Neighborhood Health Plan OF RHODE ISLAND™
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Nulibry™ (fosdenopterin)
(Intravenous)

Effective Date: 07/01/2021
Review Date: 6/24/2021, 3/17/2022, 3/2/2023, 12/14/2023, 01/04/2024

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

I. Length of Authorization

Coverage will be provided for six months* and may be renewed.

*if diagnosis is not confirmed approval will be for 3 months (one time only).

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Nulibry 9.5 mg vial for injection: 10 vials daily

B. Max Units (per dose and over time) [HCPCS Unit]:

- 95 mg daily

III. Summary of Evidence

Nulibry (fosdenopterin) was approved by the FDA in February 2021 to reduce the risk of mortality in patients with molybdenum cofactor deficiency (MoCD) Type A. Approval was based on combined efficacy data from 3 clinical trials that compared data from a genotype-matched historical control. Nulibry had a survival rate of 84% at 3 years compared to 55% for the untreated matched control patients. Nulibry is given once daily as an IV infusion at a rate of 1.5mL/min with dosing being age and weight dependent. Treatment with Nulibry can lead to increased photosensitivity and the adverse reactions reported include catheter-related complications, pyrexia, viral infection, pneumonia, otitis media, vomiting, cough/sneezing, viral upper respiratory infection, gastroenteritis, bacteremia, and diarrhea.

IV. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Universal Criteria [1,3]

- 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; **AND**

Molybdenum Cofactor Deficiency Type A (MoCD Type A) † Φ [1-3]

- Patient has a diagnosis of MoCD Type A as confirmed, by molecular genetic testing, by a mutation in the *MOCS1* gene suggestive of disease; **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 (documentation required) for the following:
  - Elevated 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

† FDA approved indication(s); ‡ Compendia recommended indication(s); **Φ** Orphan Drug

V. Renewal Criteria [1]

Authorizations can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **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 (documentation required); **AND**
    - Patient is responding to therapy compared to one or more pre-treatment baseline parameters which prompted the workup for MoCD; **AND**
  - For continued approval diagnosis must be confirmed within the first 3 months of treatment

VI. Dosage/Administration [1]

Indication	Dose
MoCD Type A	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 at least 1 year – The recommended dosage is 0.9 mg/kg administered as an IV infusion once daily. **Note all weights are based on Actual Body Weight (ABW)*
Nulibry is administered intravenously by a healthcare provider or at home by the patient's caregiver	

VII. Billing Code/Availability Information

HCPCS Code:

- J3490 – Unclassified drugs
- C9399 – Unclassified drugs or biologicals (hospital outpatient use)

NDC:

- Nulibry 9.5 mg single-dose vial as a lyophilized powder for injection: 73129-0001-xx

VIII. References

1. Nulibry [package insert]. Boston, MA; Origin Biosciences, Inc.; October 2022. Accessed November 2023.
2. Origin Biosciences. A Phase 2, Multicenter, Multinational, Open-Label, Dose-Escalation Study to Evaluate the Safety and Efficacy of ORGN001 (Formerly ALXN1101) in Pediatric Patients With Molybdenum Cofactor Deficiency (MoCD) Type A Currently Treated With Recombinant Escherichia Coli-derived Cyclic Pyranopterin Monophosphate (rcPMP). Available from: https://clinicaltrials.gov/ct2/show/NCT02047461?term=NCT02047461&draw=2&rank=1. NLM identifier: NCT02047461. Accessed Marche 3, 2021.
3. Origin Biosciences. A Phase 2/3, Multicenter, Multinational, Open Label Study to Evaluate the Efficacy and Safety of ORGN001 (Formerly ALXN1101) in Neonates, Infants and Children With Molybdenum Cofactor Deficiency (MOCD) Type A. Available from: https://clinicaltrials.gov/ct2/show/NCT02629393?term=NCT02629393&draw=2&rank=1. NLM identifier: NCT02629393. Accessed March 3, 2021.

4. Reiss J, Hahnewald R. Molybdenum cofactor deficiency: Mutations in GPHN, MOCS1, and MOCS2. Hum Mutat. 2011 Jan;32(1):10-8.
5. Veldman A, Santamaria-Araujo JA, Sollazzo S, Pitt J, Gianello R, Yaplito-Lee J, Wong F, Ramsden CA, Reiss J, Cook I, Fairweather J, Schwarz G. Successful treatment of molybdenum cofactor deficiency type A with cPMP. Pediatrics. 2010 May;125(5):e1249-54. doi: 10.1542/peds.2009-2192. Epub 2010 Apr 12.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E61.5	Molybdenum deficiency
E72.19	Other disorders of sulfur-bearing amino-acid metabolism

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Nulibry was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Nulibry according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.