09-J3000-95

Original Effective Date: 06/15/21

Reviewed: 12/11/24

Revised: 10/01/25

Subject: Fosdenopterin Hydrobromide (Nulibry)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Molybdenum Cofactor Deficiency (MoCD) is an ultra-rare, autosomal recessive, inborn error of metabolism caused by mutations in the molybdenum cofactor synthesis 1 gene (MOCS1), molybdenum cofactor synthesis 2 gene (MOCS2), and gephyrin gene (GPHN). There are three forms of MoCD: types A, B, and C. The forms have the same signs and symptoms but are distinguished by their genetic cause: MOCS1 gene mutations cause type A, MOCS2 gene mutations cause type B, and GPHN gene mutations cause type C. The proteins produced from each of these genes are involved in the biosynthesis of molybdenum cofactor. In MoCD type A, the mutation disrupts cyclic pyranopterin monophosphate (cPMP) synthesis, which is the first step in the molybdenum cofactor synthesis pathway. A deficiency in molybdenum cofactor production leads to accumulation of s-sulfocysteine (SSC), a neurotoxic metabolite of sulfite that causes rapid and progressive neurological damage.

MoCD typically presents shortly after birth and progresses very quickly with intractable seizures, autonomic dysfunction, feeding difficulties, and severe encephalopathy. MoCD type A impacts less than 150 patients globally and has a median survival age of approximately 4 years. Infants with MoCD type A who survive beyond the first few months without treatment often have severe developmental delays. Management of MoCD is mainly supportive.

Fosdenopterin hydrobromide (Nulibry) was approved by the U.S. Food and Drug Administration (FDA) in February 2021 to reduce the risk of mortality in patients with MoCD type A. Substrate replacement therapy with fosdenopterin provides an exogenous source of cPMP, which is converted to molybdopterin. Molybdopterin is then converted to molybdenum cofactor.

The safety and efficacy of fosdenopterin was evaluated in patients with genetically confirmed MoCD Type A (n=13). Of the 13 treated patients, median gestational age was 39 weeks (range, 35 to 41 weeks).

Age at first dose was 14 days or less for 10 patients (with 5 patients initiating treatment at 1 day of age) and 32 days to less than 69 days for the remaining 3 patients.

In a combined analysis of 3 studies, fosdenopterin reduced the risk of death by 82% compared with an untreated, genotype-matched, historical control group (n=18) (HR, 0.18; 95% CI, 0.04 to 0.72). The probability of survival at 3 years was 84% (95% CI, 49% to 96%) compared with 55% (95% CI, 30% to 74%) in the treated and untreated groups, respectively. In 2 of the studies, treatment with fosdenopterin led to a reduction of urine concentrations of S-sulfocysteine and the reduction was sustained with long-term treatment over 48 months. The most common adverse reactions (>25%) were catheter-related complications, pyrexia, viral infection, pneumonia, otitis media, vomiting, cough/sneezing, viral upper respiratory infection, gastroenteritis, bacteremia, and diarrhea.

POSITION STATEMENT:

Initiation of fosdenopterin hydrobromide (Nulibry) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with Molybdenum Cofactor Deficiency (MoCD) Type A
2. Member's diagnosis of MoCD Type A is confirmed by genetic testing - laboratory documentation must be provided
3. Dose does not exceed 0.9 mg/kg daily

Approval duration: 6 months

Continuation of fosdenopterin hydrobromide (Nulibry) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue in the past two years for treatment of MoCD Type A, **OR** the member has previously met all indication-specific criteria
2. Member continues to receive benefit with treatment with fosdenopterin - documentation from the medical record must be provided

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Gestational age less than 37 weeks
    - Initial Dosage: 0.4 mg/kg once daily
    - Month 1: 0.7 mg/kg once daily

    - Month 3: 0.9 mg/kg once daily
- Gestational age 37 weeks and above (up to one year of age)
    - Initial Dosage: 0.55 mg/kg once daily
    - Month 1: 0.75 mg/kg once daily
    - Month 3: 0.9 mg/kg once daily
- One year of age and older: 0.9 mg/kg once daily

Dose Adjustments

- None

Drug Availability

- For injection: 9.5 mg of fosdenopterin as a lyophilized powder or cake in a single-dose vial for reconstitution

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- Potential for photosensitivity

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J1809	Injection, fosdenopterin, 0.1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

E61.5	Molybdenum deficiency

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 11/30/24]. Available from: http://www.clinicalpharmacology.com/.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 11/30/24]. Available from: http://clinicaltrials.gov/.
3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 11/30/24].
4. Origin Biosciences. Nulibry (fosdenopterin hydrobromide) injection. 2021 [cited 4/26/21]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4f67cc4e-84ed-4f4e-a5d9-6ffbfb84eddd
5. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 11/30/24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/11/24.

GUIDELINE UPDATE INFORMATION:

06/15/21	New Medical Coverage Guideline.
01/15/24	Review and revision to guideline; updated references.
01/15/25	Review and revision to guideline; updated references.
10/01/25	Revision: Added HCPCS code J1809 and deleted code J3490.