Effective Date: 05/01/2025
Reviewed: 02/10/2025, 03/2026
Scope: Medicaid

Niemann-Pick Disease Type C (NPC)

Aqneursa (levacetylleucine) for oral suspension
Miplyffa (arimoclomol) oral capsules

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
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.

Aqneursa is indicated for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adults and pediatric patients weighing ≥15 kg

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Niemann-Pick disease type C (NPC)
Authorization of the requested drug for 6 months may be granted for treatment of Niemann-Pick disease, type C when all of the following criteria are met:

A. Documentation (e.g., chart notes) of 5-domain NPC clinical severity scale (NPCCSS) assessment to establish baseline score.
B. Documentation that the diagnosis is confirmed by one of the following:
    a. Genetically confirmed variant in both alleles of NPC1 or NPC2.
    b. Mutation in only one allele of NPC1 or NPC2 plus either positive filipin staining or elevated cholestane-triol level (>2 times the upper limit of normal).
C. Medical records (e.g., chart notes) documenting that member has neurological manifestations of disease (e.g., loss of fine motor skills, swallowing, speech, ambulation).
D. Stable on miglustat (e.g., Opfolda) for 6 months except if not recommended (i.e., if patient has advanced neurological disease and/or dementia, early-infantile NPC, or has spleen/liver enlargement only).
E. Member has the ability to walk either independently or with assistance.
F. This medication must be prescribed by or in consultation with an endocrinologist, geneticist, neurologist or physician who specializes in the treatment of metabolic disease and/or lysosomal storage disorders.
G. If request is for Aqneursa:
    a. Member is 4 years of age to 64 years of age.
    b. Documentation that member weighs ≥ 15 kg and prescribed dose is in accordance with FDA-approved labeling based on current weight.

c. The requested medication will not be used in combination with Miplyffa (arimoclomol) for the treatment of neurological manifestations of Niemann-Pick disease type C.

H. If request is for Miplyffa:
   a. Member is 2 to 19 years of age.
   b. Member does NOT have adult-onset Niemann-Pick disease type C
      Note: Adult-onset NPC is defined as the age of the first neurological symptom occurring > 15 years of age
   c. Documentation of current weight and prescribed dose is in accordance with FDA-approved labeling.
   d. The requested medication will be used in combination with miglustat (e.g., Opfolda)
   e. The requested medication will not be used in combination with Aqneursa (levacetylleucine) for the treatment of neurological manifestations of Niemann-Pick disease type C.

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for the treatment of Niemann-Pick disease type C when all of the following criteria are met:

A. Member meets the criteria for initial approval.
B. Documentation that member is experiencing benefit from therapy (e.g., stabilization or improvement in 5-domain NPCCSS score, fine motor skills, swallowing, speech, ambulation).

IV. QUANTITY LIMIT

Miplyffa 47 mg, 62 mg, 93 mg, 124 mg capsules have a quantity limit of 3 capsules per day.

Aqneursa 1 g unit dose packets have a quantity limit of 4 packets per day.

Drug	Recommended Dosage
Miplyffa	Based on actual body weight*: • 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 *Note:* For patients with an eGFR ≥ 15 to < 50 mL/minute, reduce the frequency to two times daily
Aqneursa	Based on actual body weight: • 15 kg to <25 kg - 1 g twice daily • 25 kg to <35 kg - 1 g three times daily • 35 kg or more - 2 g in the morning, 1 g in the afternoon, and 1 g in the evening

*refer to prescribing information for oral or G-Tube administration instructions for patients who have difficulty swallowing capsules

V. REFERENCES

1. Miplyffa [package insert]. Celebration, FL: Zevra Therapeutics, Inc.; September 2024.
2. Aqneursa [package insert]. Austin, TX: IntraBio, Inc.; September 2024.
3. Patterson, M. C., Lloyd-Price, L., Guldberg, C., Doll, H., Burbridge, C., Chladek, M., íDali, C., Mengel, E., & Symonds, T. (2021). Validation of the 5-domain Niemann-Pick Type C Clinical Severity Scale. *Orphanet Journal of Rare Diseases*, *16*(1). https://doi.org/10.1186/s13023-021-01719-2
4. Geberhiwot, T., Moro, A., Dardis, A. *et al.* Consensus clinical management guidelines for Niemann-Pick disease type C. *Orphanet J Rare Dis* **13**, 50 (2018). https://doi.org/10.1186/s13023-018-0785-7
5. Freihuber, C., Dahmani-Rabehi, B., Brassier, A. *et al.* Effects of miglustat therapy on neurological disorder and survival in early-infantile Niemann-Pick disease type C: a national French retrospective study. *Orphanet J Rare Dis* **18**, 204 (2023). https://doi.org/10.1186/s13023-023-02804-4

VI. APPENDIX

5- domain NPC clinical severity scale (NPCCSS) assessment

Table 1 5-domain NPCCSS

Domain	Scoring	Minimum–Maximum Score
Ambulation	0 = Normal 1 = Clumsy 2 = Ataxic unassisted gait or not walking by 18 months 4 = Assisted ambulation or not walking by 24 months 5 = Wheelchair dependent	0–5
Fine Motor Skills	0 = Normal 1 = Slight dysmetria/dystonia (independent manipulation) 2 = Mild dysmetria/Dystonia (requires little to no assistance, able to feed self without difficulty) 4 = Moderate dysmetria/dystonia (limited fine motor skills, difficulty feeding self) 5 = Severe dysmetria/Dystonia (gross motor limitation, requires assistance for selfcare activities)	0–5
Swallow	0 = Normal, no dysphagia 1 = Cough while eating Intermittent dysphagia* +1 = w/Liquids +1 = w/Solids Dysphagia* +2 = w/Liquids +2 = w/Solids 4 = Nasogastric tube or gastric tube for supplemental feeding 5 = Nasogastric tube or gastric tube feeding only	0–5
Cognition	0 = Normal 1 = Mild learning delay, grade appropriate for age 3 = Moderate learning delay, individualized curriculum or modified work setting 4 = Severe delay/plateau, no longer in school or no longer able to work, some loss of cognitive function* 5 = Minimal cognitive function	0–5
Speech	0 = Normal 1 = Mild dysarthria (easily understood 2 = Severe dysarthria (difficult to understand) 3 = Non-verbal/functional communication skills for needs 5 = Minimal communication	0–5
5-domain NPCCSS score	Sum of all scores from the 5 domains above	0–25 (higher score = more severe clinical impairment)

* Score is additive (to the "cough while eating"-score of 1) within the two subsections of intermittent dysphagia and dysphagia (example: for intermittent dysphagia with solids and dysphagia with liquids a score of 4 applies (1 + 1 + 2))

Adapted from Patterson et al.