dates initiated of statin 2) Baseline LDL-C (untreated) 3) Recent LDL-C 	<p>Yes: Confirm documentation; go to #5</p> <p>1. Statin: Dose: Date Initiated:</p> <p>Baseline LDL-C _____ Date: _____</p> <p>Recent LDL-C _____ Date: _____</p>	<p>No: Go to #4</p>
<p>4. Does the patient have a history of:</p> <ul style="list-style-type: none"> • rhabdomyolysis caused by a statin, OR • a history of creatinine kinase (CK) levels >10-times upper limit of normal with muscle symptoms determined to be caused by a statin, OR • statin intolerance, defined as one or more adverse effects associated with statin therapy that improves with dose reduction or discontinuation and a trial of at least 2 statin medications at the lowest approved daily dose? <p>Note: Prescriber must provide chart documentation of diagnosis or CK levels. A recent LDL-C level (within last 12 weeks) must also be submitted.</p>	<p>Yes: Confirm chart documentation of diagnosis or labs and go to #5</p> <p>1. Statin #1: Dose: Date Initiated:</p> <p>2. Statin #2 Dose: Date Initiated:</p> <p>Recent LDL-C _____ mg/dL Date: _____</p>	<p>No: Pass to RPh; deny for medical appropriateness</p>
<p>5. Has the patient taken ezetimibe 10 mg daily for at least 3 months and still requires additional LDL-C lowering (LDL-C still ≥ 70 mg/dl with ASCVD or ≥ 100 mg/dl with HeFH or HoFH or high-risk CVD), OR have a contraindication to ezetimibe?</p>	<p>Yes: Go to #6</p>	<p>No: Pass to RPH; deny for medical appropriateness</p>

Approval Criteria

6. Is the patient adherent with a high-intensity statin and/or ezetimibe?

Yes: Approve for up to 12 months

Note: pharmacy profile may be reviewed to verify >80% adherence (both lipid-lowering prescriptions refilled 5 months' supply in last 6 months)

No: Pass to RPh; deny for medical appropriateness

High- and Moderate-intensity Statins.

High-intensity Statins (≥50% LDL-C Reduction)	Moderate-intensity Statins (30 to <50% LDL-C Reduction)	
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Fluvastatin 80 mg Lovastatin 40-80 mg	Pitavastatin 1-4 mg Pravastatin 40-80 mg Simvastatin 20-40 mg Rosuvastatin 5-10 mg

P&T / DUR Review: 12/23 (MH), 08/20 (MH)
Implementation: 1/1/24; 9/1/20