Original Effective Date: 03/28/2025
Current Effective Date: 10/09/2025
Last P&T Approval/Version: 07/30/2025
Next Review Due By: 07/2026
Policy Number: C29062-A

Miplyffa (arimoclomol)

PRODUCTS AFFECTED

Miplyffa (arimoclomol)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Niemann-Pick Disease Type C

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. NIEMANN-PICK DISEASE TYPE C:
   1. Documented diagnosis of Niemann-Pick disease, type C
      AND
   2. Documentation diagnosis was confirmed by genetic testing that identifies both disease-causing alleles in NPC1 or NPC2 [DOCUMENTATION REQUIRED]

AND

3. Documentation of neurological manifestations (see APPENDIX)
   AND
4. Documentation of concurrent treatment with miglustat

CONTINUATION OF THERAPY:

A. NIEMANN-PICK DISEASE TYPE C:

1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
2. Documentation of concurrent treatment with miglustat

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified neurologist, geneticist, metabolic specialist, or physician experienced in the management of Niemann-Pick disease. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests.]

AGE RESTRICTIONS:

2 years of age and older

QUANTITY:

The recommended oral dosage of Miplyffa (arimoclomol) is based on actual body weight.

Body weight	Recommended oral dosage if eGFR ≥ 50 mL/minute
8 kg to 15 kg	47 mg three times a day
> 15 kg to 30 kg	62 mg three times a day
> 30 kg to 55 kg	93 mg three times a day
> 55 kg	124 mg three times a day

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:

Psychotherapeutic and Neurological Agents – Misc.

FDA-APPROVED USES:

Indicated for use in combination with miglustat for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adult and pediatric patients 2 years of age and older.

COMPENDIAL APPROVED OFF-LABELED USES:

None

APPENDIX

APPENDIX:

Symptoms of NPD-C are progressive and may present differently depending on age.

