

<b>Heraeus</b>	<b>Safety Data Sheet</b>	Date of issue: 08.06.2004
<b>W. C. Heraeus GmbH &amp; Co. KG</b>		Rev. no.: 1
	Trade name: <b>Thiotepa</b>	Identity no.: 89730026

## 1. Identification of the substance/preparation and company

Identity number : 89730026  
 Empirical formula : C<sub>6</sub>H<sub>12</sub>N<sub>3</sub>PS  
 Molecular weight : 189,22 [g/Mol]

### 1.1 Trade name

Thiotepa

Synonym: Thiotriethylenphosphoramid; Triethylenethiophosphoramid;  
 Tris(1-aziridinyl)phosphine sulphide

### 1.2 Application

The substance is used as cytostatica in cancer therapy.

### 1.3 Informations about manufacturer/supplier

W. C. Heraeus GmbH & Co. KG  
 Chemicals Division - Pharma  
 Heraeusstraße 12-14, D-63450 Hanau, Germany  
 Post box 1553, D-63405 Hanau, Germany

Marketing manager: Mr. M. Schwarz Phone: 06181/35-5255  
 Fax: 06181/35-4302

## 2. Composition/information on ingredients

### **Chemical characterization (substance)**

Aziridine, 1, 1', 1'', -phoshinothioylidynetris-

CAS-No.	EINECS-No.	Index-No.	Elincs-No.
52-24-4	200-137-7	---	---

## 3. Hazards identification

### **Characterization of hazards**

Very toxic.  
 Irritant.

### **Hazards information**

May cause cancer. May cause heritable genetic damage. May impair fertility. May cause harm to the unborn child. Very toxic by inhalation, in contact with skin and if swallowed. Irritating to eyes, respiratory system and skin. May cause sensitization by inhalation and skin contact.

**Handle with extreme care!!!**

### **Usual adult dose:**

The usual adult dose (intravenous) of thiotepa is up to 40 mg every 1 to 4 weeks.  
 This material has a slow onset of action.

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**Adverse effects:**

Adverse effects include dizziness, hives, loss of appetite, nausea and vomiting, missing menstrual periods, hair loss, bone marrow depression characterized by blood disorder (may take up to 30 days to appear), fever, chills, cough, sore throat or tightness, headache, abnormal burning or prickling sensation, lower back or side pain, painful or difficult urination, unusual bleeding or bruising, bloody urine or black, tarry stools, joint pain, swollen feet or legs, and impaired fertility. Possible allergic reaction to material if inhaled, ingested or in contact with skin.

#### 4. First-aid measures

**General information**

Remove from exposure, lie down. Remove contaminated clothing. Persons developing serious hypersensitivity (anaphylactic reactions) must receive immediate medical attention. If person is not breathing give artificial respiration. If breathing is difficult give oxygen. Obtain medical attention.

- Acute:** Causes eye, gastrointestinal tract and respiratory tract irritation. Possible skin irritation.
- Chronic:** Possible hypersensitization, increased skin pigmentation, contact allergic reactions, bone marrow depression and cancer (leukemia).
- After inhalation:** Causes irritation. Avoid inhalation. Supply with fresh air. Seek medical advice immediately
- After contact with skin:** May cause irritation. Flush with copious quantities of water. Avoid contact since systemic toxicity may occur following skin absorption. Seek medical advice immediately
- After contact with eyes:** Causes irritation. Flush with copious quantities of tepid water for 15 minutes. Seek medical advice immediately
- After ingestion:** Causes irritation. Flush out mouth with water. This material is unreliably and incompletely absorbed from the gastrointestinal tract. Seek medical advice immediately

**Overdose treatment:**

There is no known antidote for overdose treatment with thiotepa. If oral exposure occurs, induced vomiting with syrup of ipecac leads to a mean recovery of only 30% of the ingested dose, but it is still probably useful. Monitor hemograms and WBC counts to assess the level of intoxication to the hematopoietic system. Transfusions of whole blood or platelets or leukocytes have proven beneficial in combating this toxicity.

**Medical conditions**

- Aggravated by Exposure:** Hypersensitivity to material, bone marrow depression, chickenpox (including recent exposure), herpes zoster, history of gout or kidney stones, impaired liver or kidney function, and infection.
- Pregnancy comments:** Because thiotepa is generally teratogenic in humans, its use during pregnancy should be avoided, especially during the first trimester.

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## 5. Fire-fighting measures

### Suitable extinguishing media

Use extinguishing media that are appropriate to the environment.

