Clinical Policy: Fosdenopterin (Nulibry)

Reference Number: ERX.SPA.384
Effective Date: 02.26.21
Last Review Date: 05.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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);
   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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents;

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 and laboratory 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, elevated urinary sulfite and/or SSC, elevated xanthine in urine or blood, 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

Age Range	# Vials/Day
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. Boston, MA: Origin Biosciences, Inc.; February 2021. Available at: www.nulibry.com. Accessed February 27, 2022.
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 March 8, 2021.
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 March 8, 2021.
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 March 8, 2021.
7. WHO growth charts: Data table for weight-for-age charts, birth-24 months. Available at: https://www.cdc.gov/growthcharts/who/boys_length_weight.htm and https://www.cdc.gov/growthcharts/who/girls_length_weight.htm. Accessed March 25, 2021.
8. CDC growth charts: Data table for weight-for-age charts, 2-20 years. Available at: https://www.cdc.gov/growthcharts/html_charts/wtage.htm. Accessed March 25, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	03.03.20	05.20
2Q 2021 annual review: drug is now FDA approved – criteria updated per FDA labeling: removed age restriction; added pathway to initial approval for presumptive diagnosis in neonates (genetic confirmation is required upon re-authorization); prescriber requirement: added neonatologist and modified	04.13.21	05.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
specialist in MoCD to specialist in inborn errors of metabolism; removed requirement for documentation of baseline urinary SSC, xanthine, and uric acid since primary outcome of interest is survival; added requirement for documentation of body weight; increased continued approval duration from 6 to 12 months; added MoCD type B as a diagnosis/indication not covered; references reviewed and updated.		
2Q 2022 annual review: no significant changes; references reviewed and updated.	02.27.22	05.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.