2. Winner P, *et al.* Twelve-month tolerability and safety of sumatriptan-naproxen sodium for the treatment of acute migraine. *Mayo Clin Proc* 2007; **82:** 61–8.

3. Brandes JL, *et al.* Sumatriptan-naproxen for acute treatment of migraine: a randomized trial. *JAMA* 2007; **297:** 1443–54.

4. Sargent J, *et al.* A comparison of naproxen sodium to propranolol hydrochloride and a placebo control for the prophylaxis of migraine headache. *Headache* 1985; **25:** 320–4.

5. Welch KMA, *et al.* Successful migraine prophylaxis with naproxen sodium. *Neurology* 1985; **35:** 1304–10.

6. Sances G, *et al.* Naproxen sodium in menstrual migraine prophylaxis: a double-blind placebo controlled study. *Headache* 1990; **30:** 705–9.

Malignant neoplasms. Some NSAIDs such as naproxen may be of value both for the differential diagnosis and the management of neoplastic fever[1-4] as they appear to be more effective in reducing this type of fever than against fever associated with infections. However, the reliability of naproxen in the diagnosis of neoplastic fever has been questioned.[5] In a group of 72 patients, naproxen decreased body temperature in 55% of patients with neoplastic disorders and 38% of patients with other conditions. Thus, the sensitivity of the test was calculated as 55% and its specificity as 62%, which the authors considered to be too low to be reliable.

1. Chang JC, Gross HM. Neoplastic fever responds to the treatment of an adequate dose of naproxen. *J Clin Oncol* 1985; **3:** 552–8.

2. Azeemuddin SK, *et al.* The effect of naproxen on fever in children with malignancies. *Cancer* 1987; **59:** 1966–8.

3. Economos K, *et al.* The effect of naproxen on fever in patients with advanced gynecologic malignancies. *Gynecol Oncol* 1995; **56:** 250–4.

4. Cunha BA, *et al.* Fever of unknown origin (FUO) caused by multiple myeloma: the diagnostic value of the Naprosyn test. *Heart Lung* 2006; **35:** 358–62.

5. Vanderschueren S, *et al.* Lack of value of the naproxen test in the differential diagnosis of prolonged febrile illnesses. *Am J Med* 2003; **115:** 572–5.

