

Medical benefit drug policies are a source for WyoBlue Advantage medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 04/10/2025

Nulibry® (fosdenopterin)

HCPCS: J3490, C9399

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. FDA approved indication
 - b. FDA approved age
 - c. Confirmed genetic diagnosis of molybdenum cofactor deficiency (MoCD) Type A (MOCS1 mutation) and/or biochemical profile consistent with MoCD Type A
 - i. Examples: elevated urinary sulfite and/or S-sulfocysteine (SSC), elevated xanthine in urine or blood, or low or absent uric acid in the urine or blood
 - d. Documentation of clinical presentation consistent with MoCD Type A
 - i. Examples: intractable seizures, exaggerated startle response, high-pitched cry, axial hypotonia, limb hypertonia, feeding difficulties
 - e. No current or planned treatment for MoCD Type A with another investigational drug or device
 - i. Exception: Recombinant Escherichia coli-derived cyclic pyranopterin monophosphate (rcPMP) through day 1
 - f. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in WyoBlue Advantage's utilization management medical drug list
- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limits: Align with FDA recommended dosing
 - b. Initial Authorization Period: Two months
 - c. Renewal Authorization Period: Six months
 - d. Renewal Criteria: If not provided on initial approval, genetic confirmation of MoCD Type A (MOCS1 mutation) is required. Additionally, clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit.

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Nulibry is a cyclic pyranopterin monophosphate (cPMP) substrate replacement therapy indicated for the treatment of molybdenum cofactor deficiency (MoCD) Type A.
- MoCD is an autosomal recessive disorder that results from one of several single gene defects in the biosynthetic pathway of molybdenum cofactor. Molybdenum cofactor deficiency is caused by mutations in the molybdenum cofactor synthesis 1 (MOCS1), MOCS2, or GPHN gene. There are three forms of the disorder, named types A, B, and C (or complementation groups 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.
- Approximately two-thirds of patients have MoCD type A, in which mutations in MOCS1 result in the inability to synthesize the first intermediate in the pathway, cyclic pyranopterin monophosphate (cPMP), and the toxic accumulation of sulfites in blood and urine. Tests reveal that affected individuals have high levels of sulfite, S-sulfocysteine, xanthine, and hypoxanthine in the urine and low levels of uric acid in the blood. A positive sulfite dipstick finding of very fresh urine is highly suggestive of sulfite oxidase deficiency and MoCD; however, a negative dipstick finding should not eliminate suspicion, as urinary sulfite is an unstable compound and prone to false-negative results related to drugs and bacterial degradation.
- MoCD is a rare condition characterized by encephalopathy that worsens over time. Babies with this condition appear normal at birth, but within a week they have difficulty feeding and develop intractable seizures. Brain abnormalities, including atrophy of brain tissue, lead to severe developmental delay; affected individuals usually do not learn to sit unassisted or to speak.
- Biochemical tests, when paired with clinical presentation, can confirm a suspected MoCD diagnosis. A genetic test is the only way to distinguish between MoCD subtypes, and genetic results can take weeks.
- In patients with a presumptive diagnosis of MoCD Type A based on biochemical tests and clinical presentation, confirmation of the diagnosis of MoCD Type A via genetic testing should commence immediately after initiation of Nulibry treatment. Nulibry should be discontinued if the MoCD Type A diagnosis is not confirmed by genetic testing.
- MoCD is estimated to occur in 1 in 100,000 to 200,000 newborns worldwide with a median survival of less than 4 years. More than 100 cases have been reported in the medical literature, although it is thought that the condition is underdiagnosed, so the number of affected individuals may be higher.
- Prior to the development of the synthetic form of cPMP (Nulibry), an E.coli derived recombinant form of cPMP (rcPMP) was in development. Studies for the approval of Nulibry include this rcPMP which has the same active moiety and biologic activity as Nulibry. Studies showed the safety and efficacy of switching patients from rcPMP to cPMP.

References:

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3. Origin Biosciences. Safety & Efficacy Study of ORGN001 (Formerly ALXN1101) in Pediatric Patients With MoCD Type A Currently Treated With rcPMP. Available from: <https://clinicaltrials.gov/ct2/show/NCT02047461> ClinicalTrials.gov Identifier: NCT02047461. Accessed 11.2.2020
4. NIH U.S. National Library of Medicine. MedlinePlus: Molybdenum cofactor deficiency. <https://medlineplus.gov/genetics/condition/molybdenum-cofactor-deficiency/>
5. Bridgebio. BridgeBio Pharma And Affiliate Origin Biosciences Announces FDA Acceptance Of Its New Drug Application For Fosdenopterin For The Treatment Of MoCD Type A. Press release from 9.29.2020. <https://bridgebio.com/news/bridgebio-pharma-and-affiliate-origin-biosciences-announces-fda-acceptance-of-its-new-drug-application-for-fosdenopterin-for-the-treatment-of-mocd-type-a>
6. Shellhaas R MD. Etiology and prognosis of neonatal seizures. UpToDate. <https://www.uptodate.com/contents/etiology-and-prognosis-of-neonatal-seizures> Accessed 11.2.2020
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8. Mechler K et al. Genet Med. 2015;17(12):965-9
9. Zaki MS et al. Molybdenum cofactor and isolated sulphite oxidase deficiencies: Clinical and molecular spectrum among Egyptian patients. Eur J PaediatrNeurol. 2016;20(5):714-722.

Policy History		
#	Date	Change Description
1.0	Initial Effective Date: 01/01/2026	New policy

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.*