MEDICAL MUTUAL®

Drug Policy

Policy:	Aqneursa™ (levacetylleucine for oral suspension – IntraBio)	Annual Review Date: 08/21/2025 Last Revised Date: 08/21/2025

OVERVIEW

Aqneursa, a modified amino acid, is indicated for the treatment of neurological manifestations of **Niemann Pick disease type C** (NPC) in patients weighing ≥ 15 kg.[1]

POLICY STATEMENT

This policy involves the use of Aqneursa. Prior authorization is recommended for pharmacy benefit coverage of Aqneursa. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Aqneursa as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Aqneursa be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Aqneursa is recommended in those who meet the following criteria:

1. **Niemann-Pick disease type C.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy: Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):
     - **i.** Patient is ≥ 4 years of age; AND
     - **ii.** Patient weighs ≥ 15 kg; AND
     - **iii.** Patient has one or more neurologic symptom(s) of Niemann-Pick disease type C; AND
       Note: Examples of neurologic symptoms of Niemann-Pick disease type C are loss of motor function, difficulty swallowing, and speech and cognitive impairment.
     - **iv.** The diagnosis is established by a genetic test showing biallelic pathogenic variants in either the NPC1 gene or NPC2 gene*; AND
     - **v.** The medication is prescribed by or in consultation with a geneticist, endocrinologist, metabolic disorder subspecialist, neurologist, or a physician who specializes in the treatment of Niemann-Pick disease type C or related disorders; AND
     - **vi.** The patient meets one of the following (a or b):

a) Aqneursa is prescribed in combination with miglustat; OR
b) History of failure, contraindication, or intolerance to miglustat.

B) Patient is Currently Receiving Aqneursa. Approve for 1 year if the patient meets BOTH of the following (i and ii):
i. According to the prescriber, patient has derived benefit from treatment defined as disease stabilization, slowed progression, or improvement; AND
ii. The medication is prescribed by or in consultation with a geneticist, endocrinologist, metabolic disorder subspecialist, neurologist, or a physician who specializes in the treatment of Niemann-Pick disease type C or related disorders;
iii. The patient meets one of the following (a or b):
a) Aqneursa is prescribed in combination with miglustat; OR
b) History of failure, contraindication, or intolerance to miglustat.

Initial Approval/ Extended Approval.
A) *Initial Approval: 6 months*
B) *Extended Approval: 1 year*

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Aqneursa has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Ataxia-Telangiectasia.** A multinational, multicenter, open-label, rater-blinded prospective Phase II study is underway to assess the safety and efficacy of levacetylleucine for the treatment of Ataxia-Telangiectasia.[7,9] The primary completion date is anticipated in December 2024. Results are not yet available.

2. **Combination use with Miplyffa (arimoclomol capsules).** Miplyffa, in combination with miglustat is indicated for the treatment of neurologic manifestations of Niemann-Pick disease type C in patients ≥ 2 years of age.[13] There are no data available regarding combination use of Miplyffa and Aqneursa.

3. **GM2 Gangliosidoses**. GM2 gangliosidoses (Tay-Sachs and Sandhoff diseases) are rare, autosomal recessive, neurodegenerative diseases. Levacetylleucine (4 g per day in patients ≥ 13 years of age and weight-based doses for patients 6 to 12 years of age) was evaluated in a Phase IIb multinational, open-label, rater-blinded study in patients ≥ 6 years of age with a genetically confirmed diagnosis of GM2 gangliosidoses (n = 30).[7,8] The study met its Clinical Impression of Change in Severity primary endpoint, as well as secondary measures of ataxia and global impression. Additional study is needed.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

***Documentation Requirements:**
The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not

medically necessary, investigational, or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Aqneursa™ granules [prescribing information]. Austin, TX: IntraBio; September 2024.
2. Bremova-Ertl T, Ramaswami U, Brands M, et al. Trial of N-acetyl-L-leucine in Niemann-Pick type C. *N Engl J Med*. 2024;390(5):421-431.
3. Fields T, Bremova-Ertl TM, Billington I, et al. N-acetyl-L leucine for Niemann-Pick type C: a multinational double-blind randomized placebo-controlled crossover study. *Trials*. 2023;24:361.
4. Geberhiwot T, Moro A, Dardis A, et al; on behalf of the International Niemann-Pick Disease Registry (INPDR). Consensus clinical management guidelines for Niemann-Pick disease type C. *Orphanet J Rare Dis.* 2018;13:50
5. Patterson M. Niemann-Pick Disease Type C. 2000 Jan 26 [updated 2020 Dec 10]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024.
6. Berry-Kravis E. Nieman-Pick disease type C: diagnosis, management and disease-targeted therapies in development. *Semin Pediatric Neurol.* 2021;31:100879.
7. Fields T, Patterson M, Bremova-Ertl T, et al. A master protocol to investigate a novel therapy acetyl-L-leucine for three ultra-rare neurodegenerative diseases: Niemann-Pick type C, the GM2 ganliosidoses, and ataxia telangiectasia. *Trials*. 2021;22:84.
8. Martakis K, Claassen J, Gascon-Bayari J, et al. Efficacy and safety of N-acetyl-L-leucine in children and adults with GM2 gangliosidoses. *Neurology*. 2023;100(10):e1072-e1083.
9. IntraBio. N-Acetyl-L-Leucine for ataxia-telangiectasia. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2024 Sept 25]. Available at: https://clinicaltrials.gov/study/NCT03759678?intr=IB1001&rank=5. NLM Identifier: NCT03759678.
10. Park J, Bremova-Ertl T, Brands M, et al. Assessment of the reliability, responsiveness, and meaningfulness of the scale for the assessment and rating of ataxia (SARA) for lysosomal storage disorders. *J Neurol.* 2024;271(10):6888-6902..
11. Bremova-Ertl T, Ramaswami U, Rohrback M, et al. Long-term findings of N-acetyl-L-leucine for Niemann-Pick disease type C [oral presentation]. Presented at: the 10th Congress of the European Academy of Neurology; Helsinki, Finland; June 29 to July 2, 2024.
12. Data on file. IntraBio. September 26, 2024.
13. Miplyffa™ capsules [prescribing information]. Frederiksberg, Denmark/Celebration, FL: Zevra Denmark A/S/Zevra Therapeutics; September 2024.