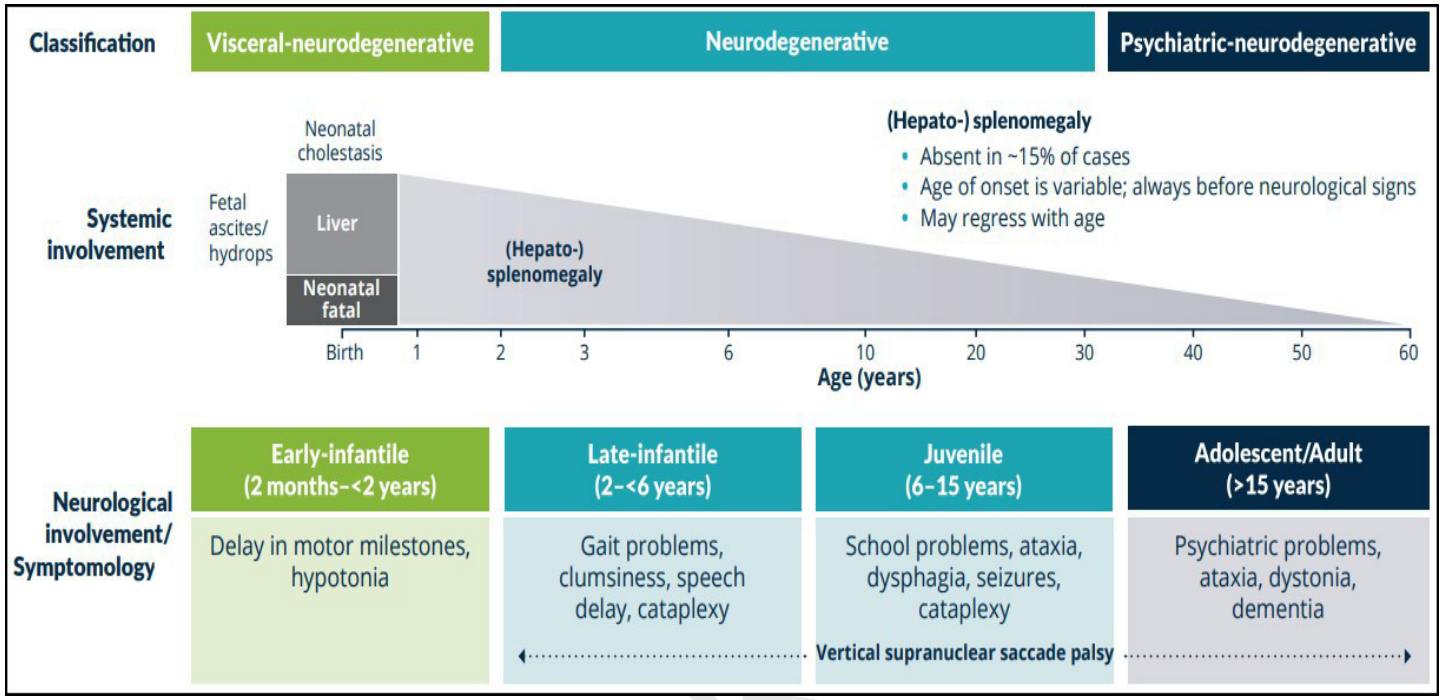

Figure 1: NPC Guidelines; Recommendations for the diagnosis and management of Niemann-Pick disease type C: an update. Journal of Molecular Genetics and Metabolism July 2012.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Niemann-Pick disease (NPD), also called sphingomyelin-cholesterol lipidosis, is a group of autosomal recessive disorders associated with splenomegaly, variable neurologic deficits, and the storage of lipids including sphingomyelin and cholesterol. Niemann-Pick disease originally was defined in terms of its histology as a reticuloendotheliosis. There are three types of NPD: type A (NPD-A), type B (NPD-B) and type C (NPD-C).

Niemann-Pick disease types A and B are allelic disorders caused by pathogenic variants in the sphingomyelin phosphodiesterase-1 (SMPD1) gene and characterized by a primary deficiency of acid sphingomyelinase activity. Type C is caused by pathogenic variants of the NPC1 or NPC2 genes that result in impaired cellular processing and transport of low-density lipoprotein (LDL) cholesterol.

Most patients with NPD-C have disease onset in middle to late childhood after normal early development. These patients typically have cerebellar involvement characterized by clumsiness and gait problems progressing to frank ataxia, and slow cognitive deterioration. Vertical supranuclear ophthalmoparesis is another early manifestation. Progressive dystonia, dysarthria, and dysphagia occur, eventually impairing oral feeding, and approximately one-third of patients develop seizures. Death typically occurs from aspiration pneumonia in the second or third decade of life.

Neonatal onset of NPD-C may occur, presenting with severe hepatic disease from infiltration of the liver. In addition, pulmonary disease with respiratory failure secondary to alveolar proteinosis or an alveolar proteinosis-like syndrome may accompany neonatal hepatic disease or occur as the initial presentation. Fetal onset of NPD-C is most often associated with ultrasonographic findings of splenomegaly,

hepatomegaly, and ascites or fetal hydrops. A separate infantile form presents with hypotonia and developmental delay with little or no hepatic and pulmonary involvement.

Adult onset of NPD-C may present with ataxia, supranuclear vertical gaze palsy, cognitive impairment, and other symptoms similar to earlier onset disease, except that progression is generally much slower. Other adults present with cognitive dysfunction or psychiatric disturbances. In some cases of NPD-C, subtle premonitory signs or symptoms in childhood, such as splenomegaly, hepatomegaly, learning difficulty, deafness, or impaired vertical gaze, may precede neurologic deterioration in adulthood.

NPD-A is the acute neuronopathic form. Affected patients present with hepatosplenomegaly, feeding difficulties, and loss of early motor skills in the first few months of life. Rapid, progressive, and profound loss of neurologic function leading to death occurs by two to three years of age. Additional manifestations include peripheral neuropathy, hypotonia, loss of reflexes, and interstitial lung disease. Macular cherry red spots are eventually present in all affected individuals.

NPD-B is pan-ethnic and generally later in onset and less severe than NPD-A, with a good prognosis for survival into adulthood. Hepatosplenomegaly develops during infancy or childhood. Other systemic manifestations include short stature with delayed skeletal maturation, interstitial lung disease, hyperlipidemia, and ocular abnormalities. The natural history is one of progressive hypersplenism and gradual deterioration of pulmonary function.

