

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use AQNEURSA safely and effectively. See full prescribing information for AQNEURSA.

**AQNEURSA® (levacetylleucine) for oral suspension**  
Initial U.S. Approval: 2024

### RECENT MAJOR CHANGES

Indications and Usage (1.2) 9/2026  
Dosage and Administration (2.2, 2.3) 9/2026

### INDICATIONS AND USAGE

AQNEURSA is indicated for the treatment of:

- neurological manifestations of Niemann-Pick disease type C (NPC) in adults and pediatric patients weighing  $\geq 15$  kg. (1.1)
- ataxia in adults and pediatric patients with ataxia-telangiectasia (A-T) weighing  $\geq 15$  kg. (1.2)

### DOSAGE AND ADMINISTRATION

- For females of reproductive potential, verify that the patient is not pregnant prior to initiating treatment. (2.1)
- Recommended dosage (2.2)

| Patient Body Weight | Morning Dose | Afternoon Dose | Evening Dose |
|---------------------|--------------|----------------|--------------|
| 15 to <25 kg        | 1 g          | No Dose        | 1 g          |
| 25 to <35 kg        | 1 g          | 1 g            | 1 g          |
| 35 kg or more       | 2 g          | 1 g            | 1 g          |

- See the full prescribing information for administration instructions. (2.3)

### DOSAGE FORMS AND STRENGTHS

For oral suspension: 1 gram levacetylleucine in a unit-dose packet. (3)

### CONTRAINDICATIONS

None. (4)

### WARNINGS AND PRECAUTIONS

**Embryo-Fetal Toxicity:** May cause fetal harm. Advise females of reproductive potential to use effective contraception during treatment and for 7 days after the last dose if AQNEURSA is discontinued. (5.1)

### ADVERSE REACTIONS

In NPC, the most common adverse reactions (incidence  $\geq 5\%$  and greater than placebo) are abdominal pain, dysphagia, upper respiratory tract infections, and vomiting. (6.1)

In A-T, the most common adverse reactions (incidence  $\geq 5\%$  and greater than placebo) are fall, skin laceration, and urinary tract infection. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact IntraBio Inc. at 1-833-306-9677 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

- N-acetyl-DL-leucine* or *N-acetyl-D-leucine*: Avoid concomitant use with AQNEURSA. (7.1)
- P-glycoprotein (P-gp) Transporter Substrates*: Monitor for adverse reactions if used with AQNEURSA. (7.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 9/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Niemann-Pick Disease Type C

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

1.2 Ataxia-Telangiectasia

AQNEURSA is indicated for the treatment of ataxia in adults and pediatric patients with ataxia-telangiectasia (A-T) weighing ≥15 kg.

2 DOSAGE AND ADMINISTRATION

2.1 Important Recommendation Prior to AQNEURSA Treatment Initiation

For females of reproductive potential, verify that the patient is not pregnant [see Use in Specific Populations (8.1, 8.3)].

2.2 Recommended Dosage

The recommended dosage of AQNEURSA to be administered orally, with or without food, is based on the patient’s actual body weight (kg), as shown in Table 1 [see Clinical Studies (14)].

For AQNEURSA doses of 2 grams, prepare two packets individually [see Dosage and Administration (2.3)].

Table 1: Recommended Dosage of AQNEURSA Based on Body Weight (kg)

| Patient’s Body Weight    | Morning Dose | Afternoon Dose | Evening Dose |
|--------------------------|--------------|----------------|--------------|
| 15 kg to less than 25 kg | 1 gram       | No Dose        | 1 gram       |
| 25 kg to less than 35 kg | 1 gram       | 1 gram         | 1 gram       |
| 35 kg or more            | 2 grams      | 1 gram         | 1 gram       |

One AQNEURSA packet contains 1 gram levacetylleucine.

Missed Dose

If a dose of AQNEURSA 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.

## 2.3 Preparation and Administration Instructions

### Oral Administration

For oral administration, administer AQNEURSA as follows:

1. Obtain the required number of AQNEURSA packets for the prescribed dose (one or two packets).
2. Open and empty the entire contents of one AQNEURSA packet into a container with 40 mL of water, orange juice, almond milk, or yogurt. Do not use hot liquid.
3. Stir to form a suspension.
4. Swallow the suspension immediately (within 30 minutes).
5. For doses requiring two AQNEURSA packets, repeat steps 2 to 4.
6. Discard unused AQNEURSA suspension if not administered within 30 minutes.

