PDL DRUG REVIEW

Proprietary Name: Aqneursa®
Common Name: levacetylleucine granule, for suspension
PDL Category: Neurologics

Comparable Products	Preferred Drug List Status
Miplyffa	Non-Preferred

Pharmacology/Usage: Levacetylleucine, the active ingredient of Aqneursa®, is a modified amino acid. The distinct molecular target for levacetylleucine in the treatment of Niemann-Pick disease type C is not known.

Indication: For the treatment of neurological manifestations of Niemann-Pick disease type C (NPD-C) in adults and pediatric patients weighing ≥15kg.

There is no pregnancy category for this medication; however, the risk summary indicates that based on findings from animal studies, Aqneursa® may cause embryo-fetal harm when administered during pregnancy. There are no available data on use in pregnant females to assess a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Advise a pregnant female of the potential risk to the fetus. The decision to continue or discontinue Aqneursa® treatment during pregnancy should consider the female's need for Aqneursa®, the potential drug-related risks to the fetus, and the potential adverse outcomes from untreated maternal disease. For a female of reproductive potential, verify that the patient is not pregnant prior to starting treatment. In addition, advise females of reproductive potential to use effective contraception during treatment and for 7 days after the last dose. The safety and efficacy of use have not been established in the pediatric population weighing <15kg.

Dosage Form: For oral suspension: 1gm levacetylleucine as strawberry flavored granules in a unit-dose packet.

Recommended Dosage: For females of reproductive potential, verify that the patient is not pregnant.

The recommended dosage is based on the patient's actual body weight (kg) to be administered orally up to three times daily. Aqneursa® can be taken with or without food.

For 2gm levacetylleucine doses, prepare two Aqneursa® packets individually. One packet contains 1 gm.

Patient's body weight	Morning dose	Afternoon Dose	Evening dose
15kg to less than 25kg	1gm	No dose	1gm
25kg to less than 35kg	1gm	1gm	1gm
35kg or more	2gm	1gm	1gm

If a dose is missed, skip the missed dose and take the next dose at the scheduled time. Do not take 2 doses at the same time to make up for a missed dose.

For oral administration, obtain the required number of packets for the prescribed dose. Open and empty the entire contents of one packet into a container with 40ml of water, orange juice, or almond milk. Do not use hot liquid. Stir to form a suspension and swallow immediately (within 30 minutes). For doses requiring two Aqneursa® packets, repeat the above steps. Discard unused suspension if not administered within 30 minutes.

Aqneursa® may also be administered via gastrostomy tube (G-tube).

Drug Interactions: Avoid concomitant use of Aqneursa® with N-acetyl-DL-leucine and N-acetyl-D-leucine. The D-enantiomer, N-acetyl-D-leucine, competes with levacetylleucine for monocarboxylate transporter uptake, which may reduce the levacetylleucine efficacy.

Levacetylleucine inhibits P-gp. However, the clinical significance of this finding has not been fully characterized. Monitor more frequently for P-gp substrate related adverse reactions when used concomitantly with Aqneursa®.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Aqneursa®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included upper respiratory tract infection (14%), abdominal pain (7%), dysphagia (7%), and vomiting (7%).

Contraindications: There are no contraindications listed with this product.

Manufacturer: IntraBio, Inc.

Analysis: The safety and efficacy of Aqneursa® for the treatment of NPD-C were assessed in a randomized, double-blind, placebo-controlled, two-period crossover study that included patients (N=60) aged 4 years or older with a confirmed diagnosis of NPD-C. 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 to one of the two treatment sequences:

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

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

Fifty-nine patients (98%) completed the study and received both placebo and Aqneursa®. One patient withdrew based on healthcare provider decision during Aqneursa® treatment. Of the randomized patients (N=37 adults and N=23 pediatrics), 27 were female and the median age at treatment initiation was 25 years (range 5 to 67 years). In addition, 90% of patients were white and most (85%) received miglustat treatment prior to randomization and during the trial.

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 only of 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 the worst, with a total score ranging from 0 to 16.

The fSARA score was assessed at baseline, 6 weeks, 12 weeks (the end of Period I), 18 weeks, and 24 weeks (the end of Period II). 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. Results are presented in the table below, which was adapted from the prescribing information.

Variable	fSARA Total Score	
	Treatment Sequence I: Aqneursa® - placebo	Treatment Sequence II: Placebo - Aqneursa®
Baseline	N=30	N=30
Mean	5.2	6.3
Period I	N=29	N=30
Mean	4.5	6.0
Period II	N=28	N=30
Mean	5.1	5.6
Estimated mean fSARA Score by Treatment		
Aqneursa®	5.1	
Placebo	5.6	
Treatment Difference	-0.4 (p<0.001)	

Patients who received Aqneursa® in Period I followed by placebo in Period II (Treatment Sequence 1) demonstrated a greater improvement in the fSARA score in Period I with a mean change from baseline of -0.5, compared to Period II with a mean change from baseline of 0. Similarly, patients who received placebo in Period I followed by Aqneursa® in Period II (Treatment Sequence 2) experienced greater improvement in the fSARA score while receiving Aqneursa® in Period II with a mean change of -0.7, compared to a mean change of -0.3 in Period I.

Results on the fSARA were supported by consistent results demonstrated on the original SARA.

Place in Therapy: Aqneursa® is the first standalone treatment indicated for the treatment of neurological manifestations of Niemann-Pick disease type C (NPD-C) in adults and pediatric patients weighing ≥15kg. NPD-C is a rare autosomal recessive disorder that results in progressive neurological symptoms and organ dysfunction. To date, there is supportive treatment for physical manifestations of the disease through physical therapy.[2] The current treatment comparator for Aqneursa® is a combination therapy of Miplyffa® given in conjunction with miglustat, which was recently approved by the FDA (09/24). To date, there is no comparator trial between Aqneursa® and Miplyffa®. Each drug trial also looked at different functional scoring criteria outcomes.

For females of reproductive potential, verify that the patient is not pregnant prior to starting treatment. The safety and efficacy of Aqneursa® were assessed in a randomized, double-blind, placebo-controlled, two-period crossover study, with the primary efficacy outcome assessed using a modified version of the Scale for Assessment and Rating of Ataxia (SARA), referred to as the functional SARA (fSARA). The estimated treatment difference for the fSARA total score was -0.4, which was statistically significant (p<0.001). Results on the fSARA were supported by consistent results demonstrated on the original SARA.

Summary

It is recommended that Aqneursa® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

References

[1] Aqneursa [package insert]. Austin, TX: IntraBio Inc; 2024.
[2] UpToDate online. Overview of acid sphingomyelinase deficiency and Niemann-Pick disease type C. Accessed February 2025.

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