NPD-C can present from the perinatal period until late adulthood. Most patients with NPD-C have disease onset in middle to late childhood, typically with vertical supranuclear gaze palsy, cerebellar symptoms, slow cognitive deterioration, and progressive dystonia, dysarthria, and dysphagia.

The diagnosis of NPD first depends upon an appreciation of the variable phenotypic manifestations. The definitive diagnosis of NPD-A and NPD-B is made by detection of both disease-causing alleles in SMPD1 or by demonstration of acid sphingomyelinase deficiency (ASMD). The diagnosis of NPD-C is based upon abnormal biomarker screening for oxysterols and genetic confirmation of a pathogenic variants involving both alleles of NPC1 or NPC2.

The management of all forms of NPD is supportive. There is no treatment for NPD that is proven to modify the onset or neurologic progression of the disease, or to prolong lifespan. However, limited data suggest that olipudase alfa may improve certain non-neurologic manifestations of ASMD (NPD-B) and that miglustat may delay the progression of the neurologic manifestations of NPD-C in children without severe neurologic symptoms at the start of treatment.

The efficacy of arimoclomol was studied in a 12-month multi-center, randomized, double-blind, placebo-controlled trial in patients with NPD-C. Patients treated with arimoclomol, in combination with miglustat, showed slower disease progression (as measured by the Rescored 4-Domain NPC Clinical Severity Scale [R4DNPCCSS] score) at 12 months compared to treatment with miglustat alone. The R4DNPCCSS is a measure of NPD-C disease progression that looks at four items that patients with NPD-C, their caregivers and physicians have identified as most relevant including ambulation, speech, swallow and fine motor skills. Higher scores signify a greater severity of the disease.

There is insufficient data to determine the effectiveness of the use of arimoclomol without miglustat for the treatment of neurological manifestations in patients with NPD-C.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Miplyffa (arimoclomol) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Miplyffa (arimoclomol) include: no labeled indications. Based on findings from animal reproduction studies, Miplyffa (arimoclomol) may cause embryofetal harm when administered during pregnancy. There are no available data on Miplyffa (arimoclomol) use in

pregnant females to evaluate a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Advise pregnant females of the potential risk to the fetus.

OTHER SPECIAL CONSIDERATIONS:

The recommended Miplyffa (arimoclomol) dosage in combination with miglustat in patients with an eGFR 15 mL/minute to < 50 mL/minute is lower than the recommended dosage (less frequent dosing) in patients with normal renal function.

Body weight	Recommended oral dosage if eGFR ≥ 15 to < 50 mL/minute
8 kg to 15 kg	47 mg two times a day
> 15 kg to 30 kg	62 mg two times a day
> 30 kg to 55 kg	93 mg two times a day
> 55 kg	124 mg two times a day

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:

Miplyffa CAPS 47MG
Miplyffa CAPS 62MG
Miplyffa CAPS 93MG
Miplyffa CAPS 124MG

REFERENCES

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3. Vanier, M.T. Niemann-Pick Disease Type C, Orphanet Journal of Rare Diseases, 2010;5(16):1-18. doi:10.1186/1750-1172-5-16.
4. Patterson MC, Clayton P, Gissen P, et al. Recommendations for the detection and diagnosis of Niemann-Pick disease type C: an update. American Academy of Neurology: Neurology Clinical Practice. 2017;7(6):499-511. doi:10.1212/CPJ.0000000000000399. PMID: 29431164.
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Niemann-Pick disease type C. Orphanet Journal of Rare Diseases. 2018;13(1):1-19. doi:10.1186/s13023-018-0785-7
6. Patterson et al. Recommendations for the diagnosis and management of Niemann-Pick disease type C: An update. Mol Genet Metab. 2012;106(3):330-344. doi:10.1016/j.ymgme.2012.03.012. Epub 2012 May 8. PMID: 22572546.
7. Wasserstein MP, Schuchman EH. Acid sphingomyelinase deficiency. GeneReviews 2023, Adam MP, Feldman J, Mirzaa GM, et al (Eds.), University of Washington, Seattle. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1370/ (Accessed on October 31, 2024).

SUMMARY OF REVIEW/REVISIONS	DATE
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q3 2025
NEW CRITERIA CREATION	Q1 2025