Tepylute®
(thiotepa) injection

TEPYLUTE® is the First and Only Ready-to-Dilute Formulation of Thiotepa

Not Actual Size

ABOUT TEPYLUTE®

- TEPYLUTE® is a ready-to-dilute thiotepa formulation which does not require reconstitution and is ready to dilute in 0.9% NaCl
- Adoption of TEPYLUTE® may reduce manual compounding time by ~30% vs lyophilized thiotepa
- Single and multi-dose vials for improved flexibility:
  - Vial Size: 3 mL single-use vial containing 15 mg thiotepa and 1.5 mL of polyethylene glycol 400
  - Vial Size: 10 mL multi-dose vial containing 100 mg thiotepa and 10 mL of polyethylene glycol 400
- Once compounded, TEPYLUTE® is stable for 24 hours when stored in the refrigerator and for 4 hours when stored at room temperature
- Partially used multi-dose vials are stable for 14 days when properly stored (2°C to 8°C)
- Introducing TEPYLUTE® may result in cost savings for institutions
  - In modeling, switching from lyophilized thiotepa to ready-to-dilute TEPYLUTE® resulted in cost savings for the hospital
  - The following factors resulted in cost offsets:
    - Drug acquisition costs were reduced due to the lower cost of TEPYLUTE® compared to TEPADINA® and 15 mg vials of generic thiotepa
    - Administration costs, where adopting TEPYLUTE® resulted in reduced compounding time, saving time for pharmacists
    - Drug wastage, where TEPYLUTE® resulted in fewer remade doses due to reduced preparation errors
- Physiochemical studies demonstrated comparability of ready-to-dilute/reconstituted and final diluted solutions of TEPYLUTE® and TEPADINA®

INDICATIONS

TEPYLUTE® is indicated for the treatment of adenocarcinoma of the breast or ovary.

WARNING: SEVERE MYELOSUPPRESSION AND CARCINOGENICITY

- **TEPYLUTE® may cause severe marrow suppression, and high doses may cause marrow ablation with resulting infection or bleeding. Monitor hematologic laboratory parameters.**
- **TEPYLUTE® should be considered potentially carcinogenic in humans.**

SHORLA ONCOLOGY®

For full Prescribing Information, please visit shorlaoncology.com/tepylute.

TEPYLUTE® Ordering Information

Tepylute® (thiotepa) injection

TEPYLUTE® WAC $2350

- TEPYLUTE® is available through GPO contracts
- TEPYLUTE® is available for order through existing hazardous drug distributors
- Shorla has applied for a TEPYLUTE® J Code (Effective 7/1/25)

Vial Size	NDC	WAC Price	Vials/Case
15 mg	81927-105-15	$557.10	24
100 mg	81927-106-01	$3714.00	24

Order Direct

Shorla Oncology representatives are available to assist you Monday through Friday from 8 AM to 5 PM CT.

CALL
1-844-974-6752

FAX
414-501-3169

EMAIL
shorlacs@eversana.com

SHORLA ONCOLOGY®

For full Prescribing Information, please visit shorlaoncology.com/tepylute.

TEPYLUTE® (thiotepa) Injection for Intravenous Use

INDICATIONS

TEPYLUTE® is an alkylating drug indicated for the treatment of adenocarcinoma of the breast or ovary.

WARNING: SEVERE MYELOSUPPRESSION AND CARCINOGENICITY

- **TEPYLUTE® may cause severe marrow suppression, and high doses may cause marrow ablation with resulting infection or bleeding. Monitor hematologic laboratory parameters.**
- **TEPYLUTE® should be considered potentially carcinogenic in humans.**

CONTRAINDICATIONS

TEPYLUTE® is contraindicated in patients with severe hypersensitivity to thiotepa and in concomitant use with live or attenuated vaccines.

WARNINGS AND PRECAUTIONS

Myelosuppression: For patients receiving TEPYLUTE® for treatment of adenocarcinoma of the breast or adenocarcinoma of the ovary, if the bone marrow has been compromised by prior irradiation or chemotherapy, or is recovering from chemotherapy, the risk of severe myelosuppression with TEPYLUTE® may be increased. Perform periodic complete blood counts during the course of treatment with TEPYLUTE®. Provide supportive care for infections, bleeding, and symptomatic anemia. Inform patients of the possibility of developing low blood cell counts and the need for hematopoietic progenitor cell infusion. Instruct patients to immediately report to their healthcare provider if bleeding or fever occurs.

Hypersensitivity: Clinically significant hypersensitivity reactions, including anaphylaxis, have occurred following administration of thiotepa. If anaphylactic or other clinically significant allergic reaction occurs, discontinue treatment with TEPYLUTE®, initiate appropriate therapy, and monitor until signs and symptoms resolve. Counsel patients on the signs and symptoms of hypersensitivity and to seek immediate emergency assistance if they develop any of these signs and symptoms.

