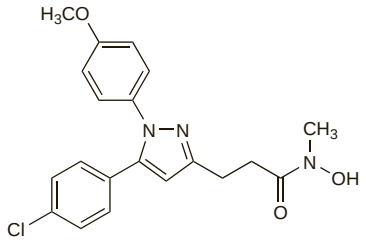
Tepoxalin *(USAN, rINN)*

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.



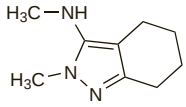
Profile
Tepoxalin, a propionic acid derivative, is an NSAID used in veterinary medicine for the treatment of inflammation and pain in dogs.

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.



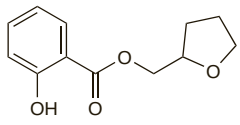
Profile
Tetridamine is an NSAID (p.96) that has been used as the maleate as a douche in the treatment of vaginitis.

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.

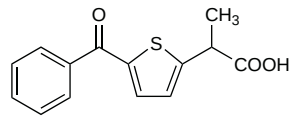
Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austral.:*** Biosal Arthritis; ***Belg.:*** Transvane; ***Irl.:*** Transvasin; ***UK:*** Transvasin Heat Rub.

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.

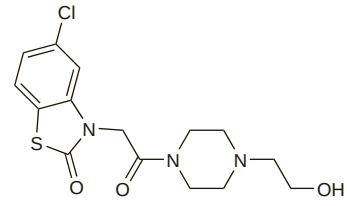
Preparations
Proprietary Preparations (details are given in Part 3)
Austral.: Surgam; ***Canad.:*** Albert Tiafen†; Surgam; ***Cz.:*** Surgam; Thialgin; ***Denm.:*** Surgamyl; ***Fin.:*** Surgamyl; ***Fr.:*** Flanid; Surgam; ***Ger.:*** Surgam; ***Hung.:*** Surgam; ***Irl.:*** Surgam; ***Ital.:*** Suralgan†; 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.

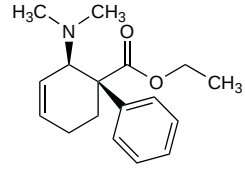
Preparations
Proprietary Preparations (details are given in Part 3)
Jpn: Solantal†.

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