Preparations

BP 2008: Gastro-resistant Naproxen Tablets; Naproxen Oral Suspension; Naproxen Suppositories; Naproxen Tablets;
USP 31: Naproxen Delayed-Release Tablets; Naproxen Oral Suspension; Naproxen Sodium Tablets; Naproxen Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Aleve; Algioprux†; Alidase; Bumaflex N; Causalon Pro†; Congex; Debril; Fabralgina; Fadalivio; Flaxvan; Flogocefal†; Melgar; Monarit; Naprofidex; Naprogen; Naprontag; Naprux; Neuralprona; Sicadentol Plus†; Tundra; Veradol†; Xicane†; ***Austral.:*** Aleve†; Anaprox; Chemists Own Period Pain Tablets; Crysanal; Femme Free; Inza; Naprogesic; Naprosyn; Nurolasts†; Proxen; ***Austria:*** Aleve; Miranax; Naprobene; Nycopren; Proxen; ***Belg.:*** Aleve; Apranax; Naproflam; Naprosyne; ***Braz.:*** Flanax; Napronax; Naprosyn; Naprox; ***Canad.:*** Anaprox; Apo-Napro-Na; Naprosyn; Naxen†; Novo-Naprox; Nu-Naprox; Synflex†; ***Chile:*** Atac; Deucoval; Eurogesic; Inveoxel†; Naprogesic; Reprost†; Triox NF; ***Cz.:*** Aleve; Emoxen; Nalgesin; Naprobene†; Naprosyn†; Napsynt†; ***Denm.:*** Bonyl; Miranax†; Naprosyn; ***Fin.:*** Alpoxen; Miranax; Naprometin; Napromex; Naprosyn†; Naxopren; Pronaxen; ***Fr.:*** Aleve; Apranax; Naprosyne; ***Ger.:*** Alacetan NNA; Aleve; Dolormin mit Naproxen; Dysmenalgit; prodolor†; Proxen; ***Gr.:*** Anaprox; Naprosyn; Nycopren-E; ***Hong Kong:*** Apo-Napro-Na; Inza; Naprorex; Naprosyn; Napxen; Noflam-N; Proxen†; Soden; Soren†; Synflex†; ***Hung.:*** Aleve; Apranax; Napmel; Naprosyn; ***India:*** Artagen; Easy Dayz; Naprosyn; Xenobid; ***Indon.:*** Naxen; Synflex; ***Irl.:*** Gerinap; Napmel†; Naprex†; Naprosyn; Synflex; ***Israel:*** Naproxi; Narocin; Naxyn; Point; ***Ital.:*** Aleve; Algonapril; Aperdan; Axer†; Floginax; Flogogin†; Floxalin; Gibixen; Gynestrel; Laser; Momendol; Napreben†; Naprius; Naprocet; Naprorex†; Naprosyn; Neo Eblimon; Nitens; Prexan; Proxagol; Synalgo; Synflex; Ticoflex†; Uninapro; Xenar†; ***Malaysia:*** Apo-Napro-Na; Inza†; Roxyn†; Seladin; Sunprox; Synflex; ***Mex.:*** Actiquim; Analgen; Anapsyl; Arsenal; Artron†; Arxen; Atiflan; Bioxan; Bixen; Dafloxen; Deflamox; Diferbest; Dolxen; Donaprox; Edem; Faraxen; Flanax; Flavoxen; Flaxendol; Flexen†; Flogen; Fuxen; Genalgen†; Inflanox; Iqfasol; Kenaprox†; Lixogan†; Lorexen†; Messelxen; Naflapen; Napoxol; Naprodil; Nasocan†; Navixen; Naxen; Naxopaar; Neonaxil; Nixal†; Novaxen; Pactens; Praxedol; Pronat; Pronax-P†; Pronaxil; Pronoxen; Propional†; Proxalin; Proxem†; Salupran†; Sertrixen; Sodixen; Tandax; Tanizona; Unirelaxed; Vantin; Velsay; ***Neth.:*** Aleve; Femex†; Momendol; Naprelan; Naprocoat; Naprovite; Nycopren†; ***Norw.:*** Alpoxen†; Ledox; Napren; Naprosyn; ***NZ:*** Naprogesic; Naprosyn; Naxen; Noflam; Synflex; ***Philipp.:*** Alpron; Flanax; Naprelan; Naprosyn; Sanomed; ***Pol.:*** Aleve; Anapran; Boloxen; Emochol†; Natrax; ***Port.:*** Momendol; Naprocet; Naprosyn; Reuxen; ***Rus.:*** Nalgesin (Налгезин); ***S.Afr.:*** Acusprain; Aleve; Fibroxyn†; Nafasol; Napflam; Naprel†; Naproscript†; Naprosyn†; Synflex; Traumox; ***Singapore:*** Aleve; Apo-Napro-Na; Bipronyl†; Gesiprox†; Inza; Noflam-N†; Nuprafen†; Seladin; Soden; Soproxen; Zynal†; ***Spain:*** Aleve; Aliviomas; Antalgin; Denaxpren; Lundiran; Momen; Naprosyn; Naproval; Tacron; ***Swed.:*** Alpoxen; Naprosyn; Pronaxen; ***Switz.:*** Aleve; Apranax; Naprosyn†; Nycopren; Proxen; ***Thai.:*** Annoxen; Naproflex; Naprosian; Naprosyn; Napsen†; Napxen†; Narzen†; Polyxen; Proxen; Roxen†; Serviproxan; Sonap; Soproxen; Synflex; U-Proxyn; Vinsen; ***Turk.:*** A-Nox; Aleve; Anaprotab; Apraljin; Apranax; Aprol; Apromed; Aprowell; Bonmin; Kapnax; Karoksen; Naponal; Napradol; Napren; Naprodeva; Naprosyn; Naprotab; Opraks; Relokap; Romaksen; Romatim; Rumazolidin; Synax; Syndol; ***UK:*** Arthrosin†; Arthroxen; Feminax Ultra; Napratec; Naprosyn; Nycopren†; Synflex; Timpron†; ***USA:*** Aleve; Anaprox; Naprelan; Naprosyn; Prevacid NapraPAC; ***Venez.:*** Apranax†; Synaprosyn†.

