

Demodan Plus; Erylik; Stievamycin; Tri-Luma; **Cz.**: Aknemycin Plus; **Fin.**: Wicaraan; **Fr.**: Erylik; **Ger.**: Aknemycin Plus; Balisa VAS; Carbamid + VAS; Clinesfar; Pigmnorm; Ureotop + VAS; **Hong Kong:** Dermabaz; Erylik; Tri-Luma; **Hung.**: Verra-med; **Indon.**: Medi-Kin TR; **Israel:** Aknemycin Plus; **Ital.**: Psorinase; **Malaysia:** Aknemycin Plus; Tri-Luma; **Mex.**: Stievamycin; Tri-Luma; **Philipp.**: Tri-Luma; **Pol.**: Aknemycin Plus; **Singapore:** Aknemycin Plus; Tri-Luma; **Spain:** Acmsidin Retinoico; Loderm Retinoico; **Switz.**: Carbamide + VAS; Pigmnorm; Sebo-Psor; Verra-med; **Thal.**: Tri-Luma; **UK:** Aknemycin Plus; **USA:** Solage; Tri-Luma; Ziana; **Venez.**: Tri-Luma.

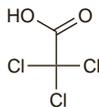
Trichloroacetic Acid

Acide trichloroacétique; Acidum trichloroaceticum; Acidum Trichloroaceticum; Kwas trichlorooctowy; Kyselina trichloroctová; Trichloroacetic Acid; Trichloracto rūgštis; Trichloressigsäure; Trichloroacético, ácido; Triklloorietikkahappo; Triklorättiksyra; Triklórecetsav.

Трихлоруксусная Кислота

$C_2HCl_3O_2 = 163.4$.

CAS — 76-03-9.



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

Ph. Eur. 6.2 (Trichloroacetic Acid). A very deliquescent white or almost white crystalline mass or colourless crystals. Very soluble in water, in alcohol, and in dichloromethane. Store in airtight containers.

Adverse Effects and Treatment

As for Hydrochloric Acid, p.2322.

Uses and Administration

Trichloroacetic acid is caustic and astringent. When used as an escharotic for warts it is applied as a strong solution; a range of concentrations have been used including 50% and 80%. The surrounding areas of skin should be protected. Trichloroacetic acid has also been used for the removal of tattoos and in cosmetic surgery for chemical peeling of the skin.

Tattoo removal. References to the use of trichloroacetic acid in the removal of tattoos.

1. Hall-Smith P, Bennett J. Tattoos: a lasting regret. *BMJ* 1991; **303**: 397.

Warts. References to the use of trichloroacetic acid in the treatment of genital warts (p.1584).

- Godley MJ, et al. Cryotherapy compared with trichloroacetic acid in treating genital warts. *Genitourin Med* 1987; **63**: 390-2.
- Davis AJ, Emans SJ. Human papilloma virus infection in the pediatric and adolescent patient. *J Pediatr* 1989; **115**: 1-9.
- Boothby RA, et al. Single application treatment of human papillomavirus infection of the cervix and vagina with trichloroacetic acid: a randomized trial. *Obstet Gynecol* 1990; **76**: 278-80.
- Abdullah AN, et al. Treatment of external genital warts comparing cryotherapy (liquid nitrogen) and trichloroacetic acid. *Sex Transm Dis* 1993; **20**: 344-5.

Preparations

Proprietary Preparations (details are given in Part 3)

Hong Kong: AccuPeel†; **Ital.**: CL tre; Verrupor; **Singapore:** AccuPeel†; **USA:** Tri-Chlor.

Multi-ingredient: **Spain:** Callicida Brum†; **Turk.**: IL-33.

Trioxysalen (INN)

NSC-71047; 4,5',8-Trimethylpsoralen; Trioksisaleni; Trioxisalen; Trioxisalen; Trioxsalen (USAN); Trioxysalène; Trioxysalenum. 2,5,9-Trimethyl-7H-furo[3,2-g][1]benzopyran-7-one.

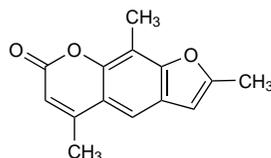
Триоксизален

$C_{14}H_{12}O_3 = 228.2$.

CAS — 3902-71-4.

ATC — D05AD01; D05BA01.

ATC Vet — QD05AD01; QD05BA01.



Pharmacopoeias. In *US*.

