CARECONTINUUM™

# UTILIZATION MANAGEMENT MEDICAL POLICY

**POLICY:** Oncology (Injectable) – Thiotepa Products Utilization Management Medical Policy
- Tepadina® (thiotepa intravenous, intracavitary, or intravesical injection – Adienne and Amneal, generic)
- Tepylute® (thiotepa intravenous injection – Shorla)

**REVIEW DATE:** 06/03/2026

## OVERVIEW

Thiotepa, an alkylating agent, is indicated for:
- **Beta-thalassemia**, to reduce the risk of graft rejection when used in conjunction with high-dose busulfan and cyclophosphamide as a preparative regimen for allogeneic hematopoietic progenitor (stem) cell transplantation for pediatric patients with Class 3 disease.[1]
- **Bladder cancer**, for superficial papillary carcinoma of the urinary bladder.[1,2]
- **Breast adenocarcinoma**.[1,2]
- **Neoplastic diseases of various serosal cavities**, for controlling intracavitary effusions secondary to diffuse or localized disease.[1,2]
- **Ovarian adenocarcinoma**.[1,2]

Tepylute (brand), an alkylating agent, is indicated for:
- **Breast adenocarcinoma.**[16]
- **Ovarian adenocarcinoma.**[16]

## Guidelines

The use of thiotepa is recommended across multiple National Comprehensive Cancer Network (NCCN) guidelines and the NCCN Compendium.[3,4,11-13,15] Recommendations with a category of evidence of 2B or higher support the approval criteria outlined below.

## POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of thiotepa. 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. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with thiotepa as well as the monitoring required for adverse events and long-term efficacy, approval requires thiotepa to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

I. Coverage of Tepadina (generic) is recommended in those who meet one of the following criteria:

**FDA-Approved Indications**

1. **Beta-Thalassemia.** Approve for 1 month 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 Class 3 beta-thalassemia; AND
   **C)** The medication will be used prior to allogeneic hematopoietic stem cell transplantation; AND
   **D)** The medication will be used in combination with high-dose busulfan and cyclophosphamide; AND
   **E)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Approve two doses, not to exceed 5 mg/kg each, administered intravenously.

2. **Bladder Cancer.** Approve for 1 month if the patient meets ALL of the following (A, B, and C):
   **A)** Patient is ≥ 18 years of age; AND
   **B)** Patient has superficial papillary carcinoma of the urinary bladder; AND
   **C)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Each individual dose must not exceed 60 mg instilled into the urinary bladder once weekly for up to 4 weeks.

3. **Breast Cancer.** Approve for 6 months if the patient meets BOTH of the following (A and B):
   **A)** Patient is ≥ 18 years of age; AND
   **B)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Each individual dose must not exceed 0.4 mg/kg administered intravenously no more frequently than once weekly.

4. **Malignant Effusions.** Approve for 6 months if the patient meets ALL of the following (A, B, and C):
   **A)** Patient is ≥ 18 years of age; AND
   **B)** Patient has intracavitary effusions secondary to diffuse or localized neoplastic disease; AND
   **C)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Each individual dose must not exceed 0.8 mg/kg instilled into the cavity no more frequently than once weekly.

5. **Ovarian Cancer.** Approve for 6 months if the patient meets BOTH of the following (A and B):
   **A)** Patient is ≥ 18 years of age; AND
   **B)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Each individual dose must not exceed 0.4 mg/kg administered intravenously no more frequently than once weekly.

**Other Uses with Supportive Evidence**

6. **Hematopoietic Cell Transplantation.** Approve for 1 month if the patient meets BOTH of the following (A and B):
   **A)** Patient is undergoing ONE of the following (i, ii, or iii):
      **i.** Autologous transplant; OR
      **ii.** Allogeneic transplant; OR
      **iii.** Umbilical cord blood transplant; AND
   **B)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Approve ONE of the following regimens (A or B):
   **A)** Approve up to two doses, not to exceed 10 mg/kg each, administered intravenously.
   **B)** Approve a single 10 mg/m$^2$ intravenous dose.

7. **Leptomeningeal Metastases**. Approve for 6 months if the patient meets BOTH of the following (A and B):
   **A)** Patient is ≥ 18 years of age; AND
   **B)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Each individual dose must not exceed 10 mg administered intrathecally up to twice weekly.