### Use of Gastrostomy Tube (G-Tube) for Feeding Tube Administration

For patients who have a G-tube (French size 12 or larger) in place, administer AQNEURSA as follows:

1. Prepare AQNEURSA suspension immediately before administration via gastrostomy tube.
2. Obtain the required number of AQNEURSA packets for the prescribed dose (one or two packets).
3. Open and empty the entire contents of one AQNEURSA packet into a container with 40 mL of water ONLY. Do not use hot liquid.
4. Stir to form a suspension.
5. Draw up the suspension into a catheter tip syringe.
6. Administer the suspension immediately through the G-tube.
7. Flush any residual suspension in the catheter tip syringe with an additional 20 mL of water.
8. Flush the G-tube again, as needed, until no residual suspension is left in the syringe or feeding tube.
9. For doses requiring two AQNEURSA packets, repeat steps 3 to 8.
10. Discard unused AQNEURSA suspension if not administered immediately.

## 3 DOSAGE FORMS AND STRENGTHS

For oral suspension: 1 gram levacetylleucine as white to off-white strawberry flavored granules in a unit-dose packet.

## 4 CONTRAINDICATIONS

None.

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Embryo-Fetal Toxicity

Based on findings from animal reproduction studies, AQNEURSA may cause embryo-fetal harm when administered during pregnancy. Administration of levacetylleucine to pregnant rats and rabbits during the period of organogenesis caused an increase in embryo-fetal death (post implantation loss/resorption) and skeletal malformations at a dose that was approximately 1.4-fold and 6-fold, respectively, the maximum recommended human dose (MRHD) of 4 g/day of levacetylleucine (based on body surface area).

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 females of reproductive potential, verify that the patient is not pregnant prior to initiating treatment with AQNEURSA. Advise females of reproductive potential to use effective contraception during treatment with AQNEURSA and for 7 days after the last dose if AQNEURSA is discontinued [see *Use in Specific Populations* (8.1, 8.3)].

## **6 ADVERSE REACTIONS**

### **6.1 Clinical Trials Experience**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

#### **Niemann-Pick Disease Type C**

The safety of AQNEURSA was evaluated in Trial 1, which included a total of 60 patients with Niemann-Pick disease Type C (NPC), in a placebo-controlled, randomized, crossover trial [see *Clinical Studies* (14.1)]. The mean (SD) treatment duration of AQNEURSA was 86.2 (4.7) days (69 min, 97 max); the mean (SD) treatment duration on placebo was 87.3 (4.8) days (78 min, 113 max).

Table 2 summarizes adverse reactions that occurred in patients who were treated with AQNEURSA in Treatment Period I of Trial 1.

**Table 2: Adverse Reactions that Occurred in Adult and Pediatric Patients with NPC at an Incidence of  $\geq 5\%$  in Treatment Period I of Trial 1**

| Adverse Reaction                  | AQNEURSA<br>N=30<br>n (%) | Placebo<br>N=30<br>n (%) |
|-----------------------------------|---------------------------|--------------------------|
| Upper respiratory tract infection | 5 (17)                    | 1 (3)                    |
| Abdominal pain                    | 2 (7)                     | 0 (0)                    |
| Dysphagia                         | 2 (7)                     | 0 (0)                    |
| Vomiting                          | 2 (7)                     | 0 (0)                    |

#### *Rosacea*

One patient experienced an exacerbation of rosacea during Trial 1 that responded to treatment. AQNEURSA was not discontinued.

#### *Laboratory Findings*

Thrombocytopenia with platelets  $< 100 \times 10^3$  cells/ $\mu\text{L}$  was observed in four patients during Treatment Period 1 of Trial 1, all of whom were receiving miglustat for 42 days or longer at the time of enrollment. In two of these patients, the thrombocytopenia was present at baseline. In the other two patients, the thrombocytopenia developed during Trial 1.

#### Ataxia-Telangiectasia

The safety of AQNEURSA was evaluated in Trial 2, which included a total of 73 patients with ataxia-telangiectasia (A-T) in a placebo-controlled, randomized, crossover trial [see *Clinical Studies (14.2)*]. The mean (SD) treatment duration of AQNEURSA was 84.5 (11.2) days (9 min, 97 max); the mean (SD) treatment duration on placebo was 85.5 (3.6) days (77 min, 94 max).

Table 3 summarizes common adverse reactions that occurred in patients who were treated with AQNEURSA in Treatment Period I of Trial 2.

**Table 3: Adverse Reactions that Occurred in Adult and Pediatric Patients with A-T at an Incidence of  $\geq 5\%$  in Treatment Period I of Trial 2**

| Adverse Reaction        | AQNEURSA<br>N=36<br>n (%) | Placebo<br>N=37<br>n (%) |
|-------------------------|---------------------------|--------------------------|
| Fall                    | 2 (6)                     | 1 (3)                    |
| Skin laceration         | 2 (6)                     | 0 (0)                    |
| Urinary tract infection | 2 (6)                     | 1(3)                     |

#### *Laboratory Findings*

Thrombocytopenia with platelets  $< 100 \times 10^3$  cells/ $\mu$ L was observed in one patient during Trial 2. The patient had thrombocytopenia at baseline, which decreased further during the trial while the patient was receiving placebo.

