

## Preparations

**Proprietary Preparations** (details are given in Part 3)

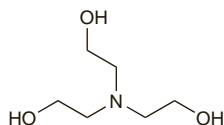
**Multi-ingredient:** **Chile:** Agua Sulfatada Picrica; **Spain:** Oftalmol Ocular.

## Trolamine (pINN)

Trietanolamina; Triethanolamine; Trolamini; Trolamin; Trolamina; Trolaminas; Trolaminum.

Троламин

CAS — 102-71-6.



**Description.** Trolamine is a variable mixture of bases containing mainly 2,2',2''-nitrilotriethanol (trolamine (CH<sub>2</sub>OH.CH<sub>2</sub>)<sub>3</sub>N), together with 2,2'-iminobisethanol (diolamine) and smaller amounts of 2-aminoethanol (monoethanolamine).

**Pharmacopoeias.** In *Eur.* (see p.vii). Also in *USNF*.

**Ph. Eur. 6.2** (Trolamine; Triethanolamine BP 2008). A clear, viscous, colourless or slightly yellow, very hygroscopic liquid. Miscible with water and with alcohol; soluble in dichloromethane. Store in airtight containers. Protect from light.

**USNF 26** (Trolamine). A mixture of alkanolamines consisting largely of trolamine containing some diolamine and monoethanolamine. A colourless to pale yellow, viscous, hygroscopic liquid having a slight ammoniacal odour. Miscible with water and with alcohol; soluble in chloroform. Store in airtight containers. Protect from light.

## Adverse Effects

Trolamine salts may be irritating to the skin and mucous membranes. Contact dermatitis has been reported after the use of ear drops containing trolamine polypeptide oleate-condensate.

**Carcinogenicity.** Because of concern about the possible production of carcinogenic nitrosamines in the stomach, the Swiss authorities restricted the use of trolamine to preparations for external use.<sup>1</sup>

1. Anonymous. Trolamine: concerns regarding potential carcinogenicity. *WHO Drug Inf* 1991; **5**: 9.

## Uses and Administration

Trolamine is used with fatty acids such as stearic and oleic acids as an emulsifier and as an alkalinising agent. It has also been used to reduce dithranol-induced staining of the skin.

Ear drops containing trolamine polypeptide oleate-condensate 10% are used for the removal of impacted ear wax (p.1725).

Trolamine salicylate (p.132) has also been used.

**Radiotherapy.** An emulsion of trolamine has been widely used in the treatment and prevention of radiation-induced dermatitis in patients undergoing radiotherapy. However, several studies have suggested that it is of little or no benefit.<sup>1-3</sup>

1. Fisher J, *et al.* Randomized phase III study comparing best supportive care to Biafine as a prophylactic agent for radiation-induced skin toxicity for women undergoing breast irradiation: Radiation Therapy Oncology Group (RTOG) 97-13. *Int J Radiat Oncol Biol Phys* 2000; **48**: 1307-10.
2. Szmacher E, *et al.* Phase II study assessing the effectiveness of Biafine cream as a prophylactic agent for radiation-induced acute skin toxicity to the breast in women undergoing radiotherapy with concomitant CMF chemotherapy. *Int J Radiat Oncol Biol Phys* 2001; **51**: 81-6.
3. Elliott EA, *et al.* Phase III trial of an emulsion containing trolamine for the prevention of radiation dermatitis in patients with advanced squamous cell carcinoma of the head and neck: results of Radiation Therapy Oncology Group Trial 99-13. *J Clin Oncol* 2006; **24**: 2092-7.

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**Arg.:** Biafine; Orla-Wax†; Solucer; **Austral.:** Neutrogena; **Belg.:** Xerumenex; **Canada:** Cerumenex; **Chile:** Biafine; **Fr.:** Biafine; Lamiderm; **Ger.:** Cerumenex N; **Hong Kong:** Biafine; **Israel:** Biafine; **Malaysia:** Biafine†; **Mex.:** Orlawax; **S.Afr.:** Cerumenex†; **Singapore:** Biafine†; **Switz.:** Biafine; Cerumenex; **USA:** Biafine; Cerumenex†; **Venez.:** Biafine.

**Multi-ingredient:** **Arg.:** Eucos-L†; Onixol†; Tereonit†; **Braz.:** Cerumin; Paraqueimol; **Canada:** Soropon; **Ital.:** Dopo Pk; **USA:** Maxilube.

## Trometamol (BAN, hINN) ⊗

NSC-6365; THAM; Trihydroxymethylaminomethane; TRIS; Tris(hydroxymethyl)aminometan; Tris(hydroxymethyl)aminomethane; Trométamol; Trometamoli; Trometamolisi; Trometamolium; Tromethamine (*USAN*). 2-Amino-2-(hydroxymethyl)propane-1,3-diol.

Трометамол

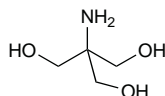
C<sub>4</sub>H<sub>11</sub>NO<sub>3</sub> = 121.1.

