Draft New Policy: Do Not Implement

Zilganersen (Zanvastro™)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Zanvastro is a glial fibrillary acidic protein (GFAP)-directed antisense oligonucleotide indicated for the treatment of Alexander disease in pediatric and adult patients.
All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Initial Requests:

- Medical records (e.g., chart notes and/or laboratory reports) documenting all of the following:
  - Genetic testing results demonstrating a pathogenic variant in the glial fibrillary acidic protein (GFAP) gene.
  - Clinical phenotype consistent with Alexander disease (e.g., seizures, developmental delay, failure to thrive, ocular movement abnormalities, bulbar symptoms).
  - Brain magnetic resonance imaging (MRI) findings consistent with a diagnosis of Alexander disease.
  - Applicable baseline functional assessment:
    - Gross Motor Function Measure-88 (GMFM-88) standing (Dimension D) and walking/running/jumping (Dimension E) subscale scores for member ≥ 2 years and < 5 years of age; OR
    - 10 Meter Walk Test (10MWT) results for member ≥ 5 years of age.

Continuation Requests:

- Medical records and/or laboratory reports documenting a clinically positive response to therapy
- Applicable baseline and follow-up functional assessment(s) test results:
  - Gross Motor Function Measure-88 (GMFM-88) standing (Dimension D) and walking/running/jumping (Dimension E) subscale scores for member ≥ 2 years and < 5 years of age; OR
  - 10 Meter Walk Test (10MWT) results for member ≥ 5 years of age.

PRESCRIBER SPECIALITIES

This medication must be prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of Alexander disease.

COVERAGE CRITERIA

Alexander Disease

Authorization of 6 months may be granted for treatment of Alexander disease when all of the following criteria are met:

- Member is 2 years to less than 65 years of age.
- Member has a genetically confirmed diagnosis of Alexander disease, with documentation of pathogenic variant in the glial fibrillary acidic protein (GFAP) gene.
- Member exhibits documented clinical phenotype consistent with Alexander disease (e.g., seizures, developmental delay, failure to thrive, ocular movement abnormalities, bulbar symptoms).
- Member has documented brain MRI consistent with a diagnosis of Alexander disease.
- Gross Motor Function Mesaure-88 (GMFM-88) standing (Dimension D) and walking/running/jumping (Dimension E) subscale scores for member ≥ 2 years and < 5 years of age or 10 Meter Walk Test (10MWT) results for member ≥ 5 years of age have been assessed at baseline and will be monitored as clinically appropriate.
- Member does not have moderate or severe renal impairment, end-stage renal disease, or moderate or severe hepatic impairment.
- Member has not received gene therapy, cell transplantation, or any other experimental brain surgery previously.
- Member does not have obstructive hydrocephalus.
- Member does not have a functional ventriculoperitoneal shunt for the drainage of cerebrospinal fluid (CSF) or an implanted central nervous system (CNS) catheter.
- Member has been evaluated prior to intrathecal administration for factors that increase risks associated with lumbar puncture.
- Member does not have brain or spinal disease that would interfere with lumbar puncture or cerebrospinal fluid circulation.

CONTINUATION OF THERAPY

Authorization of 6 months may be granted for members requesting continuation of therapy when the member demonstrates a clinically positive response to therapy as evidenced by stabilization or improvement in applicable functional assessment test results (i.e., GMFM-88 subscale scores, 10MWT) from baseline.

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

REFERENCES

1. Zanvastro [package insert]. Carlsbad, CA: Ionis Pharmaceuticals, Inc.; September 2026. Accessed October 27,2026.
2. ClinicalTrials.gov. A Study to Evaluate Efficacy and Safety of ION373 in Participants With Alexander Disease (NCT04849741). https://clinicaltrials.gov/study/NCT04849741. Accessed October 28, 2026.
3. Prust M, Wang J, Morizono H, et al. GFAP mutations, age at onset, and clinical subtypes in Alexander disease. *Neurology*. 2011;77(13):1287-1294. doi:10.1212/WNL.0b013e3182309f72. Accessed October 28,2026.
4. Lexi-Comp Online. (2026, October). AHFS DI. Zanvastro. Retrieved October 2026 from Lexi-Comp Online with AHFS.
5. MICROMEDEX Healthcare Series. Drugdex Evaluations. (2026, September). Zilganersen. Retrieved October 2026 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE

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This document has been classified as public information