Superoxide dismutases are also under investigation for their free-radical scavenging properties in a variety of conditions including the prevention of bronchopulmonary dysplasia in neonates.

Bronchopulmonary dysplasia. Use of sudismase in premature infants treated for respiratory distress syndrome did not prevent development of bronchopulmonary dysplasia (p.1500) in the first month.[1] However, treated infants subsequently showed a lower incidence of severe respiratory disease and hospitalisations in the first year, suggesting a reduction in chronic lung injury. The antoxidant was given intratracheally in a dose of 5 mg/kg every 48 hours as long as intubation and ventilation were necessary. A systematic review[2] was unable to reach a firm conclusion about the efficacy of superoxide dismutases in preventing chronic lung disease.

1. Davis JM, *et al.* Pulmonary outcome at 1 year corrected age in premature infants treated at birth with recombinant human CuZn superoxide dismutase. *Pediatrics* 2003; **111:** 469–76.
2. Suresh GK, *et al.* Superoxide dismutase for preventing chronic lung disease in mechanically ventilated preterm infants. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2001 (accessed 09/05/05).

Head injury. Pegorgotein was found[1] to be little more effective than placebo in improving neurological outcome or reducing mortality in patients with severe head injury.

1. Young B, *et al.* Effects of pegorgotein on neurologic outcome of patients with severe head injury: a multicenter, randomized controlled trial. *JAMA* 1996; **276:** 538–43.

Motor neurone disease. A small percentage of patients with familial amyotrophic lateral sclerosis (see Motor Neurone Disease, p.2380) have been shown to have a mutation in the gene encoding for the enzyme copper-zinc superoxide dismutase but there has been no consensus as to whether patients with this mutation should be given superoxide dismutase supplements.[1]

1. Orrell RW, deBelleroche JS. Superoxide dismutase and ALS. *Lancet* 1994; **344:** 1651–2.

Radiotherapy. Although some studies[1,2] indicate that orgotein can ameliorate the adverse effects of radiotherapy for bladder tumours, another study[3] was terminated prematurely because of unacceptable hypersensitivity reactions and apparent inefficacy.

1. Sanchiz F, *et al.* Prevention of radioinduced cystitis by orgotein: a randomized study. *Anticancer Res* 1996; **16:** 2025–8.
2. Valencia J, *et al.* The efficacy of orgotein in the treatment of acute toxicity due to radiotherapy on head and neck tumors. *Tumori* 2002; **88:** 385–9.
3. Nielsen OS, *et al.* Orgotein in radiation treatment of bladder cancer: a report on allergic reactions and lack of radioprotective effect. *Acta Oncol* 1987; **26:** 101–4.

Preparations

Proprietary Preparations (details are given in Part 3)
Spain: Ontosein†.

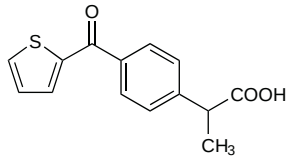
Multi-ingredient: ***Arg.:*** Vitix; ***Indon.:*** Glisodin.

Suprofen *(BAN, USAN, rINN)*

R-25061; Suprofeeni; Suprofène; Suprofeno; Suprofenum; Sutoprofen. 2-[4-(2-Thenoyl)phenyl]propionic acid.

Супрофен

$C_{14}H_{12}O_3S$ = 260.3.
CAS — 40828-46-4.
ATC — M01AE07.
ATC Vet — QM01AE07.



Pharmacopoeias. In *US.*
USP 31 (Suprofen). A white to off-white powder, odourless or having a slight odour. Sparingly soluble in water.

Profile
Suprofen is an NSAID (p.96). Suprofen has been used as 1% eye drops to inhibit the miosis that may occur during ocular surgery.

It was formerly given orally in mild to moderate pain and in osteoarthritis and rheumatoid arthritis but, after reports of adverse renal reactions, marketing of the oral dose form was suspended worldwide.

Preparations

USP 31: Suprofen Ophthalmic Solution.

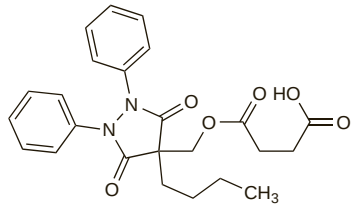
Proprietary Preparations (details are given in Part 3)
USA: Profenal†.

