VENTURA COUNTY
HEALTH CARE PLAN

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: 06/25/2025

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

Thiotepa is addressed in National Comprehensive Cancer Network (NCCN) guidelines:
- **Bladder cancer:** Guidelines (version 1.2025 – March 25, 2025) state that intravesical thiotepa does not appear to be effective. NCCN recommends gemcitabine and mitomycin for intravesical chemotherapy.[5]
- **Breast cancer:** Guidelines (version 4.2025 – April 17, 2025) do not provide any recommendations on the use of thiotepa in the management of breast cancer.[3]
- **Central nervous system (CNS) cancers:** Guidelines (version 5.2024 – March 18, 2025) recommend thiotepa, in combination with methotrexate, cytarabine, and rituximab for induction therapy, in combination with other chemotherapy agents for relapsed or refractory disease, or in combination with carmustine or busulfan and cyclophosphamide, with stem cell rescue for consolidation therapy of primary CNS lymphoma.[6] NCCN recommends intra-cerebrospinal fluid thiotepa for the treatment of leptomeningeal metastases.
- **Hematopoietic Cell Transplantation:** Guidelines (version 1.2025 – February 28, 2025) recommend thiotepa as a component of a variety of conditioning regimens for autologous, allogeneic, and umbilical cord blood transplants.[13,14]
- **Neuroblastoma:** Guidelines (version 1.2025 – April 16, 2025) recommend thiotepa as standard consolidation therapy in combination with cyclophosphamide, carboplatin, etoposide, and melphalan with tandem autologous stem cell rescue and radiation therapy following induction therapy for high risk disease.[13,15]
- **Ovarian cancer:** Guidelines (version 2.2025 – May 23 2025) do not provide any recommendations on the use of thiotepa in the management of ovarian cancer.[4]

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

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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 intravenous.

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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.

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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.

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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.

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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

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6. Hematopoietic Cell Transplantation. Approve for 1 month if the patient meets ALL 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.

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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.

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8. 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.

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9. 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) If the medication is given as conditioning for hematopoietic stem cell transplantation, it is given 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 three 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

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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.

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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

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3. Hematopoietic Cell Transplantation. Approve for 1 month if the patient meets ALL 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):
C) Approve up to two doses, not to exceed 10 mg/kg each, administered intravenously.
D) 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)** If the medication is given as conditioning for hematopoietic stem cell transplantation, it is given 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 three 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; March 2020.
2. Thiotepa for injection [prescribing information]. Schaumberg, IL: Sagent; May 2018.
3. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 4.2025 – April 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.
4. The NCCN Ovarian Cancer Clinical Practice Guidelines in Oncology (version 2.2025 – May 23, 2025). © 2025 National Comprehensive Cancer Network. Available at; http://www.nccn.org. Accessed on May 30, 2025.
5. The NCCN Bladder Cancer Clinical Practice Guidelines in Oncology (version 1.2025 – March 25, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025..
6. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 5.2024 – March 18,, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.
7. 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.
8. 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.
9. 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.
10. 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.
11. 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.
12. Mack F, Baumert BG, Schafer N, et al. Therapy of leptomeningeal metastasis in solid tumors. *Cancer Treat Rev*. 2016;43:83-91.

13. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025. Search term: thiotepa.
14. The NCCN Hematopoietic Cell Transplantation (HCT) Clinical Practice Guidelines in Oncology (version 1.2025 – February 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.
15. The NCCN Neuroblastoma Clinical Practice Guidelines in Oncology (version 1.2025 – April 16, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.
16. Tepylute® injection [prescribing information]. Cambridge, MA: Shorla; February 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	12/13/2023
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. **Breast adenocarcinoma:** Added new condition of approval for Tepylute. **Ovarian adenocarcinoma:** Added new condition of approval for Tepylute. **Hematopoietic Cell Transplantation:** Added new condition of approval for Tepylute. **Primary Central Nervous System Lymphoma:** Added new condition of approval for Tepylute.	06/25/2025