

Coverage of any drug intervention discussed in a Medica prior authorization guideline is subject to the limitations and exclusions outlined in the member's benefit certificate or policy and applicable state and/or federal laws.

Commercial (Small & Large Group) **ASO** **Exchange/ACA**
 Medicare Advantage (MAPD)

LEQVIO[®] (inclisiran)**MB2227****Covered Service:** NO**Prior Authorization Required:** NO**Additional Information:** Prescribed by (or in consultation with) cardiology specialists with prior authorization through The Plan Pharmacy Services.**Medicare Policy:** Prior authorization is not required for Medicare Cost products (Dean Care Gold) and Medicare Supplement (Select) when this drug is provided by participating providers. Prior authorization is required if a member has Medicare primary and the plan secondary coverage. This policy is not applicable to our Medicare Replacement products.**Wisconsin Medicaid Policy** Coverage of prescription drug benefits is administered by the Wisconsin Medicaid program. Coverage of medical drug benefits is administered by the Wisconsin Medicaid fee-for-service program. Medical drugs not paid on a fee-for-service basis by the Wisconsin Medicaid program are covered by the plan with no PA required.**1.0 FDA Indication****1.1 LEQVIO[®]**

1.1.1 Inclisiran (LEQVIO[®]; Novartis) was approved by the U.S. Food and Drug Administration under a New Drug Application (NDA) for adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD) who require additional lowering of low-density lipoprotein cholesterol (LDL-C). This indication was approved based on a reduction of LDL-C, a surrogate marker for increased risk for ASCVD.¹

1.2 Institute for Clinical and Economic Review (ICER):

1.2.1 In March 2021, ICER released guidance on high cholesterol treatment. In this review, the following clinical determinations were made

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regarding Inclisiran (Inclisiran was not FDA-approved at the time): a unanimous vote the evidence was judged adequate to demonstrate a net health benefit over usual care alone.^{6,7}

- 1.2.1.1 Inclisiran did not reduce the risk of all-cause mortality or cardiovascular mortality, and there was no statistically significant difference in the occurrence of stroke and MI when compared to placebo.^{1,3,4}
- 1.2.1.2 Inclisiran would represent a low-to-intermediate long-term value for money⁶
- 1.2.1.3 No studies reported data on the impact of inclisiran on health related-related quality of life^{2,6,7}
- 1.2.1.4 Other PCSK9 inhibitors can be preferred until studies show that inclisiran shows positive clinical effects

1.3 Treatment Guidelines/Consensus statements:

1.3.1 The US ACC/AHA 2018 Guideline on the Management of Blood Cholesterol

- 1.3.1.1 In patients with very high risk for CVD whose LDL-C level remains \geq 70 mg/dL on maximally tolerated statin and ezetimibe therapy, adding a PCSK9 inhibitor is reasonable (Class IIa recommendation), although long term safety (> 3 years) is uncertain and cost effectiveness is low at mid-2018 list prices.
- 1.3.1.2 The guideline came out before inclisiran was FDA approved
- 1.3.1.3 The guideline does not favor one PCSK9 inhibitor (evolocumab or alirocumab) over another

2.0 Policy / Criteria:

- 2.1 LEQVIO[®] is considered not covered due to insufficient evidence to demonstrate clinical efficacy for treatment of heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD) based on all of the following:
 - 2.1.1 LEQVIO[®] was approved based on an observed reduction in LDL-C levels, but it is unknown if that reduction is clinically significant. Currently there is no clear threshold for the amount of LDL reduction required to reduce CV mortality or morbidity.^{1,2,3}
 - 2.1.2 True clinical benefit has not been established based the following:
 - 2.1.2.1 There is no evaluation to demonstrate clinical efficacy to reduce the risk of all-cause mortality or cardiovascular mortality, and there was no statistically significant difference in the occurrence of stroke and MI when compared to placebo.^{1,2,6,7}

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2.1.2.2 No studies reported data on the impact of inclisiran on health related-related quality of life ^{6,7}

3.0 Policy Rationale

3.1 The clinical benefit of LEQVIO[®] for the treatment of heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD) has not been established based on Practice and Consensus guidelines, ICER and clinical studies.^{6,7}

3.2 Practice and Consensus Guidelines have not been updated to include inclisiran.^{2,7}

Comment(s):

1.0 *Codes and descriptors listed in this document are provided for informational purposes only and may not be all inclusive or current. Listing of a code in this drug policy does not imply that the service described by the code is a covered or non-covered service. Benefit coverage for any service is determined by the member's policy of health coverage with the plan. Inclusion of a code in the table does not imply any right to reimbursement or guarantee claim payment. Other drug or medical policies may also apply.

1.1 NDC and HCPCS codes

Medication Name		How Supplied	National Drug Code (NDC)	HCPCS code
Brand	Generic			
LEQVIO	inclisiran	284 mg/1.5mL prefilled syringe	00078-1000-60	J1306
REPATHA	evolocumab	140 mg/mL prefilled syringe	55513-0760-02	
PRALUENT	alirocumab	75 mg/mL prilled syringe	61755-0020-02	

Committee/Source

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References:

1. LEQVIO [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2021.
2. 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. 2018 Nov 8. pii: S0735-1097(18)39034-X. doi: 10.1016/j.jacc.2018.11.003.
3. 3. Ray KK, Wright RS, Kallend D, et al. Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol. N Engl J Med. 2020;382(16):1507-1519.
4. 4. Austin MA, Hunter CM, Zimmern RL, Humphries SE. Genetic causes of monogenic heterozygous familial hypercholesterolemia: a HuGE prevalence review. Am J Epidemiol. 2004;160(5):407-420.
5. 5. Raal FJ, Kallend D, Ray KK, et al. Inclisiran for the Treatment of Heterozygous Familial Hypercholesterolemia. N Engl J Med. 2020;382(16):1520-1530.
6. ICER, Institute for Clinical and Economic Review, Alirocumab for High Cholesterol – Final New Evidence Update. Published February 15, 2019. https://icer.org/wp-content/uploads/2020/10/ICER_Reference_Case_013120.pdf.
7. Arnett DK, Blumenthal RS, Albert MA, et al 2019. ACC/AHA guidelines on the primary prevention of cardiovascular Disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical practice guideline. Circulation. 2019 Sept 19. Pii : Vol 140, No11. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines | Circulation (ahajournals.org).