Suxibuzone *(BAN, rINN)*

Suksibutsoni; Suksibuzonas; Suxibuzon; Suxibuzona; Suxibuzonum; Szuxibuzon. 4-Butyl-4-hydroxymethyl-1,2-diphenylpyrazolidine-3,5-dione hydrogen succinate (ester).

Суксибузон

$C_{24}H_{26}N_2O_6$ = 438.5.
CAS — 27470-51-5.
ATC — M02AA22.
ATC Vet — QM01AA90; QM02AA22.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Suxibuzone). A white or almost white, crystalline powder. Practically insoluble in water; soluble in alcohol; freely soluble in acetone; practically insoluble in cyclohexane.

Profile
Suxibuzone, a derivative of phenylbutazone (p.117), is an NSAID (p.96) that has been applied topically at a concentration of about 7% in musculoskeletal and joint disorders. Concern over safety and toxicity after oral use has led to its withdrawal from the market in many countries.

Preparations

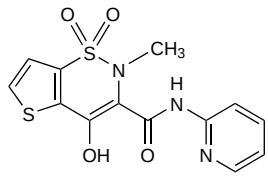
Proprietary Preparations (details are given in Part 3)
Spain: Danilon.

Tenoxicam *(BAN, USAN, rINN)*

Ro-12-0068; Ro-12-0068/000; Tenoksikaami; Tenoksikam; Tenoksikamas; Ténoxicam; Tenoxicamum; Tenoxikám; Tenoxikam. 4-Hydroxy-2-methyl-*N*-(2-pyridyl)-2*H*-thieno[2,3-e][1,2]thiazine-3-carboxamide 1,1-dioxide.

Теноксикам

$C_{13}H_{11}N_3O_4S_2$ = 337.4.
CAS — 59804-37-4.
ATC — M01AC02.
ATC Vet — QM01AC02.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Tenoxicam). A yellow, polymorphic, crystalline powder. Practically insoluble in water; very slightly soluble in dehydrated alcohol; sparingly soluble in dichloromethane; it dissolves in solutions of acids and alkalis. Protect from light.

Stability. An admixture of tenoxicam 0.02% and ceftazidime 0.5% (as the sodium salt) in glucose injection 5% appeared stable when stored for up to 120 hours at 25° in glass bottles;[1] when stored in PVC bags, the admixture was stable for up to 72 hours at 25° and for up to 144 hours at 4°.

1. Wang D-P, *et al.* Compatibility and stability of ceftazidime sodium and tenoxicam in 5% dextrose injection. *Am J Health-Syst Pharm* 2004; **61:** 1924–7.

Adverse Effects, Treatment, and Precautions
As for NSAIDs in general, p.96.

Incidence of adverse effects. Adverse effects associated with tenoxicam have been reviewed.[1] The majority of adverse effects relate to the gastrointestinal tract (11.4%), nervous system (2.8%), or skin (2.5%).

Gastrointestinal disturbances including nausea and vomiting (14.7%) and dyspepsia (2.3%), surgical site bleeding (4.3%), wound infection (2.7%), dizziness (5.7%), and headache (10.7%) were the most common adverse effects reported in a placebo-controlled study involving 1001 patients following the perioperative use of oral and intravenous tenoxicam.[2] It was noted, however, that the incidence of dizziness, nausea and vomiting, and headache was greater in the placebo group and that the difference in the incidence of dyspepsia between the 2 groups was not significant.

1. Todd PA, Clissold SP. Tenoxicam: an update of its pharmacology and therapeutic efficacy in rheumatic diseases. *Drugs* 1991; **41:** 625–46.
2. Merry AF, *et al.* Clinical tolerability of perioperative tenoxicam in 1001 patients – a prospective, controlled, double-blind, multicentre study. *Pain* 2004; **111:** 313–22.

Effects on the kidneys. A review[1] of the effects of tenoxicam on renal function concluded that tenoxicam could be given at normal recommended doses to elderly patients or those with mild to moderate renal impairment who were not at high risk of renal failure or receiving potentially nephrotoxic therapy. Data from the manufacturer's database[1] on 67 063 patients, including 17 005 over 65 years of age, who had received tenoxicam indicated that there had been 45 adverse events relating to urinary system function, described as severe in 7. The prevalence of adverse events was similar in elderly and non-elderly patients, the most common effects being dysuria and renal pain.

1. Heintz RCA. Tenoxicam and renal function. *Drug Safety* 1995; **12:** 110–19.

Effects on the liver. A report[1] of acute hepatitis associated with the use of tenoxicam.

