

**USA:** Aftate; Blis-To-Sol; Dr Scholl's Athlete's Foot; Genaspor; Lamisl AF Defense; Podactin; Quinsana Plus; Tinactin; **Venez:** Tinaderm; Tolnaftan.

**Multi-ingredient Arg:** Bacticro Complex; Cevaderm; Quadiderm; **Austral:** Mycil Healthy Feet; **Braz:** Cremederme; Permut; Poliderm; Quadiderm; Quadrikin; Quadrilon; Quadriplus; Qualiderm; Tetraderm; **Hong Kong:** Alber T†; Dermafacte; Mycil; Quadiderm; Triditol-G; **India:** Fourderm; Quiss; **Irl:** Mycil; Tinaderm-M; **Israel:** Phytoderm Compositum; **Malaysia:** Elan-Forte; **Philipp:** Quadiderm; Quadrotopic; **S.Afr:** Duo-derm; Quadiderm; **Singapore:** Quadiderm; **Spain:** Cuatroderm; **Switz:** Quadiderm; **Thai:** Alber T; Ezon-T; **UK:** Mycil; Tinaderm-M; **USA:** Absorbine Athletes Foot Care; Dermasept Antifungal.

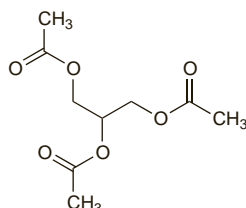
### Triacetin (rINN)

E1518; Glycerin-triacetát; Glycerol Triacetate; Glycerolum Triacetate; Glyceryl Triacetate; Triacetina; Triacetinas; Triacétine; Triacetinum; Triacetyna; Triasetiini. 1,2,3-Propanetriol triacetate.

Триацетин

$C_9H_{14}O_6 = 218.2$ .

CAS — 102-76-1.



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

**Ph. Eur. 6.2** (Triacetin). A clear, colourless, slightly viscous, oily liquid. Soluble in water; miscible with dehydrated alcohol and with toluene. Store in well-filled containers.

**USP 31** (Triacetin). A colourless, somewhat oily liquid with a slight, fatty odour. Soluble in water; slightly soluble in carbon disulfide; miscible with alcohol, with chloroform, and with ether. Store in airtight containers.

### Profile

Triacetin is reported to possess fungistatic properties based on the liberation of acetic acid. It has been applied topically in the treatment of superficial dermatophyte infections. It has also been used as a plasticiser in oral preparations.

Triacetin may destroy rayon fabric. It should not come into contact with metals.

### Preparations

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

**Multi-ingredient Braz:** Micosan†; **Hong Kong:** Alber T†; **Thai:** Alber T; Ezon-T.

### Trimetrexate Glucuronate (BANM, USAN, rINN)

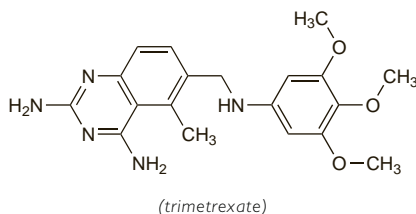
Cl-898 (trimetrexate); Glucuronato de trimetrexato; JB-11 (trimetrexate); NSC-352122; NSC-249008 (trimetrexate); NSC-328564 (trimetrexate); Triméthexate, Glucuronate de; Trimetrexati Glucuronatum. 5-Methyl-6-(3,4,5-trimethoxyanilinoethyl)quinazolin-2,4-diyldiamine mono-D-glucuronate.

Триметрексата Глюкуронат

$C_{19}H_{23}N_5O_3 \cdot C_6H_{10}O_7 = 563.6$ .

CAS — 52128-35-5 (trimetrexate); 82952-64-5 (trimetrexate glucuronate).

ATC — P01AX07.



(trimetrexate)

**Incompatibility.** Trimetrexate is reported to be incompatible with foscarnet. Trimetrexate should not be mixed with folic acid or chloride ions, since precipitation occurs instantly.

### Adverse Effects, Treatment, and Precautions

Trimetrexate is a dihydrofolate reductase inhibitor and therefore adverse effects and precautions are similar to those of methotrexate, p.745. It must be given with folic acid, which should be continued for 72 hours after the last dose of trimetrexate.

The symbol † denotes a preparation no longer actively marketed

### Interactions

Studies in *animals* suggest that cimetidine and imidazole antifungals such as clotrimazole and ketoconazole may inhibit trimetrexate metabolism, and there is a risk of possible interactions with all drugs that affect hepatic cytochrome P450 systems.

