Clinical Policy: Fosdenopterin (Nulibry)

Reference Number: PA.CP.PHAR.471
Effective Date: 07/2021
Last Review Date: 04/2025

Description
Fosdenopterin (Nulibry™) is a cyclic pyranopterin monophosphate (cPMP) replacement therapy.

FDA Approved Indication(s)
Nulibry is indicated to reduce the risk of mortality in patients with molybdenum cofactor deficiency (MoCD) type A.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Nulibry is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Molybdenum Cofactor Deficiency Type A (must meet all)**:**

1. One of the following (a or b):
   a. Diagnosis of MoCD type A confirmed by genetic testing (i.e., presence of molybdenum cofactor synthesis gene 1 [MOCS1] mutation) (*see Appendix D*);
   b. Age ≤ 28 days old, and diagnosis of MoCD type A is presumed based on onset of clinical and laboratory signs/symptoms consistent with MoCD type A (*see Appendix D*);
2. Prescribed by or in consultation with a neonatologist, neurologist, or specialist with expertise in the management of inborn errors of metabolism (e.g., pediatric geneticist);
3. Documentation of member's current weight in kilograms;
4. Dose does not exceed any of the following (a or b):
   a. Age < 1 year: the titration schedule as outlined in section V, then 0.9 mg/kg per day (*see Appendix E for vial quantity recommendations*);
   b. Age ≥ 1 year: 0.9 mg/kg per day (*see Appendix E for vial quantity recommendations*).

Approval duration:
Genetically confirmed diagnosis – 6 months
Presumptive diagnosis – 1 month

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Molybdenum Cofactor Deficiency Type A (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. If the diagnosis of MoCD type A was presumptive at the time of initial authorization, it has since been confirmed by genetic testing (i.e., presence of MOCS1 mutation) (*see Appendix D*);
3. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters:
   a. Clinical outcomes, such as: improved symptoms, achievement of motor milestones, decreased seizure activity, lack of clinical deterioration (e.g., no progression to severe epileptic encephalopathy);
   b. Biochemical outcomes, such as: decreased or normalized urinary s-sulfocysteine (SSC) or xanthine levels, increased or normalized uric acid levels;
4. Documentation of member's current weight in kilograms;
5. If request is for a dose increase, new dose does not exceed 0.9 mg/kg per day (*see Appendix E for vial quantity recommendations*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53;

B. MoCD type B.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

cPMP: cyclic pyranopterin monophosphate
FDA: Food and Drug Administration
MoCD: molybdenum cofactor deficiency
MOCS1: molybdenum cofactor synthesis gene 1
SSC: s-sulfocysteine

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- A list of available genetic tests for MoCD type A can be found here: https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=C1854988&filter=testtype:clinical.
- Clinical signs/symptoms consistent with MoCD type A include, but are not limited to: seizures, exaggerated startle response, high-pitched cry, axial hypotonia, limb hypertonia, feeding difficulties, microcephaly, urolithiasis, MRI signal changes in basal ganglia
- Laboratory signs/symptoms consistent with MoCD type A include, but are not limited to: elevated sulfite and/or SSC and/or thiosulfate in the urine/blood, elevated xanthine or hypoxanthine in urine/ blood, in combination with low or absent uric acid in the urine or blood.

Appendix E: Vial Quantity Recommendations

The below recommendations are based on average weight (50th percentile) by age according to WHO and CDC growth charts. Members whose actual body weight exceeds the average weight should be approved for the appropriate number of vials required to achieve the desired dose.

Age Range	# Vials/Day
0 to < 1 year	1
1 to < 5 years	2
5 to < 8 years	3
8 to < 11 years	4
11 to < 13 years	5
13 to < 15 years	6
15 to < 17 years	7
17 to 20 years	8

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

MoCD type A	Titration schedule for age < 1 year:
	• Preterm neonates (gestational age < 37 weeks):
	  ○ Initial dosage: 0.4 mg/kg IV QD
	  ○ Month 1: 0.7 mg/kg IV QD
	  ○ Month 3: 0.9 mg/kg IV QD
	• Term neonates (gestational age ≥ 37 weeks):
	  ○ Initial dosage: 0.55 mg/kg IV QD
	  ○ Month 1: 0.75 mg/kg IV QD
	  ○ Month 3: 0.9 mg/kg IV QD
	
	Age ≥ 1 year: 0.9 mg/kg IV QD
		0.9 mg/kg/day

VI. Product Availability

Lyophilized powder or cake in a single-dose vial for reconstitution: 9.5 mg

VII. References

1. Nulibry Prescribing Information. Solana Beach, CA: Sentynl Therapeutics, Inc; October 2022. Available at: www.nulibry.com. Accessed January 29, 2025.
2. ClinicalTrials.gov. Study of ORGN001 (formerly ALXN1101) in neonates with molybdenum cofactor deficiency (MOCD) type A. Available at: https://clinicaltrials.gov/ct2/show/NCT02629393. Accessed February 7, 2025.
3. ClinicalTrials.gov. Safety & efficacy study of ORGN001 (formerly ALXN1101) in pediatric patients with MoCD type A currently treated with rcPMP. Available at: https://clinicaltrials.gov/ct2/show/NCT02047461. Accessed February 7, 2025.
4. Schwahn BC, Van Spronsen FJ, Belaidi AA, et al. Efficacy and safety of cyclic pyranopterin monophosphate substitution in severe molybdenum cofactor deficiency type A: a prospective cohort study. Lancet. 2015; 386: 1955-1963.
5. Spiegel R, Schwahn B, Scribner CL, Confer N. A natural history study of molybdenum cofactor (MoCo) and isolated sulfite oxidase deficiencies (ISOD). Poster presented at the 2019 Society for the Study of Inborn Errors of Metabolism (SSIEM); September 3-6, 2019; Rotterdam, The Netherlands.
6. U.S. National Library of Medicine, Genetics Home Reference. Molybdenum cofactor deficiency. Reviewed March 2014. Available at: https://ghr.nlm.nih.gov/condition/molybdenum-cofactor-deficiency. Accessed February 7, 2025.
7. WHO growth charts: Data table for weight-for-age charts, birth-24 months. Available at: https://www.cdc.gov/growthcharts/who-charts.html. Accessed February 7, 2025.
8. CDC growth charts: Data table for weight-for-age charts, 2-20 years. Available at: https://www.cdc.gov/growthcharts/cdc-charts.htm. Accessed February 7, 2025.
9. Schwahn BC, van Spronsen F, Misko A, et al. Consensus guidelines for the diagnosis and management of isolated sulfite oxidase deficiency and molybdenum cofactor deficiencies. J Inherit Metab Dis. 2024;47(4):598-623.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3490	Unclassified drugs
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date
Policy created	07/2021
2Q 2022 annual review: no significant changes; references reviewed and updated.	04/2022
2Q 2023 annual review: no significant changes; references reviewed and updated.	04/2023

Reviews, Revisions, and Approvals	Date
2Q 2024 annual review: no significant changes; references reviewed and updated.	04/2024
2Q 2025 annual review: no significant changes; Appendix D clinical and laboratory signs/symptoms were updated per 2024 consensus guidelines; references reviewed and updated.	04/2025