

## Clinical Policy: Arimoclomol (Miplyffa)

Reference Number: PA.CP.PHAR.510

Effective Date: 02/2025

Last Review Date: 11/2025

### 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 PA Health & Wellness® 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 one of the following (a or b):
  - a. Genetic analysis indicating mutation in both alleles of *NPC1* or *NPC2*;
  - b. Genetic analysis indicating mutation in one allele of *NPC1* or *NPC2*, along with one of the following (i or ii):
    - i. Positive filipin staining test result;
    - ii. Positive biomarker result (e.g., oxysterol, lyso-sphingolipid, bile acid);
2. Prescribed by or in consultation with a geneticist, neurologist, endocrinologist, or metabolic disease specialist;
3. Age  $\geq$  2 years;
4. Member presents with at least one neurological sign or symptom of the disease (*see Appendix D*);
5. Miplyffa is prescribed in combination with miglustat;
6. For members weighing  $\geq$  15 kg: Failure of  $\geq$  3 month trial of Aqneursa®\*, unless contraindicated or clinically significant adverse effects are experienced;  
*\*Prior authorization may be required for Aqneursa*
7. Miplyffa is not prescribed concurrently with Aqneursa™;
8. Dose does not exceed both of the following (a and b):
  - a. 3 capsules per day;
  - b. Any of following, based on body weight:
    - 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**

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**II. Continued Therapy**

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by an improvement or stabilization 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. Any of following, based on body weight:
    - 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. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

**Approval duration: Duration of request or 12 months (whichever is less); or**

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**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 – PA.CP.PMN.53

**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 and may require prior authorization.*

| Drug Name                       | Dosing Regimen   | Dose Limit/<br>Maximum Dose |
|---------------------------------|--|-----------------------------|
| Aqneursa™<br>(levacetylleucine) | Recommended dose is based actual body weight administered PO up to TID: <ul style="list-style-type: none"> <li>15 kg to &lt; 25 kg: 1 g morning dose, no afternoon dose, 1 g evening dose</li> <li>25 kg to &lt; 35 kg: 1 g morning dose, 1 g afternoon dose, 1 g evening dose</li> <li>≥ 35 kg: 2 g morning dose, 1 g afternoon dose, 1 g evening dose</li> </ul> | 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: <ul style="list-style-type: none"> <li>8 kg to 15 kg: 47 mg PO TID</li> <li>&gt; 15 kg to 30 kg: 62 mg PO TID</li> <li>&gt; 30 kg to 55 kg: 93 mg PO TID</li> <li>&gt; 55 kg: 124 mg PO TID</li> </ul> | 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.; September 2024. Available at <https://miplyffa.com>. Accessed July 14, 2025.
2. Mengel E, Patterson MC, Da Rioli 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. 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.
4. 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    |
|---|---------|
| Policy created  | 01/2025 |
| 1Q 2026 annual review: Per August SDC added requirement that for members weighing $\geq 15$ kg, failure of a $\geq 3$ -month trial of Aqneursa; 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. | 11/2025 |