1. Sungur C, *et al.* Acute hepatitis caused by tenoxicam. *Ann Pharmacother* 1994; **28:** 1309.

Effects on the skin. A report of 3 cases of toxic epidermal necrolysis (Lyell's syndrome) associated with tenoxicam.[1]

For the general incidence of dermatological effects see above.

1. Chosidow O, *et al.* Toxidermies sévères au ténoxicam (Tilcotil). *Ann Dermatol Venereol* 1991; **118:** 903–4.

Interactions
For interactions associated with NSAIDs, see p.99.

Pharmacokinetics
Tenoxicam is well absorbed after oral doses; peak plasma concentrations occur within about 2 hours in fasting subjects; this may be delayed to about 6 hours when tenoxicam is given with food but the extent of absorption is not affected. It is also rapidly absorbed when given by intramuscular injection. Tenoxicam is about 99% protein bound and penetrates synovial fluid. The plasma elimination half-life ranges from 42 to 81 hours; with daily dosage, steady-state concentrations are reached within 10 to 15 days. Tenoxicam is completely metabolised to inactive metabolites which are excreted mainly in the urine; there is some biliary excretion of glucuronide conjugates of the metabolites.

◊ References.

1. Nilsen OG. Clinical pharmacokinetics of tenoxicam. *Clin Pharmacokinet* 1994; **26:** 16–43.
2. Guentert TW, *et al.* Relative bioavailability of oral dosage forms of tenoxicam. *Arzneimittelforschung* 1994; **44:** 1051–4.
3. Nilsen OG, *et al.* Single- and multiple-dose pharmacokinetics, kidney tolerability and plasma protein binding of tenoxicam in renally impaired patients and healthy volunteers. *Pharmacol Toxicol* 2001; **89:** 265–72.

Uses and Administration
Tenoxicam, a piroxicam (p.117) analogue, is an NSAID (p.99). It is used in the symptomatic management of musculoskeletal and joint disorders such as osteoarthritis and rheumatoid arthritis, and also in the short-term management of soft-tissue injury. Tenoxicam is given as a single oral daily dose usually of 20 mg. In acute musculoskeletal disorders treatment for up to 7 days is usually sufficient but in severe cases it may be given for up to a maximum of 14 days. Doses similar to those given orally have been given by intramuscular or intravenous injection for initial treatment for 1 or 2 days. Tenoxicam has also been given by rectal suppository.

◊ References.

1. Todd PA, Clissold SP. Tenoxicam: an update of its pharmacology and therapeutic efficacy in rheumatic diseases. *Drugs* 1991; **41:** 625–46.

Preparations

BP 2008: Tenoxicam Injection; Tenoxicam Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Mefenix†; ***Austria:*** Tilcotil; ***Belg.:*** Tilcotil; ***Braz.:*** Inflagel; Prodoxican; Teflan; Tenobio†; Tenocam†; Tenotec; Tenoxen†; Tilatil; Tilonax; Tiloxican†; Titenil†; ***Chile:*** Avancel†; Bioflam; Mitrotil; Recaflex; Texicam†; Tilcotil; ***Denm.:*** Tilcotil; ***Fin.:*** Tilcotil; ***Fr.:*** Tilcotil; ***Gr.:*** Admiral; Algin-Vek; Amcinafal; Ampirovix; Artroxicam; Artruic†; Aspagin; Biodruff; Docticam†; Dranat; Hobaticam; Indo-bros; Istotosal; Liaderyl; Neo-adlibamin; Neo-antiperstam; Neo-endusix; Octiveran; Oxytel; Ponsolit; Redac; Soral; Tenox†; Tentepanil; Tilcitin; Toscacalm; Velasor; Voir; Zibelant; ***Hong Kong:*** Nadamen†; Seftil†; Tilcotil; ***Hung.:*** Tilcotil; ***India:*** Tobitil; ***Indon.:*** Artricom; Meditil; Notritis; Oxaflam; Pilopil; Thenil; Tilcotil; Tilflam; Xotilon; ***Irl.:*** Mobiflex†; ***Ital.:*** Dolmen; Rexalgan; Tilcotil; ***Jpn:*** Tilcotil; ***Malaysia:*** Nadamen†; Seftil; Sinoral†; Tilcotil; ***Mex.:*** Tilcotil; ***Neth.:*** Tilcotil; ***NZ:*** Tilcotil; ***Philipp.:*** Tilcotil; ***Port.:*** Bioreucam†; Calibral†; Doxican; Tenalgin; Tilcotil; ***S.Afr.:*** Tilcotil; Tobitil†; ***Singapore:*** Nadamen†; ***Spain:*** Artriunic; Reutenox; Tilcotil†; ***Swed.:*** Alganex; ***Switz.:*** Tilcotil; ***Thai.:*** Memzotil; Nadamen†; Seftil; Sinoral; Teconam; Tenax; Tenocam; Tenox; Tenoxil; Tenxil; Tilcotil; Tonox; ***Turk.:*** Nobateks; Oksamen; Tenoksan; Tenoktil; Tenox; Tilcotil; Tilko; VienOks; Zikaral; ***UK:*** Mobiflex; ***Venez.:*** Rodix; Tecam†; Tenoxin; Tilcotil†.

