Drug Coverage Policy

Effective Date..... 08/15/2024
Coverage Policy Number..... IP0142
Policy Title..... Nulibry

Metabolic Disorders – Nulibry

- Nulibry™ (fosdenopterin intravenous infusion – Origin Biosciences)

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. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. 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.

Cigna Healthcare Coverage Policy

OVERVIEW
Nulibry, a cyclic pyranopterin monophosphate (cPMP), is indicated to reduce the risk of mortality in **molybdenum cofactor deficiency** (MoCD) **Type A**.[1] Treatment is initiated based on a confirmed diagnosis or presumptive diagnosis of MoCD. In patients with a presumptive diagnosis, Nulibry should be discontinued after genetic testing does not confirm MoCD Type A.

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. Onset of the disease is often seen at birth with median survival estimated at 4 years of age without intervention.[3] The most common symptoms of MoCD are seizures, feeding difficulties, and hypotonia. Patients usually experience irreversible neurological damage leading to severe developmental delays (trouble speaking or sitting) and brain abnormalities (atrophy of brain tissue). Biochemical features suggestive of MoCD include elevated urine S-sulfocysteine (SSC), thiosulfate, hypoxanthine, xanthine, or decreased serum uric acid. Genetic testing gives confirmation for differential diagnosis of MoCD Type A, B, or C.

Medical Necessity Criteria

Nulibry is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Molybdenum Cofactor Deficiency (MoCD) Type A.** Approve for the duration noted if the patient meets ALL of the following (A, B, and C):
   - **A)** According to the prescriber, the diagnosis was confirmed by ONE of the following (i or ii):
     - **i.** Approve for 1 year if the patient has genetic testing confirmation of biallelic pathogenic or likely pathogenic variants in the *MOCS1* gene; OR
     - **ii.** Approve for 1 month if the patient has laboratory findings suggestive of molybdenum cofactor deficiency (MoCD) and genetic testing is in progress; AND
       Note: Laboratory findings include elevated urinary S-sulfocysteine, thiosulfate, xanthine, hypoxanthine, or decreased serum uric acid.
   - **B)** According to the prescriber, based on the current condition, the patient is expected to derive benefit with Nulibry and the disease state is NOT considered to be too advanced; AND
   - **C)** The medication is prescribed by or in consultation with a pediatrician, geneticist, or a physician who specializes in molybdenum cofactor deficiency (MoCD) Type A.

   Dosing. Approve up to 0.9 mg/kg given by intravenous infusion once daily.

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.

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

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding Information

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

References

1. Nulibry intravenous infusion [prescribing information]. Boston, MA: Origin Biosciences; October 2022.
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.
3. Misko A, Mahtani K, Abbott J, et al. Molybdenum Cofactor Deficiency. 2021 Dec 2 [Updated 2023 Feb 2]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK575630/. Accessed on April 03, 2024.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Policy Name Change: Updated** Policy Name from "Fosdenopterin" to "Metabolic Disorders – Nulibry." **Molybdenum Cofactor Deficiency (MoCD) Type A: Updated** criteria for suspected MOCD to rely on laboratory findings rather than clinical presentation and added a note listing examples of such findings. **Added** dosing information.	08/15/2024
Selected Revision	**Molybdenum Cofactor Deficiency (MoCD) Type A:** Confirmation of a genetic mutation in the MOCS1 gene was rephrased to more specifically state, "genetic testing confirmation of biallelic pathogenic or likely pathogenic variants in the MOCS1 gene".	08/15/2024

The policy effective date is in force until updated or retired.