8. **Multiple Myeloma.** Approve for 6 months if the patient meets ALL of the following (A, B, and C):
   **A)** Patient is ≥ 18 years of age; AND
   **B)** The medication is used in combination with hydrocortisone; AND
   **C)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Each individual dose must not exceed 10 mg administered intrathecally up to twice weekly.

9. **Neuroblastoma**. Approve for 1 month if the patient meets ALL of the following (A, B, C, and D):
   **A)** The medication is used for consolidation therapy; AND
   **B)** Patient has high-risk disease; AND
   **C)** Patient will undergo tandem autologous stem cell rescue; AND
   **D)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Approve up to three doses of 300 mg/m$^2$ administered once daily by intravenous infusion.

10. **Primary Central Nervous System Lymphoma**. Approve for 3 months if the patient meets ALL of the following (A, B, and C):
   **A)** Patient is ≥ 18 years of age; AND
   **B)** The medication is used in ONE of the following (i or ii):
      **i.** The medication is used as a part of induction chemotherapy; OR
      **ii.** The medication is given as conditioning for hematopoietic stem cell transplantation prior to transplantation; AND
   **C)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Approve ONE of the following dosing regimens (A, B, or C):

**A)** Regimen 1: Each individual dose must not exceed 250 mg/m$^2$ administered intravenously for up to 3 days, beginning prior to hematopoietic stem cell transplantation; OR
**B)** Regimen 2: Each individual dose must not exceed 5 mg/kg administered intravenously for up to 2 days, beginning prior to hematopoietic stem cell transplantation; OR
**C)** Regimen 3 (i and ii):
  **i.** Each individual dose must not exceed 40 mg/m$^2$ administered intravenously up to two times in up to 21 day cycles; AND
  **ii.** Each individual dose must not exceed 5 mg/kg administered intravenously for up to 4 days, beginning prior to hematopoietic stem cell transplantation.

II. Coverage of Tepylute is recommended in those who meet one of the following criteria:

**FDA-Approved Indications**

1. **Breast Cancer.** Approve for 6 months if the patient meets BOTH of the following (A and B):
   **A)** Patient is ≥ 18 years of age; AND
   **B)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Each individual dose must not exceed 0.4 mg/kg administered intravenously no more frequently than once weekly.

2. **Ovarian Cancer.** Approve for 6 months if the patient meets BOTH of the following (A and B):
   **A)** Patient is ≥ 18 years of age; AND
   **B)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Each individual dose must not exceed 0.4 mg/kg administered intravenously no more frequently than once weekly.

**Other Uses with Supportive Evidence**

3. **Hematopoietic Cell Transplantation.** Approve for 1 month if the patient meets BOTH of the following (A and B):
   **A)** Patient is undergoing ONE of the following (i, ii, or iii):
     **i.** Autologous transplant; OR
     **ii.** Allogeneic transplant; OR
     **iii.** Umbilical cord blood transplant; AND
   **B)** The medication is prescribed by or in consultation with an oncologist.

   **Dosing.** Approve ONE of the following regimens (A or B):
   **A)** Approve up to two doses, not to exceed 10 mg/kg each, administered intravenously.
   **B)** Approve a single 10 mg/m$^2$ intravenous dose.

4. **Primary Central Nervous System Lymphoma**. Approve for 3 months if the patient meets ALL of the following (A, B, and C):
   **A)** Patient is ≥ 18 years of age; AND

**B)** The medication is used in ONE of the following (i or ii):
- **i.** The medication is used as a part of induction chemotherapy; OR
- **ii.** The medication is given as conditioning for hematopoietic stem cell transplantation prior to transplantation; AND

**C)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve ONE of the following dosing regimens (A, B, or C):

**A)** Regimen 1: Each individual dose must not exceed 250 mg/m$^2$ administered intravenously for up to 3 days, beginning prior to hematopoietic stem cell transplantation; OR

**B)** Regimen 2: Each individual dose must not exceed 5 mg/kg administered intravenously for up to 2 days, beginning prior to hematopoietic stem cell transplantation; OR