USP 31 (Trioxsalen). A white to off-white or greyish, odourless, crystalline solid. Practically insoluble in water; soluble 1 in 1150 of alcohol, 1 in 84 of chloroform, 1 in 43 of dichloromethane, and 1 in 100 of methyl isobutyl ketone. Protect from light.

Profile

Trioxysalen, a psoralen, is a photosensitizer used similarly to methoxsalen in photochemotherapy or PUVA therapy (p.1606).

Trioxysalen is used in idiopathic vitiligo to enhance pigmentation or increase the tolerance to sunlight in selected patients. In vitiligo an oral dose of 10 mg daily is given 2 to 4 hours before exposure to sunlight or ultraviolet radiation; prolonged therapy may be necessary. To increase tolerance to sunlight a dose of 10 mg daily is given 2 hours before exposure; treatment should not be continued for longer than 14 days.

Trioxysalen may also be used topically in the PUVA treatment of psoriasis.

References.

- Snellman E, Rantanen T. Concentration-dependent phototoxicity in trimethylpsoralen bath psoralen ultraviolet A. *Br J Dermatol* 2001; **144**: 490-4.

Preparations

USP 31: Trioxsalen Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Trisoralen†; **Fin.**: Tripsor; **Gr.**: Trisoralen; **Hong Kong:** Puvadin†; **India:** Neosoralen†; **Malaysia:** Puvadin†.

Urea ☒

Carbamida; Carbamide; E927b; Karbamid; Karbamidi; Močovina; Moczniik; Üre; Urée; Urea; Ureja; Ureum. Carbonic acid diamide.

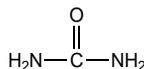
Карбамид; Мочевина

$NH_2.CO.NH_2 = 60.06$.

CAS — 57-13-6.

ATC — B05BC02; D02AE01.

ATC Vet — QB05BC02; QD02AE01.



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

Ph. Eur. 6.2 (Urea). Transparent, slightly hygroscopic, crystals or a white or almost white, crystalline powder. Very soluble in water; soluble in alcohol; practically insoluble in dichloromethane. Store in airtight containers.

USP 31 (Urea). Colourless or white, practically odourless, prismatic crystals, or white crystalline powder or pellets. May gradually develop a slight odour of ammonia on prolonged standing. Soluble 1 in 1.5 of water, 1 in 10 of alcohol, and 1 in 1 of boiling alcohol; practically insoluble in chloroform and in ether. Solutions are neutral to litmus. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Incompatibility. Urea can cause haemolysis when mixed with blood and should never be added to whole blood for transfusion or given through the same set by which blood is being infused.

Adverse Effects and Precautions

As for Mannitol, p.1330. Urea should also be used with caution in liver impairment as blood-ammonia concentrations can rise, and should be avoided in liver failure.

Urea is reported to be more irritant than mannitol, and intravenous use may cause venous thrombosis or phlebitis at the site of injection; extravasation may cause sloughing or necrosis. Only large veins should be used for infusion, and urea should not be infused into veins of the lower limbs of elderly patients. Extreme care is essential to prevent accidental extravasation of urea infusions.

Rapid intravenous injection of solutions of urea can cause haemolysis; the risk is reduced by using glucose or invert sugar solutions as diluent. Urea should not be mixed with whole blood.

Topical applications may be irritant to sensitive skin.

Infants and neonates. High plasma-urea concentrations have been reported^{1,2} in neonates after topical application of emollient creams containing urea. Since there was no evidence of dehydration^{2,3} absorption of urea through the skin was the likely cause. Raised plasma-urea concentrations have been reported⁴ in infants with erythematous skin conditions who had not been treated with urea cream and this was attributed to dehydration due to increased insensible water loss through the damaged skin.

- Beverley DW, Wheeler D. High plasma urea concentrations in colloidion babies. *Arch Dis Child* 1986; **61**: 696-8.
- Oudesluis-Murphy AM, van Leeuwen M. High plasma urea concentrations in colloidion babies. *Arch Dis Child* 1987; **62**: 212.
- Beverley DW, Wheeler D. High plasma urea concentration in babies with lamellar ichthyosis. *Arch Dis Child* 1986; **61**: 1245-6.
- Garty BZ. High plasma urea concentration in babies with lamellar ichthyosis. *Arch Dis Child* 1986; **61**: 1245.

Pregnancy. There have been reports of women suffering coagulopathy associated with urea treatment given for termination of pregnancy.^{1,2}

- Grundt MFB, Craven ER. Consumption coagulopathy after intra-amniotic urea. *BMJ* 1976; **2**: 677-8.
- Burkman RT, et al. Coagulopathy with midtrimester induced abortion: association with hyperosmolar urea administration. *Am J Obstet Gynecol* 1977; **127**: 533-6.