## **7 DRUG INTERACTIONS**

### **7.1 Effect of Other Drugs on AQNEURSA**

#### N-acetyl-DL-leucine and N-acetyl-D-leucine

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.

### **7.2 Effect of AQNEURSA on Other Drugs**

#### P-glycoprotein (P-gp) Transporter Substrates

Monitor more frequently for P-gp substrate related adverse reactions when used concomitantly with AQNEURSA.

Levacetylleucine inhibits P-gp [see *Clinical Pharmacology* (12.3)]. However, the clinical significance of this finding has not been fully characterized.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Risk Summary

Based on findings from animal reproduction studies, AQNEURSA may cause embryo-fetal harm when administered during pregnancy. In animal reproduction studies, an increase in embryo-fetal death (post implantation loss/resorption), decrease in fetal body weight, and increase in external and skeletal malformations were observed in rats and rabbits when levacetylleucine was administered in pregnant rats and rabbits during the period of organogenesis. These effects were observed in rats and rabbits at the doses that were approximately 1.4-fold and 6-fold, respectively, the maximum recommended human dose (MRHD) in patients taking 4 grams of AQNEURSA per day (see *Data*).

There are no available data on AQNEURSA use in pregnant females to evaluate 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.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, miscarriage, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

#### Data

##### *Animal Data*

In a dose-range finding rat embryo-fetal development study, doses of up to 1000 mg/kg/day oral levacetylleucine were administered daily to pregnant females during organogenesis (Gestation Day [GD] 6 through GD 17). Increases in the mean number of resorptions, mean post-implantation losses and skeletal malformations (thoracic arch of the vertebra-fused thoracic arch, misaligned thoracic arch, hemicentric thoracic centrum, and misaligned thoracic centrum; vertebral column-scoliosis, and ribs-absent costal cartilage and short rib) were observed at a dose of 600 mg/kg/day, which is 1.4-fold the 4 g/day MRHD of levacetylleucine based on body surface area.

In a dose-range finding rabbit embryo-fetal development study, doses of up to 2500 mg/kg/day oral levacetylleucine were administered daily to pregnant females during organogenesis (GD 7 through GD 19). Increased embryo-fetal death (post-implantation loss/resorption), decreased fetal body weight, and increase in external (open or partially open eyes, hyperflexion of limbs) and skeletal malformations (misshapen maxillae and premaxillae, and small interparietal bones) were observed at the dose of 1250 mg/kg/day, which is 6-fold the MRHD of levacetylleucine based on body surface area.

## **8.2 Lactation**

#### Risk Summary

There are no data on the presence of levacetylleucine or its metabolites in either human or animal milk, the effects on the breastfed infant or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for AQNEURSA and any potential adverse effects on the breastfed infant from levacetylleucine or from the underlying maternal condition.

## **8.3 Females and Males of Reproductive Potential**

AQNEURSA may cause embryo-fetal harm when administered to a pregnant female [see *Use in Specific Populations* (8.1)].

#### Pregnancy Testing

For a female of reproductive potential, verify that the patient is not pregnant prior to initiating treatment with AQNEURSA.

## Contraception

### Females

Advise a female of reproductive potential to use effective contraception during treatment and for 7 days after the last dose if AQNEURSA is discontinued.

## **8.4 Pediatric Use**

The safety and effectiveness of AQNEURSA for the treatment of NPC have been established in 23 pediatric patients weighing  $\geq 15$  kg in Trial 1. Use of AQNEURSA for this indication is supported by evidence from one adequate and well-controlled study in adults and pediatric patients weighing  $\geq 15$  kg with additional pharmacokinetic data from 40 adults and 17 pediatric patients who participated in two open-label studies [see *Clinical Studies (14.1)* and *Clinical Pharmacology (12.3)*].

The safety and effectiveness of AQNEURSA for the treatment of ataxia in patients with A-T have been established in 47 pediatric patients weighing  $\geq 15$  kg in Trial 2 [see *Clinical Studies (14.2)*].

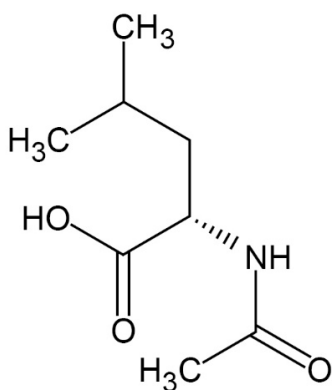
The safety and effectiveness of AQNEURSA have not been established in pediatric patients weighing  $< 15$  kg.

