LOUISIANA BLUE

levacetylleucine (Aqneursa™)

Policy # 00918
Original Effective Date: 03/01/2025
Current Effective Date: 03/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of levacetylleucine (Aqneursa™)‡ for the treatment of Niemann-Pick disease type C to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for levacetylleucine (Aqneursa) will be considered when the following criteria are met:

- Initial
  - Patient weighs ≥ 15 kg; AND
  - Patient has a genetically confirmed diagnosis of Niemann-Pick disease type C (NPC) determined by one of the following:
    - Mutations in both alleles of *NPC1* or *NPC2*; OR
    - Mutation in one allele of *NPC1* or *NPC2* AND either a positive filipin-staining or cholestane-triol level (greater than 2 times the upper limit of normal); AND
  - Patient has one or more neurologic signs of NPC. Examples of neurologic signs include loss of motor function, difficulty swallowing, speech impairment, and cognitive impairment; AND
  - Patient will not use Aqneursa in combination with arimoclomol (Miplyffa™)‡.
- Continuation
  - Patient has received an initial authorization for Aqneursa; AND
  - Provider attests that patient is experiencing a benefit from therapy as evidenced by an improvement or stabilization in a domain affected by NPC (e.g., ambulation, fine motor skills, swallowing, or speech).
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

levacetylleucine (Aqneursa™)

Policy # 00918
Original Effective Date: 03/01/2025
Current Effective Date: 03/01/2025

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the continued use of levacetylleucine (Aqneursa) when the patient has not demonstrated improvement or stabilization in a domain affected by NPC to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of levacetylleucine (Aqneursa) when the patient selection criteria are not met (except those noted to be **not medically necessary****) to be **investigational.***

Background/Overview

Aqneursa is an oral agent indicated for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in patients weighing at least 15 kg. It is supplied as 1 gram packets of powder to be mixed with water or another liquid and administered by mouth three times daily. The dose is 2-4 grams per day depending on the patient's weight. Although the exact mechanism of action is unknown, it is thought that Aqneursa works to normalize mitochondrial and lysosomal function and improve cerebellar activity in patients with NPC.

NPC is an autosomal recessive lysosomal storage disorder caused by a mutation in either the *NPC1* gene or the *NPC2* gene. These genes play a role in the lysosomal transport and metabolism of lipids, including cholesterol. Mutations in these genes cause the accumulation of cellular lipids in the cell which can result in a variety of clinical manifestations. Clinical presentation is heterogenous and ranges from severe symptoms in utero to adult-onset. The early-infantile form is rapidly progressive and leads to death in early childhood due to extensive visceral involvement. The later-onset forms are primarily neurodegenerative with symptoms such as loss of previously achieved gross and fine motor skills, ataxia, seizures, cataplexy, hearing loss, and cognitive decline. Diagnosis of NPC must be confirmed through genetic testing, including sequencing of the *NPC1* and *NPC2* genes. Most patients have a pathogenic mutation in both alleles of either *NPC1* or *NPC2*, but some patients may only have one pathogenic mutation. In this case, a positive biomarker test (cholestane-triol) or filipin staining test can confirm the diagnosis.

Prior to the approval of Aqneursa, the standard of care for treatment of NPC was off-label miglustat (available as generic or brand Zavesca® or brand Opfolda®)‡. Despite not being approved by the FDA for this indication, miglustat is widely used in the U.S. and is approved in Europe and other countries for the treatment of the neurologic complications of NPC in pediatric and adult patients. Another drug, arimoclomol (Miplyffa), was approved 4 days prior to Aqneursa and is indicated for use in combination with miglustat to treat the neurological manifestations of NPC in patients 2 years of age and older. Treatment guidelines have not been updated to reflect the approval of these two new agents.

levacetylleucine (Aqneursa™)

Policy # 00918
Original Effective Date: 03/01/2025
Current Effective Date: 03/01/2025

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Aqneursa was approved in September 2024 for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adults and pediatric patients weighing ≥ 15 kg.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The safety and efficacy of Aqneursa for the treatment of NPC were evaluated in a randomized, double-blind, placebo-controlled, two-period crossover study that evaluated the efficacy of Aqneursa in 60 patients. To be eligible for the study, patients had to be aged 4 years or older with a confirmed diagnosis of NPC. Patients were required to have at least mild disease-related neurological symptoms.

Patients were assessed over a 2-week baseline period. Patients were then randomized in a 1:1 ratio to one of the two treatment sequences:

- Treatment Sequence 1 (n = 30): Aqneursa in Treatment Period 1, followed by immediate crossover to placebo in Treatment Period 2
- Treatment Sequence 2 (n = 30): placebo in Treatment Period 1, followed by immediate crossover to Aqneursa in Treatment Period 2.

Aqneursa and placebo were administered orally with or without food for 12 weeks in each period.

The primary efficacy outcome was assessed using a modified version of the Scale for Assessment and Rating of Ataxia (SARA), referred to as the functional SARA (fSARA). The SARA is a clinical assessment tool that assesses gait, stability, speech, and upper and lower limb coordination across 8 individual domains. The fSARA consists of only gait, sitting, stance, and speech disturbance domains of the original SARA with modifications to the scoring responses. Each domain was rescored from 0 to 4, where 0 is the best neurological status and 4 is the worst, with a total score ranging from 0 to 16.

The fSARA score was assessed at baseline, 6 weeks, 12 weeks, 18 weeks, and 24 weeks. 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% CI: -0.7, -0.2).

References

1. Aqneursa [package insert]. IntraBio, Inc. Austin, TX. Updated January 2025.
2. Aqneursa New Drug Review. IPD Analytics. Updated November 2024.

Policy History

Original Effective Date: 03/01/2025
Current Effective Date: 03/01/2025
02/06/2025 Medical Policy Committee review
02/12/2025 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 02/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.