Cutaneous Toxicity: TTEPYLUTE® and/or its active metabolites may be excreted in part via skin in patients receiving high-dose therapy. Treatment with TEPYLUTE® may cause skin discoloration, pruritus, blistering, desquamation, and peeling that may be more severe in the groin, axillae, skin folds, in the neck area, and under dressings. Instruct patients to shower or bathe with water at least twice daily through 48 hours after administration of TEPYLUTE®. Change the occlusive dressing and clean the covered skin at least twice daily through 48 hours after administration of TEPYLUTE®. Change bed sheets daily during treatment. Skin reactions associated with accidental exposure to TEPYLUTE® may occur. Wash the skin thoroughly with soap and water in case the TEPYLUTE® solution contacts the skin. Flush mucous membranes in case of TEPYLUTE® contact with mucous membranes.

Concomitant Use of Live and Attenuated Vaccines: Do not administer live or attenuated viral or bacterial vaccines to a patient treated with TEPYLUTE® until the immunosuppressive effects have resolved.

Hepatic Veno-Occlusive Disease: Monitor by physical examination, serum transaminases, and bilirubin, and provide supportive care to patients who develop hepatic veno-occlusive disease.

TEPYLUTE® (thiotepa) Injection for Intravenous Use

WARNINGS AND PRECAUTIONS CONTINUED

Central Nervous System Toxicity: Fatal encephalopathy has occurred in patients treated with high doses of thiotepa. Other central nervous system toxicities, such as headache, apathy, psychomotor retardation, disorientation, confusion, amnesia, hallucinations, drowsiness, somnolence, seizures, coma, inappropriate behavior, and forgetfulness have been reported to occur in a dose-dependent manner during or shortly after administration of high-dose thiotepa. Do not exceed the recommended dose of TEPYLUTE®. If severe or life-threatening central nervous system toxicity occurs, discontinue administration of TEPYLUTE® and provide supportive care.

Carcinogenicity: Like many alkylating agents, thiotepa has been reported to be carcinogenic when administered to laboratory animals. Carcinogenicity is shown most clearly in studies using mice, but there is some evidence of carcinogenicity in man. There is an increased risk of secondary malignancy with the use of TTEPYLUTE®. Inform patients that TEPYLUTE®can increase the risk of secondary malignancy.

Polyethylene glycol (PEG) 400 toxicity: TEPYLUTE® contains a high concentration of PEG 400. Based on findings in animals, administration of high amounts of PEG 400 may cause damage to the kidneys and liver at dosages higher than recommended. When prescribing TEPYLUTE®, take into consideration the PEG 400 load from concomitant medications.

Embryo-Fetal Toxicity: Based on the mechanism of action and findings in animals, TEPYLUTE® can cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies of TEPYLUTE®in pregnant women. Thiotepa given by the intraperitoneal (IP) route was teratogenic in mice at doses ≥1 mg/kg (3.2 mg/m2), approximately 8-fold less than the maximum recommended human therapeutic dose (0.8 mg/kg, 27 mg/m2), based on body-surface area. Thiotepa given by the IP route was teratogenic in rats at doses ≥3 mg/kg (21 mg/m2), approximately equal to the maximum recommended human therapeutic dose, based on body-surface area. Thiotepa was lethal to rabbit fetuses at a dose of 3 mg/kg (41 mg/m2), approximately two times the maximum recommended human therapeutic dose based on body-surface area. Advise pregnant women and females of reproductive potential of the potential risk to the fetus. Advise females of reproductive potential to use highly effective contraception during TEPYLUTE® treatment and for 6 months after therapy/the last dose. Advise females of reproductive potential to inform their healthcare provider if they are pregnant or become pregnant. Advise males with female partners of reproductive potential to use effective contraception during TEPYLUTE® treatment and for 1 year after therapy/the last dose.

ADVERSE REACTIONS

The most common adverse reactions (incidence greater than 10%) are neutropenia, anemia, thrombocytopenia, elevated alanine aminotransferase, elevated aspartate aminotransferase (AST), elevated bilirubin, mucositis, cytomegalovirus infection, hemorrhage, diarrhea, hematuria, and rash.

The clinically significant adverse reactions include myelosuppression, infection, hypersensitivity, cutaneous toxicity, hepatic veno-occlusive disease, central nervous system toxicity, and carcinogenicity.

TEPYLUTE® (thiotepa) Injection for Intravenous Use

DRUG INTERACTIONS

Effect of Cytochrome CYP3A Inhibitors and Inducers: In vitro studies suggest that thiotepa is metabolized by CYP3A4 and CYP2B6 to its active metabolite triethylene phosphoramide (TEPA). Avoid coadministration of strong CYP3A4 inhibitors (e.g., itraconazole, clarithromycin, ritonavir) and strong CYP3A4 inducers (e.g., rifampin, phenytoin) with thiotepa due to the potential effects on efficacy and toxicity. Consider alternative medications with no or minimal potential to inhibit or induce CYP3A4. If concomitant use of strong CYP3A4 modulators cannot be avoided, closely monitor for adverse drug reactions.