### Antimicrobial Action

Trimetrexate is an inhibitor of dihydrofolate reductase and consequently prevents formation of the active coenzyme tetrahydrofolate and production of DNA and RNA precursors, leading to cell death. At therapeutic doses the selective transport of trimetrexate, but not folic acid, into *Pneumocystis jirovecii* allows folic acid to protect normal host cells from the cytotoxicity of trimetrexate without inhibiting its antifungal activity. *In-vitro* trimetrexate has shown dose-related inhibition of growth of the trophozoite stage of *P. jirovecii*.

### Pharmacokinetics

The pharmacokinetics of intravenous trimetrexate have been described as both biphasic and triphasic, with a terminal elimination half-life of about 16 to 18 hours. After use with folic acid a biphasic disposition with a terminal half-life of 11 hours has also been reported. It is extensively protein bound; reports suggest that it is 95 to 98% bound at low serum concentrations, but that binding is saturable, with free fraction increasing at plasma concentrations above 1 microgram/mL. Trimetrexate is excreted mainly in the urine, as unchanged drug and metabolites, some of which may be active. The major metabolic pathway appears to be oxidative O-demethylation followed by conjugation to the sulfate or glucuronide.

### Uses and Administration

Trimetrexate is a dihydrofolate reductase inhibitor with general properties similar to those of methotrexate (p.749). It is used in the management of moderate to severe pneumocystis pneumonia in immunocompromised patients, notably patients with AIDS, where other therapy has proved ineffective (see also p.521). It has also been tried as an antineoplastic in the management of various solid tumours.

Trimetrexate is given as the glucuronate but doses are stated in terms of trimetrexate. Trimetrexate glucuronate 1.53 mg is equivalent to about 1 mg of trimetrexate. It is given by intravenous infusion, over 60 to 90 minutes. The schedule in pneumocystis pneumonia is 45 mg/m<sup>2</sup> daily for 21 days, in association with folic acid rescue for 24 days. The dosage of trimetrexate and folic acid should be adjusted according to the results of blood tests, which should be performed at least twice a week during therapy. Renal and hepatic function and haemoglobin values should also be monitored. Treatment with zidovudine and other myelosuppressive drugs should be interrupted to allow full doses of trimetrexate to be given.

### Reviews.

1. Fulton B, *et al.* Trimetrexate: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in the treatment of Pneumocystis carinii pneumonia. *Drugs* 1995; **49**: 563-76.

### Preparations

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

**Hong Kong:** Neutrexin†; **Irl:** Neutrexin†; **Spain:** Neutrexin†; **Thai:** Neutrexin†; **USA:** Neutrexin†.

### Undecenoic Acid

Acide Undécylénique; Acidum undecylenicum; 10-Hendecenoic Acid; Kyselina undecylenová; Undecilénico, ácido; Undecileno rūgštis; Undecilénasv; Undecylenic Acid; Undecylensyra; Undesenoatlar; Undesilenatlar; Undesyleinihappo. Undec-10-enoic acid.

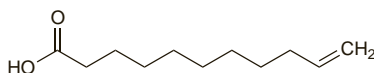
Ундеценовая Кислота

$C_{11}H_{20}O_2 = 184.3$ .

CAS — 112-38-9.

ATC — D01AE04.

ATC Vet — QD01AE04.



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

**Ph. Eur. 6.2** (Undecylenic Acid; Undecenoic Acid BP 2008). A colourless or pale yellow liquid or a white or very pale yellow crystalline mass. Practically insoluble in water; freely soluble in alcohol and in fatty and essential oils. Store in nonmetallic containers. Protect from light.

**USP 31** (Undecylenic Acid). A clear, colourless to pale yellow liquid with a characteristic odour. Practically insoluble in water; miscible with alcohol, with chloroform, with ether, with benzene, and with fixed and volatile oils. Store in airtight containers. Protect from light.

### Calcium Undecenoate

Calcium Undecylenate (*USAN*); Undecilenato de calcio. Calcium di(undec-10-enoate).

Ундециленат Кальция

$(C_{11}H_{19}O_2)_2Ca = 406.6$ .

ATC — D01AE04.

ATC Vet — QD01AE04.

**Pharmacopoeias.** In *US*.

**USP 31** (Calcium Undecylenate). A fine white powder with a characteristic odour and no grit. Practically insoluble in water, in cold alcohol, in acetone, in chloroform, and in ether; slightly soluble in hot alcohol.

### Zinc Undecenoate

Çinko undecilenatas; Çinko Undesilenat; Çink-undecilenat; Sinkiundesylenaat; Undecilenato de zinc; Undecilinato de Zinco; Undecylenan zineçnat; Zinc Undecylenate; Zinc, undécylénate de; Zinci undecylenas; Zinkundecylenat. Zinc di(undec-10-enoate).

