Zanvastro™ (zilganersen)
(Intrathecal)

Document Number: IC-0886

Last Review Date: 10/01/2026
Date of Origin: 10/01/2026
Dates Reviewed: 10/2026

I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 12 months (365 days).
- Renewal: Prior authorization validity may be renewed every 12 months (365 days) thereafter.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- 50 mg (1 vial) every 3 months

III. Initial Approval Criteria

Prior authorization validity is provided in the following conditions:

Universal Criteria [1-3]

- Member does not have obstructive hydrocephalus or any other brain or spinal disease that would interfere with the lumbar puncture (LP) process and CSF circulation; **AND**
- Confirmation that members with advanced stage of disease have been evaluated and it has determined that treatment would provide meaningful clinical benefit (*i.e., clinically meaningful function is expected to be maintained with treatment and/or a measurable symptom, functional ability, or disease parameter that can be assessed and monitored over time to evaluate treatment benefit*); **AND**

Alexander Disease (AxD) † Φ [1-3]

- Member has a confirmed diagnosis of Alexander Disease as established by a heterozygous pathogenic or likely pathogenic variant in the *GFAP* gene identified by molecular genetic testing AND suggestive brain neuroimaging (e.g., MRI) findings consistent with age-related phenotypes; **AND**
- Baseline documentation of one or more of the following:
    - Gross motor function assessments, including but not limited to, the following validated scales: Gross Motor Function Measure-88 (GMFM-88), Pediatric Low Motor Function Item Battery (P-LoMo), Gross Motor Function Classification Scale (GMFCS), modified Rankin Scale, 10-meter walk test *(note: applicable only to members who are ambulatory and able to perform it reliably)*, etc.

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- Symptom, laboratory and functional tracking:
    - Bulbar function: dysphagia, dysarthria/dysphonia, and palatal myoclonus
    - Seizure frequency
    - Spasticity, ataxia, and ocular movement abnormalities
    - Fluid biomarkers (i.e., serum or CSF GFAP levels)

† FDA Approved Indication(s), ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-3]

Prior authorization validity may be renewed based upon the following criteria:

- Member continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity which would preclude safe administration of the drug. Examples of unacceptable toxicity include: aseptic meningitis, etc.; **AND**
- Member has responded to therapy compared to pretreatment baseline in one or more of the following:
    - Stability or improvement or slowing the rate of decline in gross motor function assessments, including but not limited to, the following validated scales: Gross Motor Function Measure-88 (GMFM-88), Pediatric Low Motor Function Item Battery (P-LoMo), Gross Motor Function Classification Scale (GMFCS), modified Rankin Scale, 10-meter walk test gait speed etc.
    - Stability or improvement in symptom, laboratory and functional tracking:
        - Bulbar function: dysphagia, dysarthria/dysphonia, and palatal myoclonus
        - Seizure frequency
        - Spasticity, ataxia, and ocular movement abnormalities
        - Stability or improvement in fluid biomarkers (i.e., serum or CSF GFAP levels)

V. Dosage/Administration [1]

Indication	Dose

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<table>
<tr>
<td>Alexander Disease</td>
<td>The recommended dosage of Zanvastro is 50 mg intrathecally every 3 months. Administer Zanvastro intrathecally after dilution using a lumbar puncture by, or under the direction of, healthcare professionals experienced in performing lumbar punctures. The final dose volume of the intrathecal injection is determined by the member's age.
<table>
<tr><th>Member Age</th><th>Volume of excess aCSF diluent to withdraw from the diluent vial and discard</th><th>Volume of Zanvastro to add to the diluent vial</th><th>Volume of diluted Zanvastro to withdraw from the diluent vial for administration (dose volume)</th></tr>
<tr><td>Less than 2 years old</td><td>12.6 mL</td><td>2.8 mL</td><td>10 mL</td></tr>
<tr><td>2 to 7 years old (inclusive)</td><td>7.0 mL</td><td>2.8 mL</td><td>15 mL</td></tr>
<tr><td>8 years old and above</td><td>1.4 mL</td><td>2.8 mL</td><td>20 mL</td></tr>
</table>
<table>
<tr><th>Age</th><th>Injection Dose Volume After Dilution</th></tr>
<tr><td>Less than 2 years old</td><td>10 mL</td></tr>
<tr><td>2 years old to 7 years old (inclusive)</td><td>15 mL</td></tr>
<tr><td>8 years old and above</td><td>20 mL</td></tr>
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<tr>
<td colspan="2"><u>NOTE:</u>

Store the Zanvastro vial and diluent vial in the refrigerator between 2°C and 8°C (36°F and 46°F) in the original carton to protect from light.
Once taken out of the refrigerator, the Zanvastro vial and diluent vial can be stored at room temperature up to 30°C (86°F) in the original carton for up to 14 days. If not used within the 14 days stored at room temperature, discard Zanvastro.
Do not freeze. Do not expose to heat. Protect from light as a precaution.

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VI. Billing Code/Availability Information

<u>HCPCS code:</u>

- J3490 – Unclassified drugs

<u>NDC:</u>

- Zanvastro 56 mg/2.8 mL (20 mg/mL) solution for injection; single-dose vial: 71860-0304-xx
    - Includes one single-dose vial of artificial cerebrospinal fluid (aCSF) diluent: 21 mL of sterile, preservative free, clear and colorless solution for dilution of Zanvastro.

VII. References

1. Zanvastro [package insert]. Carlsbad, CA; Ionis Pharm., Inc.; September 2026. Accessed September 2026.
2. Waldman A, Lynch D, Tonduti D, et al. Efficacy and Safety of Zilganersen, an Investigational RNA-targeted Antisense Therapy, in People Living with Alexander Disease: Results from a Pivotal Study (PL5.003). 106 (11_Supplement_1) 941. June 9, 2026 issue. https://doi.org/10.1212/WNL.0000000000213207
3. Srivastava S, Waldman A, Naidu S. Alexander Disease. 2002 Nov 15 [Updated 2020 Nov 12]. In: Adam MP, Bick S, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA):

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University of Washington, Seattle; 1993-2026. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1172/.

Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G31.86	Alexander Disease

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)

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Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
6	MN, WI, IL	Wellpoint Federal
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	Wellpoint Federal
15	KY, OH	CGS Administrators, LLC

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