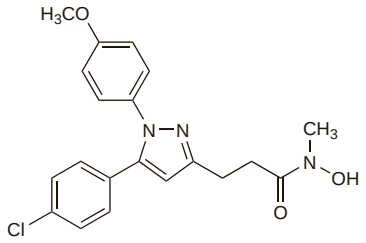
Multi-ingredient: ***Arg.:*** Mefenix Relax†.

Tepoxalin *(USAN, rINN)*

ORF-20485; RWJ-20485; Tepoksaliini; Tepoxalina; Tépoxaline; Tepoxalinum. 5-(*p*-Chlorophenyl)-1-(*p*-methoxyphenyl)-*N*-methylpyrazole-3-propionohydroxamic acid.

Тепоксалин

$C_{20}H_{20}ClN_3O_3$ = 385.8.
CAS — 103475-41-8.
ATC Vet — QM01AE92.



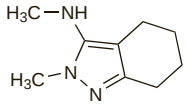
Profile
Tepoxalin, a propionic acid derivative, is an NSAID used in veterinary medicine for the treatment of inflammation and pain in dogs.

Tetridamine *(rINN)*

POLI-67; Tetridamina; Tétridamine; Tetridaminum; Tetrydamine *(USAN)*. 4,5,6,7-Tetrahydro-2-methyl-3-(methylamino)-2*H*-indazole.

Тетридамин

$C_9H_{15}N_3$ = 165.2.
CAS — 17289-49-5.



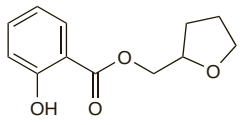
Profile
Tetridamine is an NSAID (p.96) that has been used as the maleate as a douche in the treatment of vaginitis.

Preparations
Proprietary Preparations (details are given in Part 3)
Ital.: Deb; ***Spain:*** Fomene.

Thurfyl Salicylate

Salicilato de turfilo. Tetrahydrofurfuryl salicylate.

$C_{12}H_{14}O_4$ = 222.2.
CAS — 2217-35-8.



Profile
Thurfyl salicylate is a salicylic acid derivative that has been used similarly to methyl salicylate (p.85) in topical rubefacient preparations at concentrations of up to 14% for musculoskeletal, joint, peri-articular, and soft-tissue disorders.

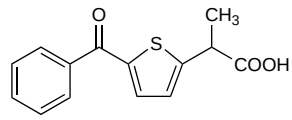
Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austral.:*** Biosal Arthritis; ***Belg.:*** Transvane; ***Irl.:*** Transvasin; ***UK:*** Transvasin Heat Rub.

Tiaprofenic Acid *(BAN, rINN)*

Acide tiaprofénique; Ácido tiaprofénico; Acidum tiaprofenicum; FC-3001; Kyselina tiaprofenová; RU-15060; Tiaprofeenihappo; Tiaprofenik Asit; Tiaprofeno rūgštis; Tiaprofensyra. 2-(5-Benzoyl-2-thienyl)propionic acid.

Тиапрофеновая Кислота

$C_{14}H_{12}O_3S$ = 260.3.
CAS — 33005-95-7.
ATC — M01AE11.
ATC Vet — QM01AE11.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Tiaprofenic Acid). A white or almost white, crystalline powder. Practically insoluble in water; freely soluble in alcohol, in acetone, and in dichloromethane. Protect from light.

Adverse Effects, Treatment, and Precautions
As for NSAIDs in general, p.96.

