Clinical Policy: Arimoclomol (Miplyffa)

Reference Number: CP.PHAR.510
Effective Date: 09.20.24
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Arimoclomol (Miplyffa™) is a molecular chaperone activator of the heat-shock proteins.

FDA Approved Indication(s)

Miplyffa is 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.

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 Miplyffa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Niemann-Pick Disease Type C (must meet all)**:**

1. Diagnosis of NPC confirmed by genetic analysis indicating biallelic pathogenic variants in either *NPC1* or *NPC2*;
2. Prescribed by or in consultation with a geneticist, neurologist, endocrinologist, or metabolic disease specialist;
3. Age ≥ 2 years;
4. Member presents with at least one neurological sign or symptom of the disease (*see Appendix D*);
5. Member is able to walk either independently or with assistance;
6. For members weighing ≥ 15 kg: Failure of ≥ 3 month trial of Aqneursa®*, unless contraindicated or clinically significant adverse effects are experienced;^
   **Prior authorization may be required for Aqneursa*
   ^ For Illinois HIM requests, the step therapy requirement above does not apply as of 1/1/2026 per IL HB 5395
7. Miplyffa is prescribed in combination with miglustat;
8. Miplyffa is not prescribed concurrently with Aqneursa™;
9. Dose does not exceed both of the following (a and b):
   a. 3 capsules per day;
   b. One of the following, based on body weight (i, ii, iii, or iv):
      i. For 8 kg to 15 kg: 141 mg per day;
      ii. For > 15 kg to 30 kg: 186 mg per day;
      iii. For > 30 kg to 55 kg: 279 mg per day;

iv. For > 55 kg: 372 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Niemann-Pick Disease Type C (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by an improvement, stabilization, or slowed disease progression in a domain affected by NPC (e.g., ambulation, fine motor skills, swallowing, sitting, speech);
3. Miplyffa is prescribed in combination with miglustat;
4. Miplyffa is not prescribed concurrently with Aqneursa;
5. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 3 capsules per day;
   b. One of the following, based on body weight (i, ii, iii, or iv):
      i. For 8 kg to 15 kg: 141 mg per day;
      ii. For > 15 kg to 30 kg: 186 mg per day;
      iii. For > 30 kg to 55 kg: 279 mg per day;
      iv. For > 55 kg: 372 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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.PHAR.21 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
NPC: Niemann-Pick disease type C

Appendix B: Therapeutic Alternatives This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Aqneursa™ (levacetylleucine)	Recommended dose is based actual body weight administered PO up to TID: • 15 kg to < 25 kg: 1 g morning dose, no afternoon dose, 1 g evening dose • 25 kg to < 35 kg: 1 g morning dose, 1 g afternoon dose, 1 g evening dose • ≥ 35 kg: 2 g morning dose, 1 g afternoon dose, 1 g evening dose	4 g/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Examples of neurological signs or symptoms of NPC include hearing loss, vertical supranuclear gaze palsy, dysarthria, ataxia, dystonia, impaired ambulation, dysarthria, dysphagia, seizures, and dementia.
- The ability to walk either independently or with assistance was an eligibility criterion for all patients in Miplyffa's pivotal trial. It is an objective measure of NPC neurological severity, and Miplyffa's efficacy evaluation was based on patients who were able to walk either independently or with assistance.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NPC	Recommended dose, in combination with miglustat, based on actual body weight: • 8 kg to 15 kg: 47 mg PO TID • > 15 kg to 30 kg: 62 mg PO TID • > 30 kg to 55 kg: 93 mg PO TID • > 55 kg: 124 mg PO TID	372 mg/day

VI. Product Availability

Oral capsules: 47 mg, 62 mg, 93 mg, 124 mg

VII. References

1. Miplyffa Prescribing Information. Celebration, FL: Zevra Therapeutics, Inc.; March 2026. Available at https://miplyffa.com. Accessed July 8, 2026.
2. Mengel E, Patterson MC, Da Riol RM, et al. Efficacy and safety of arimoclomol in Niemann-Pick disease type C: Results from a double-blind, randomised, placebo-controlled, multinational phase 2/3 trial of a novel treatment. *J Inherit Metab Dis*. 2021;44(6):1463-1480. doi:10.1002/jimd.12428
3. Hiwot T, Porter FD, Bremova-Ertl T, et al. 2025 Consensus clinical management guidelines for Niemann-Pick disease type C. J Inherit Metab Dis. 2026;49(3):e70185. doi:10.1002/jimd.70185
4. Geberhiwot T, Moro Alessandro, Dardis A, et al. Consensus clinical management guidelines for Niemann-Pick disease type C. Orphanet Journal of Rare Diseases 2018 April 6;13(1):50.
5. Patterson MC, Clayton P, Gissen P, et al. Recommendations for the detection and diagnosis of Niemann-Pick disease type C: An update. Neurol Clin Pract. 2017;7(6):499-511.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: no significant changes as drug is not yet FDA-approved. Template changes applied to other diagnoses/indications and continued therapy section.	08.01.22	11.22
4Q 2023 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	07.10.23	11.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2024 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	07.22.24	11.24
Drug is now FDA approved – criteria updated per FDA labeling: for the diagnostic criteria, the criterion for oxysterols elevated at > 2 times the upper limit of normal was revised to include more examples reflecting the consensus guideline; added neurologist and geneticist specialists and removed psychiatrist per external specialist feedback; removed upper limit of 18 years as age requirement for therapy initiation; revised ≥ 1 neurologic symptom to include option of neurologic sign; added requirement that Miplyffa is prescribed in combination with miglustat to initial and continued criteria; added exclusion for concurrent therapy with Aqneursa to initial and continued criteria; clarified continued therapy positive response criterion to improvement or stabilization in a domain affected by NPC; references reviewed and updated.	12.03.24	02.25
4Q 2025 annual review: Per August SDC added requirement that for members weighing ≥ 15 kg, failure of a ≥ 3-month trial of Aqneursa; added step therapy bypass for IL HIM per IL HB 5395; revised initial approval duration from 6 months to 12 months; for continued therapy, added positive response option of slowed disease progression in a domain affected by NPC; references reviewed and updated.	08.20.25	11.25
4Q 2026 annual review: updated NPC diagnostic criterion to require confirmation by biallelic pathogenic variants in *NPC1* or *NPC2* gene per updated international consensus guidelines; added ICHRA line of business; references reviewed and updated.	07.08.26	11.26

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.

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