CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Arsenic Trioxide Utilization Management Medical Policy
- Trisenox® (arsenic trioxide intravenous infusion – Teva, generic)

REVIEW DATE: 10/16/2024

OVERVIEW

Arsenic trioxide is indicated for **acute promyelocytic leukemia (APL)**: [1]
- In combination with tretinoin for the treatment of adults with newly diagnosed low-risk disease whose APL is characterized by the presence of the t(15;17) translocation or PML/RAR-alpha gene expression.
- For induction of remission and consolidation in patients with APL who are refractory to, or have relapsed from, retinoid and anthracycline chemotherapy, and whose APL is characterized by the presence of the t(15;17) translocation or PML/RAR-alpha gene expression.

Guidelines

Arsenic trioxide is addressed in National Comprehensive Cancer Network (NCCN) guidelines.
- **Acute Myeloid Leukemia:** Guidelines (version 3.2024 – May 17, 2024) recommend arsenic trioxide for induction and consolidation therapy in low-risk (white blood cell [WBC] count < 10,000/µL) and in high-risk (WBC > 10,000/µL) APL with or without cardiac issues.[2,3] NCCN also recommends arsenic trioxide for the first relapse (either morphologic or molecular) and as single-agent consolidation therapy in patients who are not transplant candidates and are polymerase chain reaction negative following second remission (morphologic). In addition to the FDA-approved dosing for arsenic trioxide, NCCN also recommends the following dosing regimen:
  - Induction phase: 0.3 mg/kg administered intravenously (IV) on Days 1 through 5 of Week 1, followed by 0.25 mg/kg IV twice weekly in Weeks 2 through 8.
  - Consolidation phase: 0.3 mg/kg IV on Days 1 through 5 of Week 1, followed by 0.25 mg/kg IV twice weekly in Weeks 2 through 4 of each 8-week cycle.[3,4]
- **T-Cell Lymphoma:** Guidelines (version 4.2024 – May 28, 2024) recommend arsenic trioxide as a single agent for the second-line or subsequent treatment of non-responders to first-line therapy for adult T-cell leukemia/lymphoma, acute or lymphoma subtypes.[2,5]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of arsenic trioxide. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with arsenic trioxide as well as the monitoring required for adverse events and long-term efficacy, approval requires arsenic trioxide to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of arsenic trioxide is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Acute Promyelocytic Leukemia.** Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve ONE of the following dosing regimens (A or B):
   - **A)** FDA-approved dose (i, ii, and iii):
     - **i.** Each individual dose must not exceed 0.15 mg/kg administered by intravenous infusion; AND
     - **ii.** During the induction phase, the dose is administered once daily for a maximum of 60 days; AND
     - **iii.** During the consolidation phase, the dose is administered once daily on Days 1 through 5 in the first 4 weeks of each 8-week cycle.
   - **B)** National Comprehensive Cancer Network recommended dosing (i, ii, and iii):
     - **i.** Each individual dose must not exceed 0.3 mg/kg administered by intravenous infusion; AND
     - **ii.** During the induction phase, the dose is administered on Days 1 through 5 of Week 1 and then twice weekly in Weeks 2 through 8; AND
     - **iii.** During the consolidation phase, the dose is administered on Days 1 through 5 of Week 1 and then twice weekly in Weeks 2 through 4 of each 8 week cycle.

Other Uses with Supportive Evidence

2. **Adult T-Cell Leukemia/Lymphoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has acute or lymphoma subtype; AND
   - **C)** Patient has tried chemotherapy; AND
     Note: Examples include CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone).
   - **D)** Arsenic trioxide will be used as a single agent; AND
   - **E)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve the following dosing regimen (A, B, and C):
   - **A)** Each individual dose must not exceed 0.15 mg/kg administered by intravenous infusion; AND
   - **B)** During the induction phase, the dose is administered once daily for a maximum of 60 days; AND
   - **C)** During the consolidation phase, the dose is administered once daily on Days 1 through 5 in the first 4 weeks of each 8-week cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of arsenic trioxide is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Trisenox® intravenous infusion [prescribing information]. North Wales, PA: Teva; October 2022.
2. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 8, 2024. Search term: arsenic trioxide.
3. The NCCN Acute Myeloid Leukemia Clinical Practice Guidelines in Oncology (version 3.2024 – May 17, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 8, 2024.
4. Burnett AK, Russell NH, Hills RK, et al. Arsenic trioxide and all-*trans* retinoic acid treatment for acute promyelocytic leukaemia in all risk groups (AML17): results of a randomized, controlled, phase 3 trial. *Lancet Oncol*. 2015;16:1295-1305.
5. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 4.2024 – May 28, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 8, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	10/11/2023
Annual Revision	No criteria changes.	10/16/2024