CAS — 77-86-1.

ATC — B05BB03; B05XX02.

ATC Vet — QB05BB03; QB05XX02.

The symbol † denotes a preparation no longer actively marketed



**Pharmacopoeias.** In *Eur.* (see p.vii) and *US*.

**Ph. Eur. 6.2** (Trometamol). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; sparingly soluble in alcohol; very slightly soluble in ethyl acetate. A 5% solution in water has a pH of 10.0 to 11.5.

**USP 31** (Tromethamine). A white, crystalline powder having a slight characteristic odour. Soluble 1 in 1.8 of water and 1 in 45.5 of alcohol; freely soluble in low-molecular-weight aliphatic alcohols; practically insoluble in carbon tetrachloride, in chloroform, and in benzene. pH of a 5% solution in water is between 10.0 and 11.5. Store in airtight containers.

**Incompatibilities.** There is evidence to suggest that fluorouracil degrades to cardiotoxic compounds in formulations buffered with trometamol.<sup>1</sup>

1. Lukaschek J, *et al.* Cardiotoxicity and neurotoxicity of high-dose continuous fluorouracil as a result of degradation compounds in the drug vials. *J Clin Oncol* 2004; **22**: 5022-5.

## Adverse Effects and Precautions

Great care must be taken to avoid extravasation at the injection site as solutions may cause tissue damage. Local irritation, venospasm and phlebitis have occurred.

Respiratory depression can occur and mechanical ventilation may be required. Hypoglycaemia may also occur. Trometamol is contra-indicated in anuria and uraemia, and should be used cautiously in patients with renal impairment as hyperkalaemia has been reported in such patients. Trometamol is not recommended for use in patients with respiratory acidosis alone. If it is used in patients with respiratory acidosis accompanying metabolic acidosis, ventilation should be maintained mechanically. Trometamol is contra-indicated in chronic respiratory acidosis.

Blood concentrations of bicarbonate, glucose, and electrolytes, partial pressure of carbon dioxide, and blood pH should be monitored during infusion of trometamol.

## Uses and Administration

Trometamol is an organic amine proton acceptor used as an alkalinising agent in the treatment of metabolic acidosis (p.1667). It also acts as a weak osmotic diuretic. Trometamol is mainly used during cardiac bypass surgery and during cardiac arrest. It may also be used to reduce the acidity of citrated blood for use in bypass surgery.

The dose used should be the minimum required to increase the pH of the blood to within normal limits and is based on the body-weight and the base deficit. Trometamol is given by slow intravenous infusion as a 0.3M solution; it should not be given for longer than a day except in life-threatening emergencies.

Trometamol citrate is given by mouth for the management of urinary calculi and acidosis. Trometamol acetylinate has also been used for acidosis.

## References

1. Nahas GG, *et al.* Guidelines for the treatment of acidaemia with THAM. *Drugs* 1998; **55**: 191-224.

## Preparations

**USP 31:** Tromethamine for Injection.

**Proprietary Preparations** (details are given in Part 3)

**Austral.:** Tham; **Austria:** Tris; **Ger.:** Tham; Tris; **Ital.:** Thamesol; **Swed.:** AddeX-THAM.

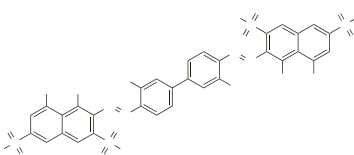
**Multi-ingredient:** **Arg.:** Solocalm Plus; **Austral.:** Blink-N-Clean; **Fr.:** Al-caphor†; **Norw.:** Tribonat; **Swed.:** Therany†; Tribonat; **Switz.:** Saltrates†.

## Trypan Blue

CI Direct Blue 14; Colour Index No. 23850; Trypanum Caeruleum. Tetrasodium 3,3'-(3,3'-dimethylbiphenyl-4,4'-diyl)bisazo]-bis[5-amino-4-hydroxynaphthalene-2,7-disulphonate].

C<sub>34</sub>H<sub>24</sub>N<sub>6</sub>Na<sub>4</sub>O<sub>14</sub>S<sub>4</sub> = 960.8.

CAS — 72-57-1.



## Profile

Trypan blue solutions are used as stains in microscopy and for visualisation of various tissues as an aid to ophthalmic surgery.

## References

1. Werner L, *et al.* Permanent blue discoloration of a hydrogel intraocular lens by intraoperative trypan blue. *J Cataract Refract Surg* 2002; **28**: 1279-86.
2. Haritoglou C, *et al.* Functional outcome after trypan blue-assisted vitrectomy for macular pucker: a prospective, randomized, comparative trial. *Am J Ophthalmol* 2004; **138**: 1-5.
3. Gouws P, *et al.* Cystoid macular oedema with trypan blue use. *Br J Ophthalmol* 2004; **88**: 1348-9.
4. Lee KL, *et al.* A comparison of outcomes after indocyanine green and trypan blue assisted internal limiting membrane peeling during macular hole surgery. *Br J Ophthalmol* 2005; **89**: 420-4.
5. Healey PR, Crowston JG. Trypan blue identifies antimetabolite treatment area in trabeculectomy. *Br J Ophthalmol* 2005; **89**: 1152-6.
6. Roos JC, Kerr Muir MG. Use of trypan blue for penetrating keratoplasty. *J Cataract Refract Surg* 2005; **31**: 1867-9.