Pharmacokinetics

Urea is fairly rapidly absorbed from the gastrointestinal tract but causes gastrointestinal irritation. Urea is distributed into extracellular and intracellular fluids including lymph, bile, CSF, and blood. It is reported to cross the placenta, and penetrate the eye. It is excreted unchanged in the urine.

Uses and Administration

Urea promotes hydration and is mainly applied topically in the treatment of ichthyosis and hyperkeratotic skin disorders (p.1580). Used intravenously it has osmotic diuretic properties similar to mannitol (p.1331) and has been used in the treatment of acute increases in intracranial pressure (p.1181), due to cerebral oedema, and to decrease intra-ocular pressure in acute glaucoma (p.1873), but has been largely superseded by mannitol. Urea has also been given intra-amniotically for the termination of pregnancy (p.2004).

When applied topically urea has hydrating and keratolytic properties. In the management of ichthyosis and other dry skin disorders it is applied in creams or lotions containing 5 to 25% urea; higher concentrations of 30% and 40% have also been used in severe cases. A preparation containing 40% may be used for nail destruction.

For the reduction of raised intracranial or intra-ocular pressure, urea is given intravenously, as an infusion of a 30% solution in glucose 5 or 10% or invert sugar 10%, at a rate not exceeding 4 mL/minute, in a dose of 0.5 to 1.5 g/kg to a maximum of 120 g daily. Doses used in children are based on the same regimen, but see also below. Rebound increases in intracranial and intra-ocular pressure may occur after about 12 hours.

Solutions of urea 40 to 50% have been given by intramniotic injection for the termination of pregnancy.

Urea labelled with carbon-13 (p.2277) is used in the *in vivo* diagnosis of *Helicobacter pylori* infection (see Peptic Ulcer Disease, p.1702). The test involves collecting a breath sample before and after oral ingestion of a single dose of ¹³C-urea. *H. pylori* produces urease which hydrolyses the urea to carbon dioxide and ammonia; therefore, an excess of carbon-13-labelled carbon dioxide in the sample, compared with a baseline sample, indicates infection. Doses of ¹³C-urea include 50 mg, 75 mg, or 100 mg depending on the kit being used. Urea labelled with the radionuclide carbon-14 (p.2053) is also used in a urea breath test for *H. pylori* detection.

Administration in children. For the reduction of raised intracranial or intra-ocular pressure in children, urea is given intravenously in dosage regimens similar to those used in adults (see above). However, for children under 2 years of age, a dose of 100 mg/kg may be adequate.

Breath test kits containing ¹³C-urea for the diagnosis of *Helicobacter pylori* infection are available for children. However, the *BNFC* states that the appropriateness of testing in children has not been established, and that endoscopy with biopsy is more accurate than *in vivo* breath testing, which is frequently unreliable in children.

Preparations

BP 2008: Urea Cream;
USP 31: Urea for Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Hidroplius; Keratop; Locherp; Nutralcon; Optiwhite†; Ureadin; Urecrem; Uremol; Xerobase; **Austria:** Aquacare; Hamilton Skin Therapy; Nutraplus; Ureacare; **Urederm**; **Austria:** Nubral; **Braz.**: Emoderm; Hidrapel Plus; Nutraplus; Ureadin; **Canada:** Dermaflex; Ultra Mide; Uree; Uremol; **Chile:** Ayr con urea; Ayr-5; Hyderrm; Nutraplus†; Uramol; Ureadin 10 and 20; **Cz.**: Elacutan; Excipial U; Linola Urea; **Fin.**: Fenurli; **Fr.**: Anti-Dessechement; Charlieu Topic†; Ictyoderme†; Nutraplus; Sedagel; **Ger.**: Balisa; Basodexal; Elacutan; Eucerin Salbe†; Hyanit N; Linola Urea; Nubral; Onychomal; Sebexol cum urea; Ureotop; **Hong Kong:** Balneum Intensiv; Carmol; Caruderm; Euderm; Nutraplus†; Ureacare; Urederm; **Hung.**: Linola Urea; **Indon.**: Calmuderm; Carmel; Moisderm; Soft U Derm; Urederm; **Irl.**: Aquadrate; Nutraplus; **Ital.**: Dermal Care; **Jpn.**: Keratinamin; **Malaysia:** Balneum Intensiv; Euderm†; Nutraplus; UO; Ureacare†; **Mex.:**