Clinical Policy: Fosdenopterin (Nulibry)

Reference Number: CP.PHAR.471
Effective Date: 02.26.21
Last Review Date: 05.21
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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.

It is the policy of health plans affiliated with Centene Corporation® 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 (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 for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit 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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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
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 March 8, 2021.
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.

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	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 from specialist in	04.13.21	05.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
MoCD to neonatologist and 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 to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.		

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.