Original Effective Date: 03/28/2025
Current Effective Date: 03/28/2025
Last P&T Approval/Version: 01/29/2025
Next Review Due By: 07/2025
Policy Number: C29063-A

Aqneursa (levacetylleucine)

PRODUCTS AFFECTED

Aqneursa (levacetylleucine)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Niemann-Pick Disease Type C

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. NIEMANN-PICK DISEASE TYPE C:
   1. Documented diagnosis of Niemann-Pick disease, type C
      AND
   2. Documentation that diagnosis was confirmed by genetic testing that identifies both disease-causing alleles in NPC1 or NPC2 [DOCUMENTATION REQUIRED]

AND

3. Documentation of neurological manifestations (see APPENDIX)
   AND
4. Documentation that member weighs at least 15 kg

CONTINUATION OF THERAPY:

A. NIEMANN-PICK DISEASE TYPE C:
   1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified neurologist, geneticist, metabolic specialist, or physician experienced in the management of Niemann-Pick disease. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests.]

AGE RESTRICTIONS:

None

QUANTITY:

The recommended oral dosage of Aqneursa (levacetylleucine) is based on actual body weight.

Body Weight	Morning Dose	Afternoon Dose	Evening Dose
15 kg to < 25 kg	1 gram	No dose	1 gram
25 kg to < 35 kg	1 gram	1 gram	1 gram
35 kg or more	2 grams	1 gram	1 gram

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:

Psychotherapeutic and Neurological Agents – Misc.

FDA-APPROVED USES:

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

COMPENDIAL APPROVED OFF-LABELED USES:

None

APPENDIX

Symptoms of NPD-C are progressive and may present differently depending on age.