## **8.5 Geriatric Use**

NPC and A-T are largely diseases of pediatric and young adult patients. Clinical studies of AQNEURSA did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.

## **11 DESCRIPTION**

AQNEURSA (levacetylleucine) for oral suspension contains the drug substance levacetylleucine, a modified amino acid. Levacetylleucine is slightly soluble in aqueous solutions. The chemical name is 2-acetamido-4-methylpentanoic acid. The empirical formula is  $C_8H_{15}NO_3$  and the molecular weight is 173.21. The chemical structure is:



Each packet of AQNEURSA granules contains 1 gram levacetylleucine and the inactive ingredients hypromellose, isomalt and strawberry flavor.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

The distinct molecular target for levacetylleucine in the treatment of NPC or A-T is unknown.

### 12.2 Pharmacodynamics

Clinical pharmacodynamic studies have not been conducted for levacetylleucine.

A relationship was not observed between increasing levacetylleucine exposure and clinical efficacy. The time course of pharmacodynamic response is unknown.

### 12.3 Pharmacokinetics

Levacetylleucine pharmacokinetic parameters at steady state are presented as mean (SD) unless otherwise specified. Levacetylleucine maximum concentration ( $C_{\max}$ ) and area under the curve from time 0 to 24 hours ( $AUC_{0-24\text{hrs}}$ ) were 8.3 (3.3)  $\mu\text{g/mL}$  and 33.2 (12.5)  $\text{h}\cdot\mu\text{g/mL}$ .

No levacetylleucine accumulation occurs after repeated administration.

#### Absorption

Levacetylleucine time to  $C_{\max}$  ( $T_{\max}$ ) is 1 hour (ranging from 0.5 to 2.5 hours).

#### Distribution

Levacetylleucine apparent (oral) volume of distribution ( $V_{\text{ss}}/F$ ) is 253 (125) L.

#### Elimination

Levacetylleucine estimated half-life is around 1 hour and the apparent (oral) clearance is 139 (59) L/h.

#### *Metabolism*

Levacetylleucine is metabolized into acetate and L-leucine by ubiquitously expressed enzymes, which are used endogenously in catabolic and metabolic pathways. Cytochrome P450 enzymes are not involved in the metabolism of levacetylleucine.

#### Specific Populations

No clinically significant differences in pharmacokinetics of levacetylleucine were observed based on age (range 4 to 67 years), gender (female 47%, male 53%), or race/ethnicity (White 92%, Asian 3%, Other or not specified 5%). The effect of renal impairment, hepatic impairment, or pregnancy on levacetylleucine pharmacokinetics is unknown.

#### *Body Weight*

The volume of distribution and clearance of levacetylleucine increases with increasing body weight (21 kg to 109 kg), but these effects on pharmacokinetics are minimized by the recommended weight-based dosing.

## Drug Interaction Studies

### In Vitro Studies

Cytochrome P450 (CYP450) enzymes: Levacetylleucine does not inhibit CYP 1A2, 2B6, 2C8, 2C9, 2C19, 2D6, or 3A4 and does not induce CYP 1A2, 2B6, or 3A4.

### Transporter Systems

Levacetylleucine is a substrate of organic anion transporter (OAT)1 and OAT3, but not organic cation transporter (OCT)2, breast cancer resistance protein (BCRP), or P-glycoprotein (P-gp). Levacetylleucine inhibits P-gp, BCRP, bile salt export pump (BSEP), OAT1 and OAT3, but does not inhibit organic anion transporting polypeptide (OATP)1B1 and OATP1B3.

## **13 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

#### Carcinogenesis

Animal studies to evaluate the carcinogenic potential of levacetylleucine have not been conducted.

#### Mutagenesis

Levacetylleucine was not mutagenic or clastogenic in a battery of *in vitro* and *in vivo* assays including bacterial reverse mutation (Ames), chromosomal aberration (in human lymphocytes) and mouse micronucleus assays.

#### Impairment of Fertility

Animal studies to evaluate effects of levacetylleucine on fertility have not been conducted.

## **14 CLINICAL STUDIES**

### **14.1 Niemann-Pick Disease Type C**

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 (Trial 1; NCT05163288). 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 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.

Patients aged ≥13 years received 4 gram per day (as 2 gram morning dose, 1 gram afternoon dose, and 1 gram evening dose). The AQNEURSA dosage in pediatric patients under 13 years was based on patient's body weight [see *Dosage and Administration* (2.2)]. The approved dosage regimen is based on body weight and not age. 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 60 randomized patients (37 adults and 23 pediatric patients), 27 were female and 33 were male. The median age at treatment initiation was 25 years (range: 5 to 67 years). 90% of the patients were White, 3% Asian, and 7% Other. The majority of the patients (n=51, 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 (95% CI: -0.7, -0.2) (Table 4).