## Preparations

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**Ital.:** Oftalblue; **Neth.:** MembraneBlue; VisionBlue; **USA:** VisionBlue.

**Multi-ingredient:** **Fr.:** Parkipan†.

## Trypsin (BAN)

Thrypsinum; Tripsina; Tripsinas; Tripszin; Trypsini; Trypsine; Trypsinum; Trypsyna.

CAS — 9002-07-7.

ATC — B06AA07; D03BA01.

ATC Vet — QB06AA07; QD03BA01.

**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), and *US*.

**Ph. Eur. 6.2** (Trypsin). A proteolytic enzyme obtained by the activation of trypsinogen extracted from mammalian pancreas. It has an activity of not less than 0.5 microkatal/mg, calculated with reference to the dried substance. A white or almost white, crystalline or amorphous powder; the amorphous form is hygroscopic. Sparingly soluble in water. A 1% solution in water has a pH of 3.0 to 6.0. Solutions have a maximum stability at pH 3 and a maximum activity at pH 8. Store at 2° to 8° in airtight containers. Protect from light.

**USP 31** (Crystallized Trypsin). A proteolytic enzyme crystallised from an extract of the pancreas of healthy bovine or porcine animals, or both. It contains not less than 2500 USP units in each mg, calculated on the dried basis. A white to yellowish-white, odourless, crystalline or amorphous powder. Store in airtight containers at temperature not exceeding 40°.

## Profile

Trypsin is a proteolytic enzyme that has been applied for the debridement of wounds. It has also been taken by mouth, usually with chymotrypsin (p.2281), and sometimes with antibacterial or other drugs, for its supposed benefit in relieving oedema and inflammation associated with infection or trauma. Trypsin solutions have been inhaled for the liquefaction of viscous sputum, and trypsin is also an ingredient of mixtures intended to relieve various gastrointestinal disorders. Trypsin has been used in oncology in a combination preparation with chymotrypsin and papain (see under Uses and Administration of Papain, p.2362).

Hypersensitivity reactions may occasionally occur.

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**Multi-ingredient:** **Arg.:** Phlogenzym†; **Austria:** Leukase; Leukase-Kegel; Phlogenzym; Rutozym; Traumazym; Wobenzym; **Braz.:** Parenzyme; Parenzyme Ampicilina; Parenzyme Analgesico; Parenzyme Tetraciclina; **Cz.:** Phlogenzym; Wobe-Mugos†; Wobenzym; **Fr.:** Ribatrin; **Ger.:** Enzym-Wied†; Mulsal N†; Phlogenzym; Wobe-Mugos E†; Wobenzym N†; **Gr.:** Chymoral; **Hung.:** Phlogenzym; Trypsin†; **India:** Alfapsin; Orthal Forte; Soluzym; **Ital.:** Essen Enzimatico†; **Jpn:** Kimotab; **Mex.:** Ochozym; Phlogenzym; Quimotrip; Ribotripsin; Wobe-Mugos; Wobenzym; Zimotris; **Port.:** Anginova; Chimar; **Rus.:** Phlogenzym (Флогензим); Wobe-Mugos E (Вобе-Мугос Е); Wobenzym (Вобэнзим); **Spain:** Bristaciadina Dental; Dertrase; Dosi Enzimatico; Doxiten Enzimatico; Kanapomada; Naso Pekamin; Oxidermiol Enzima†; Quimodril; **USA:** Allanderin-T; Dermuspray; Granulderm; Granulex; GranuMed; Xenaderm; **Venez.:** Phlogenzym; Wobenzym N.

## Tuberculin

Tuberculinas.

ATC — V04CF01.

ATC Vet — QV04CF01.

NOTE: 'PPD' is an abbreviation sometimes used for tuberculin purified protein derivative which should not be confused with para-phenylenediamine (p.2363), which is also referred to by the same abbreviation.

**Pharmacopoeias.** In *Eur.* (see p.vii) and *US*.

**Ph. Eur. 6.2** (Tuberculin for Human Use, Old). It consists of a filtrate, concentrated by heating, containing the soluble products of the culture and lysis of one or more strains of *Mycobacterium tuberculosis* and/or *M. bovis*. It contains a suitable preservative that does not give rise to false-positive reactions. In concentrated form, it is a transparent, viscous, yellow or brown liquid. Protect from light.

**Ph. Eur. 6.2** (Tuberculin Purified Protein Derivative for Human Use). A preparation obtained by precipitation from the heated

The symbol ⊗ denotes a substance whose use is restricted in certain sports (see p.vii)