Effect of TEPYLUTE® on Cytochrome CYP2B6 Substrates: In vitro studies suggest that thiotepa inhibits CYP2B6. Thiotepa may increase the exposure of drugs that are substrates of CYP2B6 in patients; however, the clinical relevance of this in vitro interaction is unknown. The administration of thiotepa with cyclophosphamide in patients reduces the conversion of cyclophosphamide to the active metabolite, 4 hydroxycyclophosphamide; the effect appears sequence-dependent with a greater reduction in the conversion to 4-hydroxycyclophosphamide when thiotepa is administered 1.5 hours before the intravenous administration of cyclophosphamide compared to administration of thiotepa after intravenous cyclophosphamide. The reduction in 4-hydroxycyclophosphamide levels may potentially reduce the efficacy of cyclophosphamide treatment.

USE IN SPECIFIC POPULATIONS

Pregnancy: TEPYLUTE® can cause fetal harm when administered to a pregnant woman based on findings from animals and the drug's mechanism of action. Limited available data on thiotepa use in pregnant women are insufficient to inform a drug-associated risk of major birth defects and miscarriage. In animal reproduction studies, administration of thiotepa to pregnant mice and rats during organogenesis produced teratogenic effects (neural tube defects and malformations of the skeletal system of the fetus) at doses approximately 0.125 and 1 times, respectively, the maximum recommended human daily dose on a mg/m2 basis. Thiotepa was lethal to rabbit fetuses at approximately 2 times the maximum recommended human therapeutic dose based on body-surface area. Consider the benefits and risks of TEPYLUTE® for the mother and possible risks to the fetus when prescribing TEPYLUTE® to a pregnant woman.

Lactation: There is no information regarding the presence of thiotepa in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for serious adverse reactions, including the potential for tumorigenicity shown for thiotepa in animal studies, advise patients not to breastfeed during TEPYLUTE® treatment and for 1 week after therapy/the last dose.

Females and Males of Reproductive Potential:
TEPYLUTE® can cause fetal harm when administered to a pregnant woman.

Pregnancy Testing - Verify the pregnancy status of females of reproductive potential before initiating TEPYLUTE® therapy.
Contraception for Females - Advise females of reproductive potential to avoid pregnancy during TEPYLUTE® treatment and for 6 months after therapy/the last dose. Advise females to immediately report pregnancy.

Contraception for Males - TEPYLUTE® may damage spermatozoa and testicular tissue, resulting in possible genetic abnormalities. Males with female sexual partners of reproductive potential should use effective contraception during TEPYLUTE® treatment and for 1 year after therapy/the last dose.

Infertility - Based on nonclinical findings, male and female fertility may be compromised by treatment with TEPYLUTE®. Advise patients that TEPYLUTE® can produce infertility. Inform male patients about the possibility of sperm conservation before the start of therapy.

TEPYLUTE® (thiotepa) Injection for Intravenous Use

USE IN SPECIFIC POPULATIONS, CONTINUED

Pediatric Use: Safety and effectiveness of TEPYLUTE® in neonates have not been established. Safety and effectiveness of TEPYLUTE® for the treatment of adenocarcinoma of the breast and adenocarcinoma of the ovary in pediatric patients have not been established.

Geriatric Use: Clinical studies of thiotepa for treatment of adenocarcinoma of the breast and adenocarcinoma of the ovary did not include sufficient numbers of subjects aged 65 years and over to determine whether elderly subjects respond differently from younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreasing hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Renal Impairment: In patients with moderate (creatinine clearance [CLcr] of 30 mL/min to 59 mL/min) renal impairment, decreased renal excretion may result in increased plasma levels of thiotepa and TEPA. This may result in increased toxicity. Monitor patients with moderate to severe (CLcr <30 mL/min) renal impairment for signs and symptoms of toxicity following treatment with TEPYLUTE® for an extended period of time.

Hepatic Impairment: Thiotepa is extensively metabolized in the liver. Patients with moderate (bilirubin levels greater than 1.5 times to 3 times the upper limit of normal and any AST) hepatic impairment may have increased plasma levels of thiotepa. This may result in toxicity. Monitor patients with moderate to severe (bilirubin levels greater than 3 times the upper limit of normal and any AST) hepatic impairment for signs and symptoms of toxicity following treatment with TEPYLUTE® for an extended period of time.

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To report suspected adverse reactions, contact Shorla Oncology at 1-844-9-SHORLA (1-844-974-6752) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please click here for full Prescribing Information.
For more information, please visit shorlaoncology.com/tepylute.

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