**Table 4: Summary of fSARA Efficacy Results in Adult and Pediatric Patients with NPC (Trial 1)**

| Variable                                            | fSARA Total Score                           |                                             |
|-----------------------------------------------------|---------------------------------------------|---------------------------------------------|
|                                                     | Treatment Sequence 1:<br>AQNEURSA - Placebo | Treatment Sequence 2:<br>Placebo - AQNEURSA |
| Baseline                                            | N=30                                        | N=30                                        |
| Mean (SD)                                           | 5.2 (3.0)                                   | 6.3 (3.3)                                   |
| Period I                                            | N=29                                        | N=30                                        |
| Mean (SD)                                           | 4.5 (2.6)                                   | 6.0 (3.4)                                   |
| Period II                                           | N=28*                                       | N=30                                        |
| Mean (SD)                                           | 5.1 (2.8)                                   | 5.6 (3.1)                                   |
| <b>Estimated Mean fSARA Score (SE) by Treatment</b> |                                             |                                             |
| AQNEURSA                                            | 5.1 (0.1)                                   |                                             |
| Placebo                                             | 5.6 (0.1)                                   |                                             |
| Treatment Difference (95% CI)                       | -0.4 (-0.7, -0.2)**                         |                                             |

CI = confidence interval; SD = standard deviation; SE = standard error.

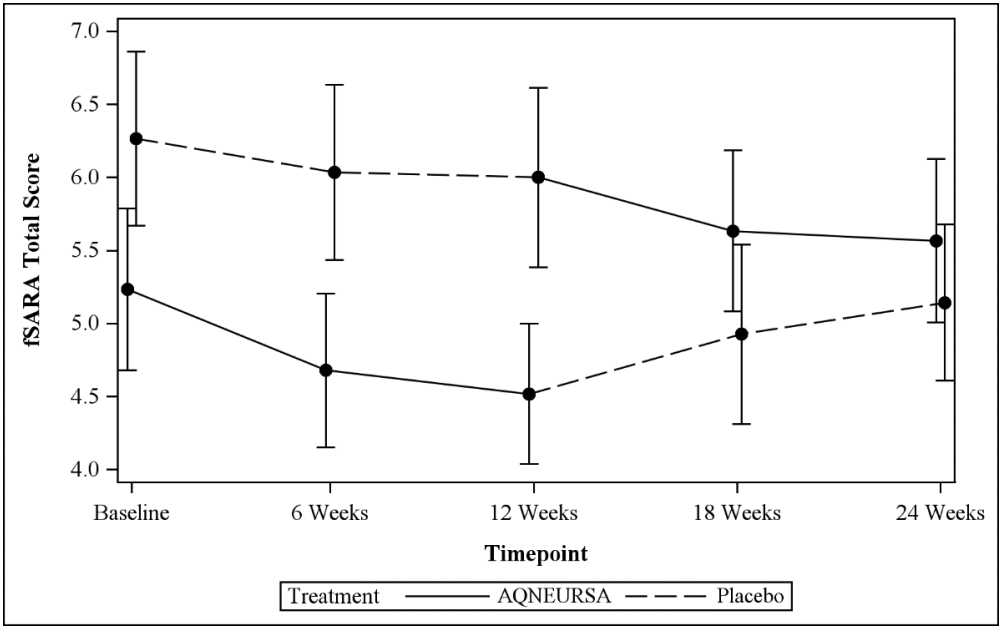
\* Two patients did not have an assessment at the end of Period II (week 24).

\*\* Two-sided p-value <0.001

Patients who received AQNEURSA in Period I followed by placebo in Period II (Treatment Sequence 1) showed a greater improvement in the fSARA score in Period I with a mean change from baseline of -0.5 (SD 1.2), compared to Period II with a mean change from baseline of 0 (1.5). 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 (0.9), compared to a mean change of -0.3 (0.9) in Period I.

**Figure 1: Mean (+/- standard error) Plot of the fSARA Total Score by Time and Treatment Sequence in Adult and Pediatric Patients with NPC (Trial 1)**



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

### 14.2 Ataxia-Telangiectasia

The safety and efficacy of AQNEURSA for the treatment of ataxia in patients with A-T were evaluated in a randomized, double-blind, placebo-controlled, two-period crossover study that evaluated the efficacy of AQNEURSA in 73 patients (Trial 2; NCT06673056). To be eligible for the study, patients had to be aged 4 years or older with a confirmed diagnosis of A-T. Patients were required to have at least mild ataxia at baseline. Ataxia may be comprised of multiple signs and symptoms, including gait ataxia, truncal ataxia, oculomotor ataxia, and difficulties with balance, speech, and hand coordination.