Water spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and materials.

### Not suitable extinguishing media

Full water jet

### Specific danger by the substance, its burning products or developing gases

This material is assumed to be combustible. As with all dry powders it is advisable to ground mechanical equipment in contact with dry material to dissipate the potential buildup of static electricity.

In case of fire dangerous gases may be formed: PO<sub>x</sub>, SO<sub>x</sub>, NO<sub>x</sub>

### Specific fire-fighting measures

As with all fires, evacuate personnel to a safe area. Firefighters should use self-contained breathing equipment and protective clothing.

## 6. Accidental release measures

### Personal precautions

Avoid contact with substance without fail.

To collect disposed material use an emergency kit consisting of:

- one-way respiratory protection filter (P3)
- tightly fitting safety glasses / goggles
- two pair high-risk gloves (wear one upon the other)
- one-way overshoes
- one-way overall
- tight bag for cytostatica waste

Evacuate area. Use safety shower and where necessary eye bath.

Remove and dispose of contaminated clothing and gloves as well as equipment and treat as hazardous waste.

### Environmental precautions

Do not allow to enter surface and ground water, the sewage system or soil.

### Methods for cleaning up/taking up

Wear approved respirator, chemically compatible gloves and protective clothing. Avoid breathing dust. Wash spill site

Collect solids and wipes in an appropriately labelled container for disposal according to local and national waste disposal regulations.

### Further information

Thiotepa can be deactivated by treatment with aqueous acidic solutions (pH < 1,5)

Label transport container of waste with "Attention Cytostatica".

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## 7. Handling and storage

### **Advice on safe handling**

Handle only in a closed equipment, in a cytostatica workbench (DIN 12980) or in a safety workbench (DIN 12950 Part 10).

Working in the cited workbenches use personal protection as mentioned in section 8.3).

Handle in accordance with good industrial hygiene and safety practise.

Do not eat, drink and smoke at working place.

Only accessible to qualified persons.

Avoid formation of respiratory particles.

### **Precautionary measures against fire and explosion**

Heating may cause decomposition. In the case of fire hazardous gases may be generated (see section 5).

### **Storage**

#### **Requirements for storage rooms and vessels**

Store in tight, light-resistant container. This material should be handled and stored per label instructions to ensure product integrity. Keep refrigerated.

Do not store together with flammable or fire promoting substances.

Keep away from food and drink.

## 8. Exposure controls / Personal protection

### 8.1 **Additional advice on system design**

Handle only in a closed equipment, in a cytostatica workbench (DIN 12980) or in a safety workbench (DIN 12950 Part 10).

### 8.2 **Advice on limits**

**MAK-List: ---**

The pharmaceutical industry recommend the reference point of 0.00005 mg/m<sup>3</sup> (LTEL 8hr TWA) for very toxic and potential carcinogen substances.

### 8.3 **Personal protection equipment**

#### **Respiratory protection:**

Using a cytostatica workbench or a safety workbench there is no respiratory protection necessary.

#### **Hand protection:**

In a cytostatica workbench or a safety workbench use 2 pairs of high risk gloves (wear one upon the other). Gloves made of rubber or PVC or similar material. Change gloves when contaminated or having 20 min in use.

#### **Eye protection:**

Using a cytostatica workbench or a safety workbench there is no eye protection is not necessary.

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**Body protection:** Using a cytostatica workbench or a safety workbench wear a laboratory smock with long sleeves. Contaminated working clothes remove immediately and clean before reuse.

**Protective and hygiene measure:** Handle in accordance with good industrial hygiene and safety practise. Do not eat or drink at work place, do not smoke. Wash hands before breaks. At the end of workday have a shower. Wear working cloths not outside the working area. Keep away from food and drink. Wash hands and face before breaks and immediately after handling the product.

## 9. Physical and chemical properties

### 9.1 Appearance

Form: fine crystalline flakes  
 Colour: white  
 Odour: faint odour

### 9.2 Aspects relevant for security

#### Test method

pH-value: 5,5 – 7,5 (10 mg/ml)  
 Melting range: between 52 – 57°C  
 Boiling point: not applicable  
 Flash point: not applicable  
 Ignition point: not applicable  
 Ignition temperature: not applicable  
 Self ignition: not applicable  
 Explosion limits lower: not applicable  
 upper: not applicable  
 Vapour pressure: not applicable  
 Density: not determined  
 Solubility in water: soluble (~ 190 g/L)

### 9.3 Further information

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## 10. Stability and reactivity

**Conditions to avoid:**  
 Avoid exposure to light and heat.

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**Materials to avoid**

Acids, acidic substances.