Tiaprofenic acid may cause cystitis, bladder irritation, and other urinary-tract symptoms (see below). It should not be given to patients with active urinary-tract disorders or prostatic disease or a history of recurrent urinary-tract disorders. It should be stopped immediately if urinary-tract symptoms occur and urinalysis and urine culture performed.

Tiaprofenic acid is contra-indicated in patients with severe hepatic or renal impairment.

Breast feeding. Although tiaprofenic acid is distributed into breast milk, the amount is considered by the *BNF* to be too small to be harmful to a breast-fed infant. Licensed product information also states that exposure to tiaprofenic acid via breast milk is unlikely to be of pharmacological significance; however, it is recommended that either treatment or breast feeding is stopped as necessary.

Effects on the urinary tract. Cystitis and bladder irritation have been associated with the use of tiaprofenic acid.[1-6] In August 1994 the UK CSM stated[4] that since the introduction of tiaprofenic acid in the UK in 1982 they had received 69 reports of cystitis and 32 other reports of urinary-tract symptoms associated with tiaprofenic acid including frequency, dysuria, and haematuria whereas only 8 cases of cystitis had been reported for all other NSAIDs combined. Analysis of spontaneous reports received by WHO[7] confirmed that cystitis was more commonly associated with tiaprofenic acid than with other NSAIDs. The Australian Adverse Drug Reactions Advisory Committee had received similar reports.[3] Since the 1994 warning, the CSM[8] had received reports of a further 74 cases of cystitis, but the majority of these had occurred before the warning was issued. The duration of treatment in patients affected had varied considerably. Most patients recovered when tiaprofenic acid was withdrawn.

The CSM recommended that tiaprofenic acid should not be given to patients with urinary-tract disorders and that it should be stopped in patients who develop urinary-tract symptoms. Patients should be advised that if they develop symptoms such as urinary frequency, nocturia, urgency, or pain on urination, or have blood in their urine they should stop taking tiaprofenic acid and consult their doctor. Older patients may be at increased risk.[9]

1. Ahmed M, Davison OW. Severe cystitis associated with tiaprofenic acid. *BMJ* 1991; **303:** 1376.
2. O'Neill GFA. Tiaprofenic acid as a cause of non-bacterial cystitis. *Med J Aust* 1994; **160:** 123–5.
3. Australian Adverse Drug Reactions Advisory Committee (ADRAC). Update on tiaprofenic acid and urinary symptoms. *Aust Adverse Drug React Bull* 1994; **13:** 6.
4. CSM/MCA. Severe cystitis with tiaprofenic acid (Surgam). *Current Problems* 1994; **20:** 11. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2015615&RevisionSelectionMethod=LatestReleased (accessed 08/11/07)
5. Harrison WJ, *et al.* Adverse reactions to tiaprofenic acid mimicking interstitial cystitis. *BMJ* 1994; **309:** 574.
6. Mayall FG, *et al.* Cystitis and ureteric obstruction in patients taking tiaprofenic acid. *BMJ* 1994: **309:** 599.
7. The ADR Signals Analysis Project (ASAP) Team. How does cystitis affect a comparative risk profile of tiaprofenic acid with other non-steroidal antiinflammatory drugs? An international study based on spontaneous reports and drug usage data. *Pharmacol Toxicol* 1997; **80:** 211–17.
8. Crawford MLA, *et al.* Severe cystitis associated with tiaprofenic acid. *Br J Urol* 1997; **79:** 578–84.
9. Buchbinder R, *et al.* Clinical features of tiaprofenic acid (surgam) associated cystitis and a study of risk factors for its development. *J Clin Epidemiol* 2000; **53:** 1013–19.

Interactions
For interactions associated with NSAIDs, see p.99.

Pharmacokinetics
Tiaprofenic acid is absorbed from the gastrointestinal tract with peak plasma concentrations being reached within about 1.5 hours after oral doses. It has a short elimination half-life of about 2 hours and is highly bound to plasma proteins (about 98%). Excretion of tiaprofenic acid and its metabolites is mainly in the urine in the form of acyl glucuronides; some is excreted in the bile. Tiaprofenic acid crosses the placenta and is distributed into breast milk.

◊ References.
1. Davies NM. Clinical pharmacokinetics of tiaprofenic acid and its enantiomers. *Clin Pharmacokinet* 1996; **31:** 331–47.