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=36): AQNEURSA in Treatment Period I, followed by immediate crossover to placebo in Treatment Period II
- Treatment Sequence 2 (N=37): 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.

Patients weighing  $\geq 35$  kg received 4 gram per day (as 2 gram morning dose, 1 gram afternoon dose, and 1 gram evening dose). The AQNEURSA dosage in patients weighing under 35 kg was based on

patient's body weight [see *Dosage and Administration* (2.2)]. Seventy patients (96%) completed the study and received both placebo and AQNEURSA.

Of the 73 randomized patients (26 adults and 47 pediatric patients), 38 were female and 35 were male. The median age at treatment initiation was 13 years (range: 4 to 50 years). 75% of the patients were White, 6% Asian, 1% Native Hawaiian or other Pacific Islander, 12% Not Reported, and 6% Other.

Efficacy was demonstrated using a modified version of the SARA, referred to as the functional SARA (fSARA) [see *Clinical Studies* (14.1)].

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 Least Squares Mean fSARA total score was 7.2 when patients were treated with AQNEURSA and 7.8 when patients were treated with placebo. The Least Squares treatment effect for the fSARA total score was -0.6 (95% CI: -0.9, -0.2) (Table 5).

**Table5: Summary of fSARA Efficacy Results in Adult and Pediatric Patients with A-T (Trial 2)**

| Variable                                                | fSARA Total Score                           |                                             |
|---------------------------------------------------------|---------------------------------------------|---------------------------------------------|
|                                                         | Treatment Sequence 1:<br>AQNEURSA - Placebo | Treatment Sequence 2:<br>Placebo - AQNEURSA |
| Baseline                                                | N=36                                        | N=37                                        |
| Mean (SD)                                               | 7.3 (2.6)                                   | 8.5 (2.5)                                   |
| Period I                                                | N=34*                                       | N=37                                        |
| Mean (SD)                                               | 6.6 (2.8)                                   | 8.5 (2.6)                                   |
| Period II                                               | N=35†                                       | N=35‡                                       |
| Mean (SD)                                               | 7.0 (3.1)                                   | 7.8 (2.7)                                   |
| <b>Least Squares Mean fSARA Score (SE) by Treatment</b> |                                             |                                             |
| AQNEURSA                                                | 7.2 (0.1)                                   |                                             |
| Placebo                                                 | 7.8 (0.1)                                   |                                             |
| Treatment Difference (95% CI)                           | -0.6 (-0.9, -0.2)**                         |                                             |

CI = confidence interval; SD = standard deviation; SE = standard error.

\* Two patients did not have an assessment at the end of Period I (week 12).

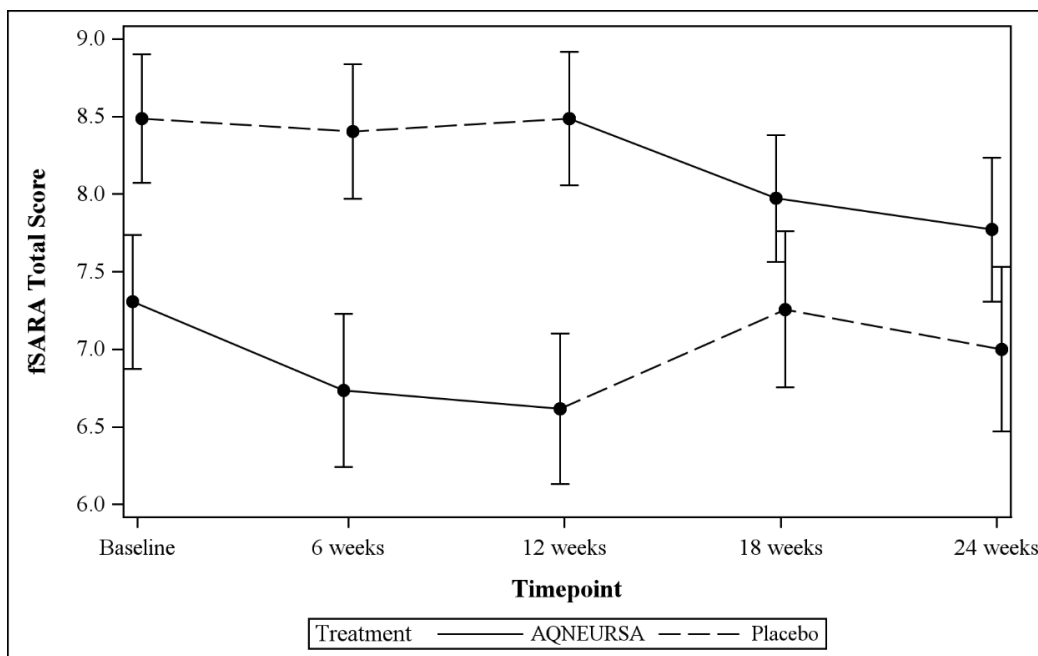
† One patient did not have an assessment at the end of Period II (week 24).

