Effective Date **8/15/2022**
Next Review Date… **8/15/2023**
Coverage Policy Number **IP0142**

Fosdenopterin

Table of Contents

Related Coverage Resources

Pharmacogenetic Testing

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for fosdenopterin (**Nulibry™**).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Fosdenopterin (Nulibry) is considered medically necessary when the following are met:

1. **Molybdenum Cofactor Deficiency (MoCD) Type A.** Individual meets **ALL** of the following criteria (A, B, and C):
    A. **ONE** of the following (i or ii):
        i. Individual has genetic testing confirmation of biallelic pathogenic or likely pathogenic variants in the *MOCS1* gene

ii. Individual has suspected molybdenum cofactor deficiency (MoCD) Type A based on clinical presentation (for example, intractable seizures, failure to thrive) and treatment is being initiated while genetic testing is pending

B. Documentation, based on the current condition, the individual is expected to derive benefit with fosdenopterin (Nulibry) and the disease state is NOT considered to be too advanced

C. The medication is prescribed by, or in consultation with, with a pediatrician, geneticist, or a physician who specializes in molybdenum cofactor deficiency (MoCD) Type A

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Fosdenopterin (Nulibry) is considered medically necessary for continued use when **ALL** of the following are met:

1. Initial criteria are met
2. There is documentation of beneficial response
3. If an individual initiated treatment based on clinical presentation for suspected MoCD Type A while genetic testing was pending, genetic testing has subsequently confirmed biallelic pathogenic or likely pathogenic variants in the *MOCS1* gene

Authorization Duration

Genetic testing confirmed biallelic pathogenic or likely pathogenic variants in the *MOCS1* gene:
Initial authorization: up to 12 months
Reauthorization: up to 12 months

Suspected MoCD Type A:
Authorization is one-time only, for 1 month, if there is no genetic testing confirmation.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Coding / Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs

Background

OVERVIEW
Nulibry, a cyclic pyranopterin monophosphate (cPMP), is indicated to reduce the risk of mortality in patients with **molybdenum cofactor deficiency** (MoCD) **Type A**.[1]

MoCD is a rare, life-threatening, autosomal-recessive disorder characterized by the deficiency of three molybdenum-dependent enzymes: sulfite oxidase (SOX), xanthine dehydrogenase, and aldehyde oxidase.[2] Patients with MoCD Type A have mutations in the *MOCS1* gene leading to deficiency of the intermediate substrate, cPMP.[1] Substrate replacement therapy with Nulibry provides an exogenous source of cPMP, which is converted to molybdopterin. Molybdopterin is then converted to molybdenum cofactor, which is needed for the activation of molybdenum-dependent enzymes, including SOX, an enzyme that reduces levels of neurotoxic sulfites.

Dosing

Recommended Dosage and Administration in Patients One Year of Age or Older:[1]
For patients one year of age or older, the recommended dosage of Nulibry is 0.9 mg/kg (based on actual body weight) administered as an intravenous infusion once daily.

Recommended Initial Dosage and Titration Schedule for Patients Less Than One Year of Age by Gestational Age:[1]

Titration Schedule	Preterm Neonates (Gestational Age Less than 37 Weeks)	Term Neonates (Gestational Age 37 Weeks and Above)
Initial Dosage	0.4 mg/kg once daily	0.55 mg/kg once daily
Dosage at Month 1	0.7 mg/kg once daily	0.75 mg/kg once daily
Dosage at Month 3	0.9 mg/kg once daily	0.9 mg/kg once daily

References

1. Nulibry intravenous infusion [prescribing information]. Boston, MA: Origin Biosciences; February 2021.
2. Mechler K, Mountford WK, Hoffmann GF, et al. Ultra-orphan diseases: a quantitative analysis of the natural history of molybdenum cofactor deficiency. *Genet Med*. 2015 Dec;17(12):965-70.