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Thiotepa for Injection

DEFINITION
Thiotepa for Injection contains NLT 95.0% and NMT 110.0% of the labeled amount of thiotepa ($C_6H_{12}N_3PS$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 13.6 g/L of monobasic potassium phosphate in water. Adjust with 35 g/L of dibasic sodium phosphate in water to a pH of 7.0.

Mobile phase: Acetonitrile and *Buffer* (13:87)

System suitability solution: Transfer 10 mg of USP Thiotepa RS to a 4-mL vial, add 2 mL of methanol, and mix. Add 50 µL of 0.1% phosphoric acid solution. Place a cap on the vial, and heat at 65° for 50 s. Cool the solution, add 1 mL of methanol, and mix. [Note—The preparation generates methoxythiotepa.]

Standard solution: 1.5 mg/mL of USP Thiotepa RS in water

Sample solution: Nominally 1.5 mg/mL of thiotepa in water from Thiotepa for Injection

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for thiotepa and methoxythiotepa are about 1.0 and 1.3, respectively.]

Suitability requirements

Resolution: NLT 3 between methoxythiotepa and thiotepa, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of thiotepa ($C_6H_{12}N_3PS$) in the portion of Thiotepa for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of thiotepa from the *Sample solution*

r_S = peak response of thiotepa from the *Standard solution*

C_S = concentration of USP Thiotepa RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of thiotepa in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–110.0%

IMPURITIES

• **Organic Impurities**

Buffer, Mobile phase, and **System suitability solution:** Proceed as directed in the *Assay*.

Peak identification solution: Dissolve 15 mg of USP Thiotepa RS in 10 mL of water, add 1 g of sodium chloride, boil in a water bath for 10 min, and cool. [Note—The preparation generates thiotepa chloroethyl analog.]

Standard solution: 3.75 µg/mL of USP Thiotepa RS in water

Sample solution: Nominally 3.75 mg/mL of thiotepa in water from Thiotepa for Injection. Pass through a suitable filter, and use the filtrate.

Chromatographic system: Proceed as directed in the *Assay*. In addition, the run time is NLT 4 times the retention time of the thiotepa peak.

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 3 between methoxythiotepa and thiotepa

Analysis

Samples: *Peak identification solution*, *Standard solution*, and *Sample solution*

Calculate the percentage of each impurity in the portion of thiotepa taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of thiotepa from the *Standard solution*

C_S = concentration of USP Thiotepa RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of thiotepa in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*. Disregard any impurity peaks less than 0.1%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Thiotepa	1.0	—
Thiotepa chloroethyl analog[a]	3.75	0.15
Any individual unspecified impurity	—	0.2
Total impurities[b]	—	0.4

[a] *P*,*P*-Bis(aziridin-1-yl)-*N*-(2-chloroethyl)phosphinothioic amide.

[b] The impurity thiotepa chloroethyl analog is excluded.

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

SPECIFIC TESTS

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 6.25 USP Endotoxin Units/mg of thiotepa

• **Sterility Tests ⟨71⟩:** Meets the requirements

• **pH ⟨791⟩**

Sample solution: 10 mg/mL of thiotepa constituted as directed in the labeling

Acceptance criteria: 5.5–7.5

• **Injections and Implanted Drug Products ⟨1⟩,** *Product Quality Tests Common to Parenteral Dosage Forms*, *Specific Tests*, *Completeness and clarity of solutions*: At the time of use, it meets the requirements.

• **Other Requirements:** It meets the requirements in *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for constitution*, and store in a refrigerator, protected from light.

• **USP Reference Standards ⟨11⟩**
USP Thiotepa RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
THIOTEPA FOR INJECTION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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