‡ Two patients did not have an assessment at the end of Period II (week 24).

\*\* Two-sided p-value = 0.0013

Patients who received AQNEURSA in Period I followed by placebo in Period II (Treatment Sequence 1) showed a greater improvement in the fSARA score while receiving AQNEURSA in Period I with a mean change from baseline of -0.7 (SD 1.0), compared to Period II with a mean change from baseline of -0.2 (1.1). Patients who received placebo in Period I followed by AQNEURSA in Period II (Treatment Sequence 2) had a mean change of 0.0 (0.9) in Period I but experienced greater improvement in the fSARA score while receiving AQNEURSA in Period II with a mean change of -0.6 (1.3).

**Figure 2: Mean (+/- standard error) Plot of the fSARA Total Score by Time and Treatment Sequence in Adult and Pediatric Patients with A-T (Trial 2)**



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

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### How Supplied

AQNEURSA (levacetylleucine) for oral suspension is supplied as white to off-white granules in a unit-dose multi-layer aluminum/polyethylene packet. Each packet contains 1.7 gram white to off-white granules, equivalent to 1 gram levacetylleucine.

NDC 83853-101-01: Carton containing 28 unit-dose packets

### Storage and Handling

Store AQNEURSA at room temperature between 20°C to 25°C (68°F to 77°F); excursion permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

## 17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (Instructions for Use).

### Embryo-Fetal Toxicity

AQNEURSA may cause embryo-fetal harm. Advise a pregnant female of the potential risk to the fetus. Advise a female of reproductive potential and caregiver to inform their healthcare provider of a known or suspected pregnancy [see *Warnings and Precautions (5.1) and Use in Specific Populations (8.1)*]. Advise a female of reproductive potential to use effective contraception during treatment and for 7 days after the last dose if AQNEURSA is discontinued [see *Use in Specific Populations (8.1, 8.3)*].

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**INSTRUCTIONS FOR USE**  
**AQNEURSA® [ak nur' sah]**  
**(levacetylleucine)**  
**for oral suspension**

This Instructions for Use contains information on how to prepare and take or give AQNEURSA oral suspension. Read this Instructions for Use before you prepare and take or give the first dose of AQNEURSA oral suspension and each time you get a refill. There may be new information. This Instructions for Use does not take the place of talking to your or your child's healthcare provider about your or your child's medical condition or treatment.

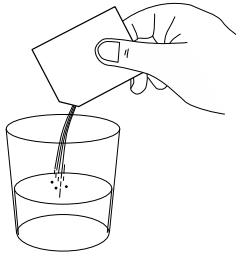
**Important Information You Need to Know Before Taking or Giving AQNEURSA Oral Suspension**

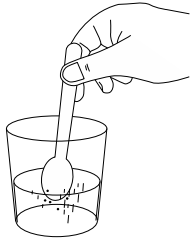
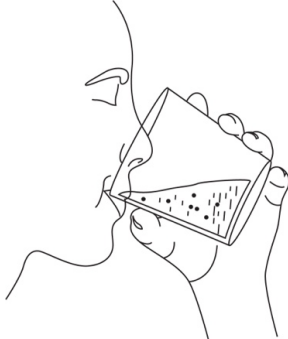
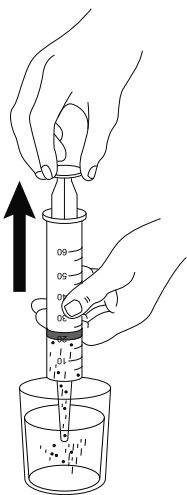
- Take or give AQNEURSA oral suspension exactly as instructed by your healthcare provider.
- Take or give AQNEURSA oral suspension with or without food.
- AQNEURSA oral suspension can be taken or given by mouth or through a gastrostomy tube (G-tube) feeding tube (French size 12 or larger).
- **Do not** use hot liquid with AQNEURSA oral suspension.
- For instructions on disposing of expired AQNEURSA packets or unused AQNEURSA oral suspension, see the end of this Instructions for Use.