Uses and Administration
Tiaprofenic acid, a propionic acid derivative, is an NSAID (p.99). It is used for the relief of pain and inflammation in musculoskeletal and joint disorders such as ankylosing spondylitis, osteoarthritis, and rheumatoid arthritis, in peri-articular disorders such as fibrositis and capsulitis, and in soft-tissue disorders such as sprains and strains. The usual oral dose is 600 mg daily given in 2 or 3 divided doses; in patients with cardiac, hepatic, or renal impairment, licensed product information suggests that the dose is reduced to 200 mg twice daily. A modified-release preparation may be available for once-daily use. Tiaprofenic acid has also been given rectally. It has been given intramuscularly as the trometamol salt in acute conditions.

◊ References.
1. Plosker GL, Wagstaff AJ. Tiaprofenic acid: a reappraisal of its pharmacological properties and use in the management of rheumatic diseases. *Drugs* 1995; **50:** 1050–75.

Administration in hepatic or renal impairment. Tiaprofenic acid is contra-indicated in patients with severe hepatic or renal impairment; for dosage details in those with more moderate impairment, see Uses and Administration, above.

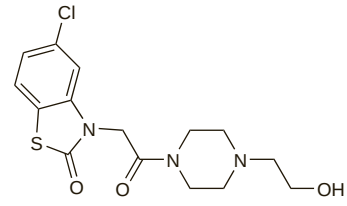
Preparations
Proprietary Preparations (details are given in Part 3)
Austral.: Surgam; ***Canad.:*** Albert Tiafen†; Surgam; ***Cz.:*** Surgam; Thialgin; ***Denm.:*** Surgamyl; ***Fin.:*** Surgamyl; ***Fr.:*** Flanid; Surgam; ***Ger.:*** Surgam; ***Hung.:*** Surgam; ***Irl.:*** Surgam; ***Ital.:*** Suralgan†; Surgamyl; Tiaprofen†; ***Mex.:*** Surgam; ***Neth.:*** Surgam; ***NZ:*** Surgam; ***Pol.:*** Surgam; ***Port.:*** Surgam; ***S.Afr.:*** Surgam; ***Thai.:*** Fengam; Surgam†; ***Turk.:*** Surgam; ***UK:*** Surgam; ***Venez.:*** Torpas.

Tiaramide Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de tiaramida; NTA-194; Tiaperamide Hydrochloride; Tiaramide, Chlorhydrate de; Tiaramidi Hydrochloridum. 5-Chloro-3-{2-[4-(2-hydroxyethyl)piperazin-1-yl]-2-oxoethyl}benzothiazolin-2-one hydrochloride.

Тиарамида Гидрохлорид

$C_{15}H_{18}ClN_3O_3S,HCl$ = 392.3.
CAS — 32527-55-2 (tiaramide); 35941-71-0 (tiaramide hydrochloride).



(tiaramide)

Pharmacopoeias. In *Jpn.*

Profile
Tiaramide hydrochloride is an NSAID (p.96) that has been given orally for the relief of pain and inflammation.

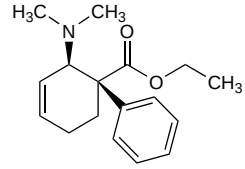
Preparations
Proprietary Preparations (details are given in Part 3)
Jpn: Solantal†.

Tilidine Hydrochloride *(USAN, pINNM)*

Gö 1261-C; Hidrocloruro de tilidina; Tilidate Hydrochloride *(BANM)*; Tilidiinihydrokloridihemihydraatti; Tilidine, Chlorhydrate de; Tilidine (chlorhydrate de) hémihydraté; Tilidin-hydrochlorid hemihydrát; Tilidinhydroklorid hemihydrat; Tilidini Hydrochloridum; Tilidini hydrochloridum hemihydricum; Tilidino hidrocloridas hemihidratas; W-5759A. (±)-Ethyl *trans*-2-dimethylamino-1-phenylcyclohex-3-ene-1-carboxylate hydrochloride hemihydrate.

Тилидина Гидрохлорид

$C_{17}H_{23}NO_2,HCl, ½H_2O$ = 318.8.
CAS — 20380-58-9 (tilidine); 27107-79-5 (anhydrous tilidine hydrochloride); 24357-97-9 (anhydrous +-trans-tilidine hydrochloride).
ATC — N02AX01.
ATC Vet — QN02AX01.



(tilidine)

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Tilidine Hydrochloride Hemihydrate). A white or almost white, crystalline powder. A suitable antoxidant may be