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, generic)

REVIEW DATE: 11/30/2022

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]
- **Neoplastic diseases of various serosal cavities**, for controlling intracavitary effusions secondary to diffuse or localized disease.
- **Ovarian adenocarcinoma**.

Guidelines

Thiotepa is addressed in National Comprehensive Cancer Network (NCCN) guidelines:
- **Bladder cancer:** Guidelines (version 2.2022 – May 20, 2022) state that intravesical thiotepa does not appear to be effective. NCCN recommends gemcitabine and mitomycin for intravesical chemotherapy.[5]
- **Breast cancer:** Guidelines (version 4.2022 – June 21, 2022) do not provide any recommendations on the use of thiotepa in the management of breast cancer.[3]
- **Central nervous system (CNS) cancers:** Guidelines (version 2.2022 – September 29, 2022) recommend thiotepa, in combination with methotrexate, cytarabine, and rituximab for induction therapy, 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 2.2022 – September 28, 2022) recommend thiotepa as a component of a variety of conditioning regimens for autologous, allogeneic, and umbilical cord blood transplants.[13,14]
- **Ovarian cancer:** Guidelines (version 5.2022 – September 16, 2022) 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

Coverage of thiotepa 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 criteria (A, B, C, D, and E):
   - **A)** Patient is ≤ 18 years of age; AND
   - **B)** Patient has class 3 beta-thalassemia; AND
   - **C)** Thiotepa will be used prior to allogeneic hematopoietic stem cell transplantation; AND
   - **D)** Thiotepa 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.

---

2. **Bladder Cancer.** Approve for 1 month if the patient meets ALL of the following criteria (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 criteria (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 criteria (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 criteria (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 ALL of the following criteria (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 criteria (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. Primary Central Nervous System Lymphoma. Approve for 3 months if the patient meets ALL of the following criteria (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** If thiotepa 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: Adienne; January 2017.
2. Thiotepa for injection [prescribing information]. Schaumberg, IL: Sagent; April 2018.
3. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 4.2022 – June 21, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 17, 2022.
4. The NCCN Ovarian Cancer Clinical Practice Guidelines in Oncology (version 5.2022 – September 16, 2022). © 2022 National Comprehensive Cancer Network. Available at; http://www.nccn.org. Accessed November 17, 2022.
5. The NCCN Bladder Cancer Clinical Practice Guidelines in Oncology (version 2.2022 – May 20, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 17, 2022.
6. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 2.2022 – September 29, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 17, 2022.
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. © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 17, 2022. Search term: thiotepa.
14. The NCCN Hematopoietic Cell Transplantation (HCT) Clinical Practice Guidelines in Oncology (version 2.2022 – September 28, 2022). © National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 17, 2022.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Bladder Cancer:** A requirement was added that the patient is ≥ 18 years of age. **Breast Cancer:** A requirement was added that the patient is ≥ 18 years of age. **Malignant Effusions:** A requirement was added that the patient is ≥ 18 years of age. **Ovarian Cancer:** A requirement was added that the patient is ≥ 18 years of age. **Leptomeningeal Metastases:** A requirement was added that the patient is ≥ 18 years of age. **Primary Central Nervous System Lymphoma:** A requirement was added that the patient is ≥ 18 years of age. The requirement that thiotepa is used as a component of high dose chemotherapy followed by hematopoietic stem cell transplantation was removed.	11/03/2021
Annual Revision	**Hematopoietic Cell Transplantation:** This indication was added as a new condition of approval. **Primary Central Nervous System Lymphoma:** A requirement was added that if the patient is undergoing hematopoietic stem cell transplantation, thiotepa is to be given before transplantation.	11/30/2022