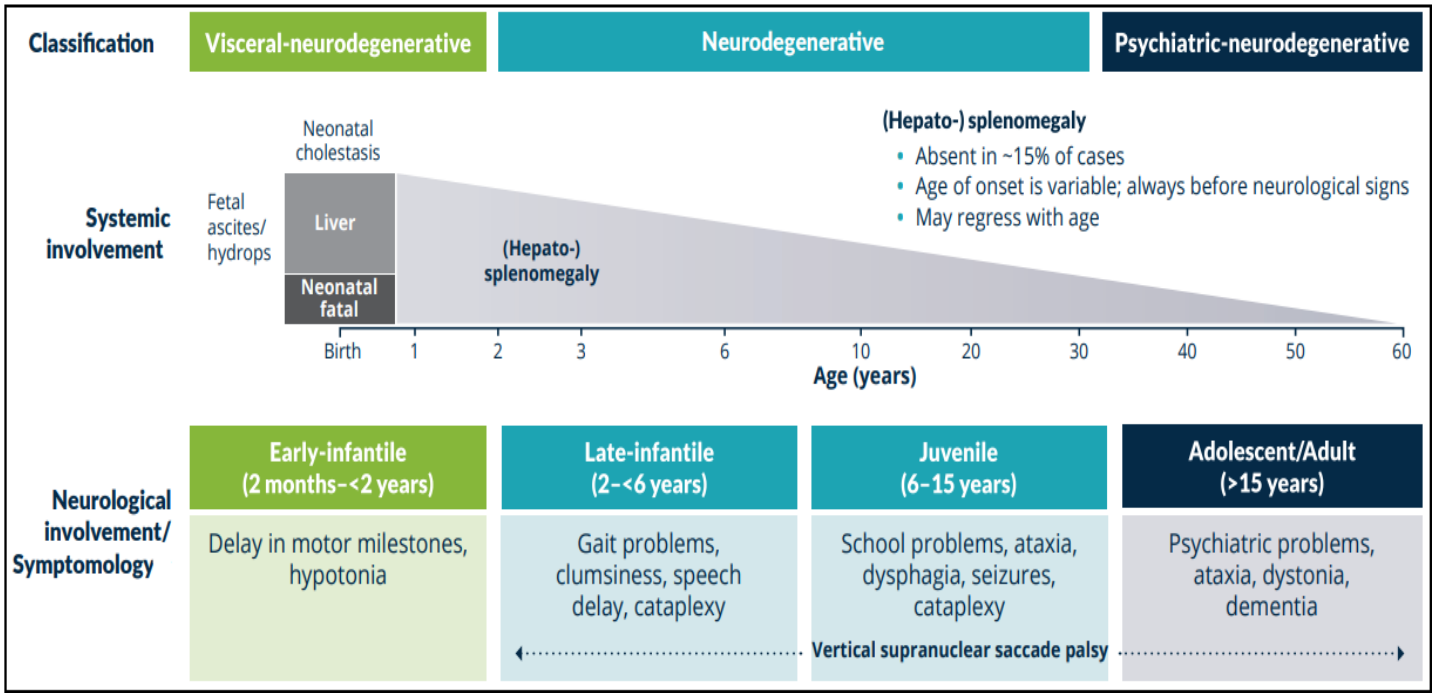

Figure 1: NPC Guidelines; Recommendations for the diagnosis and management of Niemann-Pick disease type C: an update. Journal of Molecular Genetics and Metabolism July 2012.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Niemann-Pick disease (NPD) is a group of autosomal recessive disorders characterized by the accumulation of lipids, including sphingomyelin and cholesterol, in various organs such as the spleen, liver, and brain. The condition typically presents with splenomegaly, variable neurological deficits, and other systemic effects. Historically, NPD was classified based on its histological features as a reticuloendotheliosis. There are three main types of NPD: Type A (NPD-A), Type B (NPD-B), and Type C (NPD-C).

Types A and B of Niemann-Pick disease are caused by mutations in the SMPD1 gene, which leads to a deficiency of acid sphingomyelinase, an enzyme critical for the breakdown of sphingomyelin. This results in the accumulation of sphingomyelin in various tissues. NPD-A is the more severe form, typically leading to early childhood death, while NPD-B is a less severe form, with symptoms emerging later in life and a longer survival rate.

Niemann-Pick Disease Type C (NPC) is a rare, inherited, progressive neurodegenerative disorder that primarily affects the nervous system and various organs. NPC is caused by mutations in either the NPC1 gene or, less commonly, the NPC2 gene. These genes are involved in the intracellular transport of lipids, specifically cholesterol and sphingolipids. The defective or absent function of these proteins leads to the accumulation of these lipids, particularly in the liver, spleen, and brain, resulting in progressive cellular damage.

The clinical manifestations of NPC typically emerge in childhood, though adult-onset forms are also recognized. Common early symptoms include hepatosplenomegaly, ataxia, and developmental regression, which may include speech and motor skills loss. As the disease progresses, patients develop severe neurological symptoms such as seizures, dystonia, dysphagia, cognitive decline, and psychiatric symptoms

like depression and psychosis. The disease often leads to premature death, with many patients dying in childhood or adolescence due to respiratory failure or complications related to neurological decline.

NPC is classified into two main types based on the gene mutation involved: NPC1 and NPC2. The NPC1 mutation is responsible for the vast majority of cases, while mutations in the NPC2 gene are much rarer. Both mutations result in defective lipid trafficking within cells, leading to the buildup of unprocessed lipids in the lysosomes. The NPC1 protein is located in the lysosomal membrane, while NPC2 is found in the lysosome's interior, and both are involved in the transport and esterification of cholesterol.

Diagnosis of NPC is challenging and requires a combination of clinical suspicion, biochemical testing, and genetic analysis. One of the key biochemical markers is the filipin staining test, which detects the accumulation of unesterified cholesterol in cultured skin fibroblasts. Genetic testing for mutations in the NPC1 or NPC2 genes is definitive. In some cases, a diagnostic trial with the drug miglustat, an inhibitor of glucosylceramide synthase, may show a partial response and provide further evidence of NPC.