**C)** Regimen 3 (i and ii):
- **i.** Each individual dose must not exceed 40 mg/m$^2$ administered intravenously up to two times in up to 21 day cycles; AND
- **ii.** Each individual dose must not exceed 5 mg/kg administered intravenously for up to 4 days, beginning prior to hematopoietic stem cell transplantation.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of thiotepa 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. Tepadina® injection [prescribing information]. Lugano, Switzerland and Bridgewater, NJ: Adienne and Amneal; January 2026.
2. Thiotepa for injection [prescribing information]. Schaumberg, IL: Sagent; May 2025.
3. The NCCN Bladder Cancer Clinical Practice Guidelines in Oncology (version 1.2026 – March 16, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 29, 2026.
4. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2026 – April 24, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 29, 2026.
5. DeFilipp Z, Li S, El-Jawahri A, Armand P, et al. High-dose chemotherapy with thiotepa, busulfan and cyclophosphamide and autologous stem cell transplantation for patients with primary central nervous system lymphoma in first complete remission. *Cancer*. 2017;123:3073-3079.
6. Montemurro M, Kiefer T, Schuler F, et al. Primary central nervous system lymphoma treated with high-dose methotrexate, high-dose busulfan/thiotepa, autologous stem-cell transplantation and response-adapted whole-brain radiotherapy: Results of the multicenter Ostdeutsche Studiengruppe Hamato-Onkologie OSHO-53 phase II study. *Ann Oncol*. 2007;18:665-671.
7. Illerhaus G, Muller F, Feuerhake F, et al. High-dose chemotherapy and autologous stem-cell transplantation without consolidating radiotherapy as first-line treatment for primary lymphoma of the central nervous system. *Haematologica*. 2008;93:147-148.
8. Kasenda B, Schorb E, Fritsch K, et al. Prognosis after high-dose chemotherapy followed by autologous stem-cell transplantation as first-line treatment in primary CNS lymphoma – a long-term follow-up study. *Ann Oncol*. 2012;23:2670-2675.
9. Cho KM, Kim YJ, Kim SH, et al. Salvage treatment with intracerebrospinal fluid thiotepa in patients with leptomeningeal metastasis after failure of methotrexate-based treatment. *Anticancer Res*. 2015;35:5631-5638.
10. Mack F, Baumert BG, Schafer N, et al. Therapy of leptomeningeal metastasis in solid tumors. *Cancer Treat Rev*. 2016;43:83-91.
11. The NCCN Drugs and Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 3, 2026. Search term: thiotepa.
12. The NCCN Hematopoietic Cell Transplantation (HCT) Clinical Practice Guidelines in Oncology (version 2.2026 – April 3, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 29, 2026.
13. The NCCN Neuroblastoma Clinical Practice Guidelines in Oncology (version 2.2026 – April 28, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 29, 2026.

14. Tepylute® injection [prescribing information]. Cambridge, MA: Shorla; December 2025.
15. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 5.2026 – January 9, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 29, 2026.

## HISTORY

| Type of Revision | Summary of Changes | Review Date |
|---|---|---|
| Annual Revision | **Neuroblastoma:** Added new condition of approval. | 12/11/2024 |
| Early Annual Revision | Tepylute® (thiotepa intravenous injection) was added to the policy with different approval criteria than those for the other thiotepa products.<br>**Breast adenocarcinoma:** Added new condition of approval for Tepylute.<br>**Ovarian adenocarcinoma:** Added new condition of approval for Tepylute.<br>**Hematopoietic Cell Transplantation:** Added new condition of approval for Tepylute.<br>**Primary Central Nervous System Lymphoma:** Added new condition of approval for Tepylute. | 06/25/2025 |
| Annual Revision | **Multiple Myeloma:** Added as a new condition of approval for Tepadina.<br>**Primary Central Nervous System Lymphoma:** Previously, there was a requirement in place that if the medication is given as conditioning for hematopoietic stem cell transplantation, it is given prior to transplantation. This requirement was revised such that the patient must meet one of two conditions: either the medication is given as conditioning prior to stem cell transplantation, OR the medication is used as part of induction chemotherapy. This change was made to both Tepadina and Tepylute. | 06/03/2026 |