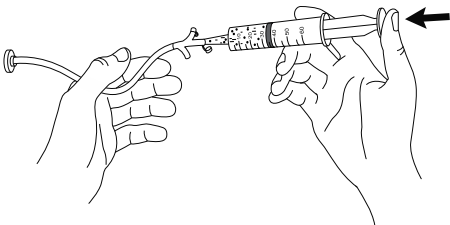
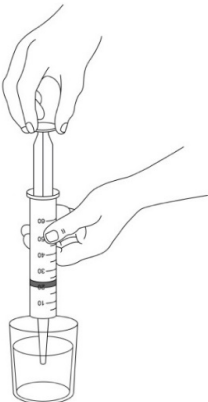
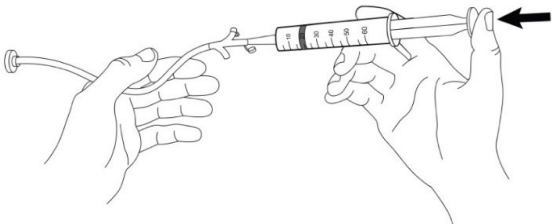
**Supplies Needed to Prepare and Take or Give AQNEURSA Oral Suspension**

Gather the following supplies on a clean flat surface:

- the number of AQNEURSA packets needed for your prescribed dose
- a clean spoon
- a container
- a measuring cup from your pharmacist
- 40 mL of water, orange juice, almond milk, or yogurt
- catheter tip syringe (if giving AQNEURSA oral suspension through G-tube)

| Preparing AQNEURSA Oral Suspension                                                                                                                                                                                                                                                                                           |                                                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| <b>Step 1:</b> Wash and dry your hands.                                                                                                                                                                                                                                                                                      |                                                                                       |
| <b>Step 2:</b> Open and empty the entire contents of 1 AQNEURSA packet into a container with 40 mL of: <ul style="list-style-type: none"><li>• water, orange juice, almond milk, or yogurt (when taken by mouth), <b>or</b></li><li>• <b>water only</b> when given through a G-tube.</li></ul> <b>Do not</b> use hot liquid. |  |

|                                                                                                                                                                                                                                                                                                                              |                                                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| <p><b>Step 3:</b> Stir to form the suspension.</p> <p><b>Note:</b></p> <ul style="list-style-type: none"> <li>Go to <b>Step 4</b> for taking AQNEURSA oral suspension by mouth, or</li> <li>Go to <b>Step 6</b> for giving AQNEURSA oral suspension through a gastrostomy tube (G-tube).</li> </ul>                          |    |
| <p><b>Taking AQNEURSA Oral Suspension by Mouth</b></p>                                                                                                                                                                                                                                                                       |                                                                                       |
| <p><b>Step 4:</b> Swallow AQNEURSA oral suspension right away (within 30 minutes).</p> <p>Throw away (dispose of) unused AQNEURSA oral suspension if not taken within 30 minutes.</p>                                                                                                                                        |    |
| <p><b>Step 5:</b> If your prescribed dose requires 2 AQNEURSA packets, repeat Steps 1 through 4.</p>                                                                                                                                                                                                                         |                                                                                       |
| <p><b>Giving AQNEURSA Oral Suspension Through a Gastrostomy Tube (G-tube)</b></p>                                                                                                                                                                                                                                            |                                                                                       |
| <ul style="list-style-type: none"> <li>Give AQNEURSA oral suspension through a G-tube that is a French size of 12 or larger.</li> <li>Follow Steps 1 through 3 to prepare AQNEURSA oral suspension.</li> </ul> <p><b>Note:</b> Only use 40 mL of water for preparing AQNEURSA oral suspension when given through G-tube.</p> |                                                                                       |
| <p><b>Step 6:</b> Draw up the prepared AQNEURSA oral suspension into a catheter tip syringe.</p>                                                                                                                                                                                                                             |  |

|                                                                                                                                                                                  |                                                                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| <p><b>Step 7:</b> Inject the AQNEURSA oral suspension through the G-tube right away.</p> <p>Throw away (dispose of) unused AQNEURSA oral suspension if not given right away.</p> |   |
| <p><b>Step 8:</b> Refill the syringe with an additional 20 mL water.</p>                                                                                                         |  |
| <p><b>Step 9:</b> Flush the G-tube with water, until no remaining AQNEURSA oral suspension is seen in the syringe or G-tube.</p>                                                 |  |
| <p><b>Step 10:</b> If your prescribed dose requires 2 AQNEURSA packets, follow Steps 1 through 3 to prepare the AQNEURSA oral suspension, then repeat Steps 6 through 9.</p>     |                                                                                     |

### Storing AQNEURSA

- Store AQNEURSA at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep AQNEURSA oral suspension and all medicines out of reach of children.

### Disposing of Expired AQNEURSA Packets or Unused AQNEURSA Oral Suspension

Throw away (dispose of) expired AQNEURSA packets or unused AQNEURSA oral suspension following the steps below:

- Mix medicine with a substance such as dirt, cat litter, or used coffee grounds.
- Place the mixture in a container such as a sealed plastic bag.
- Throw away (dispose of) the container in your household trash.

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This Instructions for Use has been approved by the U.S. Food and Drug Administration.

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