**Dangerous compounds of decomposition**

Heating may liberate dangerous fumes of PO<sub>x</sub>, SO<sub>x</sub>, NO<sub>x</sub>.

**Additional informations**

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## 11. Toxicological information

LD<sub>50</sub>/oral/rat: 23 mg/kg

(RTECS-Nr. SZ2975000, Aug. 2003)

**Acute toxicity**

Very toxic by inhalation, in contact with skin and if swallowed.

**Irritancy data**

RTECS: yes

**Listed as carcinogen**

NTP: yes

IARC: yes

OSHA: no

**Additional information**

Secondary malignancies are potential delayed effects of many antineoplastic agents, although it is not clear whether the effect is related to their mutagenic or immunosuppressive action. The effect of dose and duration of therapy is also unknown, although risk seems to increase with long-term use. Although information is limited, available data seem to indicate that the carcinogenic risk is greatest with the alkylating agents. [USP DI 12 th ed. 1992]

NCI Carcinogenesis Bioassay results: Positive in mouse and rat Thiotepa is carcinogenic and mutagenic in both animals and humans.

## 12. Ecological information

**Information on elimination; persistence and decomposition**

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**Effects on part of environment**

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**Ecotoxicity effects**

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**Further information**

Do not allow to enter surface and ground water, the sewage system or soil.

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### 13. Advice on disposal

#### Disposal

If residues of products are classified as waste from administrative bodies or recycling of precious metal is not intended, the following classification is valid:

EAK-No: 180108 Cytotoxic and cytostatic medicines

Inform disposer that delivery contains cytostatica.

#### Disposal of uncleaned packing / recommended detergents

In the same way as waste material.

### 14. Transport information

#### 14.1 Land transport (ADR/RID/GGVS/GGVE)

UN-No.: UN 2811  
 Proper Shipping Name : TOXIC SOLID, ORGANIC, N.O.S.,  
 (CYTOSTATIK DRUG)  
 Class: 6.1  
 Subsidiary risk: ---  
 Packing group: II  
 Label: 6.1

#### 14.2 Inland water ways transport

Not classified.

#### 14.3 Marine transport (IMDG/GGVSee)

UN-No.: UN 2811  
 Proper Shipping Name : TOXIC SOLID, ORGANIC, N.O.S.,  
 (CYTOSTATIK DRUG)  
 Class: 6.1  
 Subsidiary risk: ---  
 Packing group: II  
 Marine pollutant: no  
 Label: 6.1

#### 14.4 Air transport(IATA/ICAO)

UN-No.: UN 2811  
 Proper Shipping Name : TOXIC SOLID, ORGANIC, N.O.S.,  
 (CYTOSTATIK DRUG)  
 Class: 6.1  
 Subsidiary risk: ---  
 Packing group: II  
 Label: 6.1

#### 14.5 Further information

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## 15. Regulatory information

### 15.1 Labelling

T+ Very toxic

#### R-Phrases:

26/27/28 Very toxic by inhalation, in contact with skin and if swallowed.  
 36/37/38 Irritating to eyes, respiratory system and skin.  
 42/43 May cause sensitization by inhalation and skin contact.  
 45 May cause cancer.  
 46 May cause heritable genetic damage.  
 60 May impair fertility.  
 61 May cause harm to the unborn child.

#### S-Phrases:

20/21 When using do not eat, drink or smoke.  
 36/37/39 Wear suitable protective clothing, gloves and eye/face protection.  
 45 In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)  
 53 Avoid exposure – obtain special instructions before use.  
 61 Avoid release to the environment. Refer to special instructions/Safety data sheets.

### 15.2 National regulations

#### Germany:

Restriction to employ: teenager under 18 years (Jugendarbeitsschutzgesetz),  
 pregnant and nursing mothers (Mutterschutzverordnung)

Water Endangerment: WGK-class: 3 strongly water pollutant  
 (following regulation VwVwS, Annex 3)

Technical instruction on air quality control (TA Luft): carcinogenic substances (numeral 5.2.7.1.1 class I)  
 mass flow rate: 0.15 g/h or  
 concentration: 0.05 mg/m<sup>3</sup>

## 16. Other information

The data given here is based on today's stand of our knowledge and experience. The purpose of this Safety Data Sheet is to describe the product in terms of their safety requirements. The data does not signify any warranty with regard to the products properties.

Sector making out data sheet: HH-SUS