Clinical Policy: Levacetylleucine (Aqneursa)

Reference Number: CP.PHAR.682
Effective Date: 09.24.24
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Levacetylleucine (Aqneursa™) is a modified amino acid.

FDA Approved Indication(s)

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

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 Aqneursa 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. Weight is ≥ 15 kg;
4. Documentation of member's current body weight in kg;
5. Member presents with at least one neurological sign or symptom of the disease (*see Appendix D*);
6. Member meets one of the following (a or b):
   a. Member is able to walk either independently or with assistance;
   b. Scale for the Assessment and Rating of Ataxia (SARA) baseline score ≥ 7 and ≤ 34;
7. Aqneursa is not prescribed concurrently with Miplyffa™;
8. Dose does not exceed the following, based on body weight:
   a. For 15 kg to < 25 kg: 2 g (2 packets) per day;
   b. For 25 kg to < 35 kg: 3 g (3 packets) per day;
   c. For ≥ 35 kg: 4 g (4 packets) per day.

Approval duration: 12 weeks

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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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 or stabilization in a domain affected by NPC (e.g., ambulation, fine motor skills, swallowing, sitting, speech);
3. Aqneursa is not prescribed concurrently with Miplyffa;
4. If request is for a dose increase, new dose does not exceed the following by body weight:
   a. For 15 kg to < 25 kg: 2 g (2 packets) per day;
   b. For 25 kg to < 35 kg: 3 g (3 packets) per day;
   c. For ≥ 35 kg: 4 g (4 packets) 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) 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, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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.PA.154 for health insurance marketplace, 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
SARA: Scale for the Assessment and Rating of Ataxia

Appendix B: Therapeutic Alternatives
Not applicable

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.
- NPC neurological severity assessment
  - SARA domains and scoring (total score: 0-40)

8-Domains	Score Scale
Gait	0-8
Stance	0-6
Sitting	0-4
Speech disturbance	0-6
Finger chase	0-4
Nose-finger test	0-4
Fast alternating hand movements	0-4
Heel-shin slide	0-4

- A SARA baseline score of ≥ 7 and ≤ 34 was an eligibility criterion for all patients in Aqneursa's pivotal trial. This essentially excluded patients with very mild and very severe NPC.
- The ability to walk either independently or with assistance is also an objective measure of NPC neurological severity. Given the limited use of the SARA scale in general for NPC, this adds an alternative to providers for objective severity assessment.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NPC	Recommended dose is based actual body weight administered PO up to three times daily: • 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

VI. Product Availability

Granules for oral suspension: 1 g Aqneursa in a unit-dose packet

VII. References

1. Aqneursa Prescribing Information. Austin, TX: IntraBio, Inc.; September 2024. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/219132s000lbl.pdf. Accessed November 5, 2024.
2. Bremova-Ertl T, Ramaswami U, Brands M, et al. Trial of *N*-Acetyl-l-Leucine in Niemann-Pick disease type C. N Engl J Med. 2024;390(5):421-431.
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	P&T Approval Date
Policy created pre-emptively	06.04.24	08.24
Drug is now FDA approved – criteria updated per FDA labeling: added neurologist and geneticist specialists and removed psychiatrist per external specialist feedback; removed requirement for age ≥ 4 years; revised neurologic signs and symptoms from ≥ 2 to ≥ 1; added option for baseline severity assessment that member can walk either independently or with assistance; added exclusion for concurrent therapy with Miplyffa to initial and continued criteria; revised continued therapy positive response criterion to	12.03.24	02.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
improvement or stabilization in a domain affected by NPC; references reviewed and updated.		

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.

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.