Ундециленат Цинка

$(C_{11}H_{19}O_2)_2Zn = 431.9$ .

CAS — 557-08-4.

ATC — D01AE04.

ATC Vet — QD01AE04.

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

**Ph. Eur. 6.2** (Zinc Undecylenate; Zinc Undecenoate BP 2008). A fine white or almost white powder. Practically insoluble in water and in alcohol. Protect from light.

**USP 31** (Zinc Undecylenate). A fine, white powder. Practically insoluble in water and in alcohol.

### Adverse Effects

Irritation may rarely occur after the topical application of undecenoic acid or its salts.

### Antimicrobial Action

Undecenoic acid and its derivatives are active against some pathogenic fungi, including the dermatophytes *Epidermophyton*, *Trichophyton*, and *Microsporum* spp.

### Uses and Administration

Undecenoic acid and its zinc salt are applied topically in the prophylaxis and treatment of superficial dermatophytoses, particularly tinea pedis (p.521). Typical concentrations are undecenoic acid 2 to 5% and zinc undecenoate 20%. They are used in creams, ointments, solutions, or powders, often with each other. Calcium undecenoate is used as a 10 or 15% powder.

Several other salts and derivatives of undecenoic acid including methyl, phenyl, and propyl undecenoate, disodium sulfosuccinate undecenoic acid monoethanolamide, and undecenoic acid monoethanolamide and diethanolamide have been used similarly.

◊ A systematic review<sup>1</sup> of topical treatments for fungal skin or nail infections considered undecenoates to be effective, although comparative studies with other classes of topical antifungal were largely lacking.

1. Crawford F, Hollis S. Topical treatments for fungal infections of the skin and nails of the foot. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2007 (accessed 07/07/08).

### Preparations

**USP 31:** Compound Undecylenic Acid Ointment.

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

**Arg:** Bentophyto; Sinamida Pies; Umasam; **Austria:** Crino Cordes; Mayfung; Pelsana Med; **Canad:** Desenex; **Cz:** Mykoseptin; **Fr:** Mycodecyl; **Hung:** Lubex; **Indon:** Decylene; Topix; Undecyl; **Irl:** Caldesene; Desenex; **Israel:** Undecyl; **Mex:** Derman; **Pol:** Mykodermina; Unguentum Undecylenicum; **Rus:** Mykoseptin (Микосептин); **S.Afr:** Mycota; **Switz:** Funge; Lubex; Turexan Creme; Turexan Douche; **Turk:** Undo-Pate; Utalk; **UK:** Mycota; **USA:** Blis-To-Sol; Caldesene; Cruex; Decylenes; Desenex; Elon Dual Defense; Protectol; Undelenic.

**Multi-ingredient Arg:** Bacteroskin†; Bentophyto; Bifena; Champuacil; Cicatrol; Cleosvan; Dettonjab; Farm-X; Fungicida†; Fungocop; Hipoglos Cicatrizante; Laurinol Plus; LB Jabon con Purcelin†; Novo Miconol; Novofarma Champu; Pledicex†; Plusderm†; Tersoderm Anticasp†; **Austral:** Mycodecyl; Pedoz; Sebitar; Seborrol†; **Austria:** Dequafungin; Mycopol; Pelsana Med; Salvy†; **Braz:** Andriodermol; Micosan†; Micotox†; Micoz†; **Chile:** Fittig; Hansaplast Footcare†; Lady Fittig†; NP-27; **Cz:** Hexadecyl†; **Fr:** Paps; **Ger:** Gehwol Fungizid†; Gehwol Nagelpilz†; Skinnan Soft; **Gr:** Ekzegamma†; **Indon:** Decylene; Mikorex; Skintex; **Irl:** Ceanel†; **Israel:** Fungimon; Pedisol; Pitrisan; **Ital:** Balta Intimo†; Foot Zeta; Genisol; Microfoot; Propast; **Malaysia:** Acnederm†; Sebitar; **Mex:** Micotex; **NZ:** Acnederm†; Egomycol†; Grans Remedy; Sebitar; Seborrol†; **Pol:** Undofen; **Port:** Edoltar†; Micavene; **S.Afr:** AF; Mycota†; **Singapore:** Sebitar; **Switz:** Crimanex; Ederphyt; Funge; Pelsano; Pruri-med; Sebo Shampooing; Trosyd†; Turexan Emulsion†; **Turk:** Fungeyl; Undo-Talk; **UK:** Ceanel; Healthy Feet; Monphytol†; Mycota; **USA:** Breeze Mist Foot Powder†; Dermasept Antifungal; Gordochom; Phicon-F; **Venez:** Diodonato†.