Medical Policy:

Nulibry™ (fosdenopterin) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.338	March 10, 2025	June 9, 2021

Definitions

Nulibry, a cyclic pyranopterin monophosphate (cPMP), is indicated to reduce the risk of mortality in patients with molybdenum cofactor deficiency (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. Patients with MoCD Type A have mutations in the *MOCS1* gene leading to deficiency of the intermediate substrate, cPMP. 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.

Length of Authorization

Coverage will be provided for 1 year and may be renewed.

Dosing Limits [Medical Benefit]

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

Max Units (per dose and over time) [HCPCS Unit]:
95 mg daily

Guideline

I. INITIAL APPROVAL CRITERIA

1. **Molybdenum Cofactor Deficiency (MoCD) Type A:**
   A. Patient meets **ONE** of the following scenarios:
   i. Patient has a diagnosis of MoCD Type A confirmed by a mutation in the *MOCS1* gene suggestive of disease as identified on molecular genetic testing; **OR**
   ii. Patient has biochemical features suggestive of MoCD Type A (i.e., elevated sulfites in urine, low serum uric acid, elevated urinary xanthine and hypoxanthine) and will be treated presumptively while awaiting genetic confirmation; **AND**
   B. Patient has a baseline value for the following:
   i. Urinary s-sulfocysteine (SSC) normalized to creatinine; **AND**
   ii. Clinical notes regarding signs and symptoms of disease which may include, but are not limited to, seizure frequency/duration, growth, and developmental milestones; **AND**
   C. Will not be used in combination with other substrate replacement therapy (e.g., recombinant cyclic pyranopterin monophosphate, etc.); **AND**
   D. Must be prescribed by, or in consultation with, a specialist in medical genetics or pediatric neurology

II. RENEWAL CRITERIA

1. **Molybdenum Cofactor Deficiency (MoCD) Type A**:
   A. Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in Initial Criteria; **AND**
   B. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe phototoxicity, clinically significant infection, etc.; **AND**
   i. Disease response compared to pre-treatment baseline as evidenced by the following:
      a. Reduction in urinary SSC normalized to creatinine; **AND**
      b. Stabilization or improvement in one or more signs and symptoms of disease including, but not limited to, seizure frequency/duration, growth, achievement of developmental milestones; **OR**
   ii. Patient initiated therapy as an inpatient based upon a presumptive diagnosis of MoCD Type A which was subsequently confirmed by genetic testing; **AND**
      a. Patient is responding to therapy compared to one or more pre-treatment baseline parameters which prompted the workup for MoCD

Dosing/Administration

Age less than 1 year (Pre-Term neonates - gestational age < 37 weeks):
Initial dosage: 0.4 mg/kg once daily − Dosage at 1 month: 0.7 mg/kg once daily − Dosage at 3 months: 0.9 mg/kg once daily

Age less than 1 year (Full-Term neonates - gestational age ≥37 weeks)
Initial dosage: 0.55 mg/kg once daily − Dosage at 1 month: 0.75 mg/kg once daily − Dosage at 3 months: 0.9 mg/kg once daily

Age 1 year and older: The recommended dosage is 0.9 mg/kg administered as an IV infusion once daily, based on actual body weight.

Applicable Procedure Codes

Code	Description
C9399	Nulibry 9.5mg Solution Reconstituted, Unclassified drugs or biologicals
J3490	Nulibry 9.5mg Solution Reconstituted, Unclassified drugs

Applicable NDCs

Code	Description
73129-0001-xx	Nulibry Single-Dose Vial for Intravenous Infusion: 9.5 mg/vial
42358-0295-xx	Nulibry 9.5mg Single Dose Vial

ICD-10 Diagnoses

Code	Description
E61.5	Molybdenum deficiency
E72.19	Other disorders of sulfur-bearing amino-acid metabolism

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	3/10/2025	Annual Review: added 42358-0295-xx. Initial Criteria: removed to reword the following: "Coverage will be provided if the patient meets the following criteria (A, B, and C): Patient has genetic testing confirmation of a mutation in the *MOCS1* gene; AND 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 The medication is prescribed by or in consultation with a pediatrician, geneticist, or a physician who specializes in molybdenum cofactor deficiency (MoCD) Type A." reworded as: "Patient meets one of the following scenarios: Patient has a diagnosis of MoCD Type A confirmed by a mutation in the MOCS1 gene suggestive of disease as identified on molecular genetic testing; OR Patient has biochemical features suggestive of MoCD Type A (i.e., elevated sulfites in urine, low serum uric acid, elevated urinary xanthine and hypoxanthine) and will be treated presumptively while awaiting genetic confirmation; AND Patient has a baseline value for the following: Urinary s-sulfocysteine (SSC) normalized to creatinine; AND Clinical notes regarding signs and symptoms of disease which may include, but are not limited to, seizure frequency/duration, growth, and developmental milestones; AND Will not be used in combination with other substrate replacement therapy (e.g., recombinant cyclic pyranopterin monophosphate, etc.); AND Must be prescribed by, or in consultation with, a specialist in medical genetics or pediatric neurology RENEWAL CRITERIA: removed to reword the following: "Coverage can be renewed based on the following criteria: Patient continues to meet the above criteria and dosing; AND There is significant clinical improvement of the disease as determined by the prescribing physician; AND There is absence of unacceptable toxicity from the drug." Reworded and added the following:" Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc.identified in Initial Criteria; AND Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity

		include: severe phototoxicity, clinically significant infection, etc.; AND Disease response compared to pre-treatment baseline as evidenced by the following: Reduction in urinary SSC normalized to creatinine; AND Stabilization or improvement in one or more signs and symptoms of disease including, but not limited to, seizure frequency/duration, growth, achievement of developmental milestones; OR Patient initiated therapy as an inpatient based upon a presumptive diagnosis of MoCD Type A which was subsequently confirmed by genetic testing; AND Patient is responding to therapy compared to one or more pre-treatment baseline parameters which prompted the workup for MoCD"
EmblemHealth & ConnectiCare	2/1/2024	Annual Review: no criteria changes
EmblemHealth & ConnectiCare	5/30/2023	Annual Review: no criteria changes
EmblemHealth & ConnectiCare	09/13/2022	Transferred policy to new template.
EmblemHealth & ConnectiCare	9/21/2021	Updated diagnosis codes
EmblemHealth & ConnectiCare	6/9/2021	New Policy

References

1. Nulibry™ (fosdenopterin) for injection [package insert]. Boston, MA. Origin Biosciences, Inc. Updated March 10, 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4f67cc4e-84ed-4f4e-a5d9-6ffbfb84eddd
2. Nulibry™(fosdenopterin) for injection. IBM Micromedex® [database online]. Greenwood Village, CO. Truven Health Analytics. Available at: https://www.micromedexsolutions.com. Updated March 29, 2021. Accessed April 8, 2021.
3. 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