There is no cure for NPC, but treatment options aim to manage symptoms and slow disease progression. Miglustat is one of the few disease-modifying therapies approved for NPC, though it primarily slows progression rather than halting the disease. Other supportive treatments, including physical and occupational therapy, anticonvulsants for seizures, and respiratory support, are also critical in managing the symptoms and improving quality of life. Miplyffa (arimoclomol) recently received FDA-approval for treatment of NPC in combination with miglustat in adult and pediatric patients 2 years of age and older.

The safety and efficacy of Aqneursa for the treatment of NPC were evaluated in a 12-week, Phase 3, randomized, double-blind, placebo-controlled, two-period crossover study. Patients were allowed to continue current miglustat therapy. The primary efficacy outcome was a modified version of the Scale for Assessment and Rating of Ataxia (SARA), referred to as the functional SARA (fSARA). The fSARA consists only of the gait, sitting, stance, and speech disturbance domains of the original SARA. The SARA is a clinical scale that measures the severity of neurologic signs and symptoms with internal consistency in patients with spinocerebellar ataxia. However, it is not validated in patients with NPC. On average, participants treated with Aqneursa for 12 weeks showed a better outcome in their fSARA scores compared with treatment with placebo. The estimated mean fSARA total score was 5.1 when patients were treated with Aqneursa and 5.6 when patients were treated with placebo. The estimated treatment difference for the fSARA total score was −0.4 (95% confidence interval [CI]: −0.7, −0.2).

The safety and efficacy of Aqneursa for treating Niemann-Pick disease type C (NPC) were assessed in a 12-week, Phase 3, randomized, double-blind, placebo-controlled, two-period crossover study. Patients were allowed to continue their current miglustat therapy during the trial. The primary measure of efficacy was a modified version of the Scale for the Assessment and Rating of Ataxia (SARA), known as the functional SARA (fSARA), which includes only the gait, sitting, stance, and speech disturbance domains from the original SARA. While the SARA is a validated scale for measuring neurological symptoms in patients with spinocerebellar ataxia, it has not been validated for NPC. Results showed that, on average, patients treated with Aqneursa for 12 weeks had better fSARA scores compared to those who received a placebo. The estimated mean fSARA score was 5.1 for Aqneursa-treated patients and 5.6 for placebo-treated patients, with a treatment difference of −0.4 (95% confidence interval [CI]: −0.7, −0.2). Limited longer-term data has been presented at the European Academy of Neurology Congress that suggests efficacy lasting 12 months with more detailed information to follow.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Aqneursa (levacetylleucine) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Aqneursa (levacetylleucine) include: no labeled indications. Based on findings from animal reproduction studies, Aqneursa (levacetylleucine) may cause embryofetal harm when administered during pregnancy. There are no available data on Aqneursa (levacetylleucine) use in pregnant females to evaluate a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Advise pregnant females of the potential risk to the fetus.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Aqneursa PACK 1GM

REFERENCES

1. Aqneursa (levacetylleucine) for oral suspension [prescribing information]. Austin, TX: IntraBio, Inc.; September 2024.
2. Geberhiwot T, et al; International Niemann-Pick Disease Registry (INPDR). Consensus Clinical Management Guidelines for Niemann-Pick Disease Type C. *Orphanet J Rare Dis*. 2018;13(1):50. doi:10.1186/s13023-018-0785-7
3. Patterson MC, Clayton P, Gissen P, et al. Recommendations for the detection and diagnosis of Niemann-Pick disease type C: an update. American Academy of Neurology: Neurology Clinical Practice. 2017;7(6):499-511. doi:10.1212/CPJ.0000000000000399. PMID: 29431164.
4. Patterson et al. Recommendations for the diagnosis and management of Niemann-Pick disease type C: An update. Mol Genet Metab. 2012;106(3):330-344. doi:10.1016/j.ymgme.2012.03.012. Epub 2012 May 8. PMID: 22572546.
5. Vanier, M.T. Niemann-Pick Disease Type C, Orphanet Journal of Rare Diseases, 2010;5(16):1-18. doi:10.1186/1750-1172-5-16.

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q1 2025