



**POLICY:** Oncology – Thiotepa injection for intravenous, intracavitary, or intravesical use (Tepadina® – Adienne SA, generics)

**APPROVAL DATE:** 10/16/2019

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## OVERVIEW

Thiotepa is an alkylating agent indicated:

- 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 beta-thalassemia.<sup>1</sup>
- For the treatment of breast or ovarian adenocarcinoma.
- For controlling intracavitary effusions secondary to diffuse or localized neoplastic diseases of various serosal cavities.
- For the treatment of superficial papillary carcinoma of the urinary bladder.<sup>1,2</sup>

## Guidelines

The National Comprehensive Cancer Network (NCCN) breast cancer guidelines (version 3.2019 – September 6, 2019) do not provide any recommendations on the use of thiotepa in the management of breast cancer.<sup>3</sup>

The NCCN ovarian cancer guidelines (version 2.2019 – September 17, 2019) do not provide any recommendations on the use of thiotepa in the management of ovarian cancer.<sup>4</sup>

The NCCN bladder cancer guidelines (version 4.2019 – July 10, 2019) state that intravesical thiotepa does not appear to be effective. NCCN recommends gemcitabine and mitomycin for intravesical chemotherapy.<sup>5</sup>

The NCCN central nervous system (CNS) cancers guidelines (version 2.2019 – September 16, 2019) recommend thiotepa, in combination with carmustine or busulfan and cyclophosphamide, with stem cell rescue for consolidation therapy of primary CNS lymphoma.<sup>6</sup> NCCN recommends intra-cerebrospinal fluid thiotepa for the treatment of leptomeningeal metastases.

## 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 indication(s). 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.

## RECOMMENDED AUTHORIZATION CRITERIA

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Coverage of thiotepa is recommended in those who meet the following criteria:

### **FDA-Approved Indications**

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- 1. Beta-Thalassemia.** Approve for 1 month if the patient meets the following criteria (A, B, C, D, and E):
  - A) The patient is  $\leq$  18 years of age; AND
  - B) The 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) Thiotepa is prescribed by or in consultation with an oncologist.

**Dosing.** Approve two doses, not to exceed 5 mg/kg each, administered intravenously.<sup>1</sup>

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- 2. Breast Cancer.** Approve for 6 months if thiotepa 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.<sup>1,2</sup>

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- 3. Ovarian Cancer.** Approve for 6 months if thiotepa 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.<sup>1,2</sup>

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- 4. Bladder Cancer.** Approve for 1 month if the patient meets the following criteria (A and B):

- A) The patient has superficial papillary carcinoma of the urinary bladder; AND
- B) Thiotepa 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.<sup>1,2</sup>

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- 5. Malignant Effusions.** Approve for 6 months if the patient meets the following criteria (A and B):

- A) The patient has intracavitary effusions secondary to diffuse or localized neoplastic disease; AND
- B) Thiotepa 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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### **Other Uses with Supportive Evidence**

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- 6. Primary Central Nervous System Lymphoma.** Approve for 3 months if the patient meets the following criteria (A and B):
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- A) Thiotepa is used as a component of high-dose chemotherapy followed by hematopoietic stem cell transplantation; AND
- B) Thiotepa 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<sup>2</sup> administered intravenously for up to three days, beginning prior to hematopoietic stem cell transplantation;<sup>7</sup> 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;<sup>8</sup> OR
- C) Regimen 3 (i and ii):
  - i. Each individual dose must not exceed 40 mg/m<sup>2</sup> 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.<sup>9,10</sup>

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7. **Leptomeningeal Metastases.** Approve for 6 months if thiotepa is prescribed by or in consultation with an oncologist.

**Dosing.** Each individual dose must not exceed 10 mg administered intrathecally up to twice weekly.<sup>11,12</sup>

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#### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Thiotepa has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

- 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 SA; January 2017.
2. Thiotepa for injection [prescribing information]. Schaumburg, IL: Sagent Pharmaceuticals; April 2018.
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4. The NCCN Ovarian Cancer Clinical Practice Guidelines in Oncology (Version 2.2019 – September 17, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed September 20, 2019.
5. The NCCN Bladder Cancer Clinical Practice Guidelines in Oncology (Version 4.2019 – July 10, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. accessed on September 20, 2019.
6. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (Version 2.2019 – September 16, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 20, 2019.
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.

**HISTORY**

Type of Revision	Summary of Changes	Approval Date
New Policy	--	10/16/2019