Multi-ingredient: ***Arg.:*** Naprontag Flex; Papasine; ***Ital.:*** Momendol; ***Mex.:*** Acxen†; Analgen Forte; Arsenal Compuesto; Arxen Compositum; Bifardol; Blocacid; Brax; Contraxen; Dafloxen-F; Decosil; Deflamox Plus; Dolotandax; Drunen; Farxen; Febrax; Fiverdol; Flucol; Grifed; Kensedal; Movex; Naprodil Plus; Naxodol; Nedoxal; Neorpan Plus; Onexmol; Pensodil; Polet; Profenlax; Proxalin Plus; Raxenol; Reucortil; Somalgesic; Taxenan; Ulpafie-N; Velsay-S Compuesto; Viplus; ***Rus.:*** Cefecon N (Цефекон Н); Pentalgin-N (Пенталгин-Н).

Nefopam Hydrochloride

(BANM, USAN, rINNM)

Benzoxazocine; Fenazoxine; Hidrocloruro de nefopam; Néfopam, Chlorhydrate de; Nefopami Hydrochloridum; R-738. 3,4,5,6-Tetrahydro-5-methyl-1-phenyl-1*H*-2,5-benzoxazocine hydrochloride.

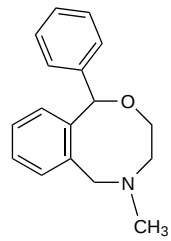
Нефопама Гидрохлорид

$C_{17}H_{19}NO,HCl$ = 289.8.

CAS — 13669-70-0 (nefopam); 23327-57-3 (nefopam hydrochloride).

ATC — N02BG06.

ATC Vet — QN02BG06.



(nefopam)

Pharmacopoeias. In *Chin.*

Adverse Effects and Treatment

Adverse effects occurring with nefopam include gastrointestinal disturbances, such as nausea and vomiting, sweating, drowsiness, insomnia, urinary retention, dizziness, hypotension, tremor, paraesthesia, palpitations, lightheadedness, nervousness, confusion, blurred vision, headache, dry mouth, syncope, angioedema, allergic reactions, and tachycardia. Euphoria, hallucinations, and convulsions have occasionally been reported, as has temporary pink discoloration of the urine. Symptoms of overdosage have included CNS and cardiovascular toxicity.

Effects on the urinary tract. In January 1989, the UK CSM[1] reported that it had received 53 reports in which nefopam was associated with the development of urinary retention or symptoms of hesitancy, poor stream, or dribbling. In one case there was a history of prostatism.

1. CSM. Nefopam hydrochloride (Acupan). *Current Problems 24* 1989. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024431&RevisionSelectionMethod=LatestReleased (accessed 14/07/08)

Overdosage. There have been reports of fatal overdoses with nefopam.[1-3] One report[1] also provided details of 9 other patients who recovered with routine supportive treatment.

1. Piercy DM, *et al.* Death due to overdose of nefopam. *BMJ* 1981; **283:** 1508–9.

2. Urwin SC, Smith HS. Fatal nefopam overdose. *Br J Anaesth* 1999; **83:** 501–2.

3. Tracqui A, *et al.* Fatal overdosage with nefopam (Acupan). *J Anal Toxicol* 2002; **26:** 239–43.

Precautions

Nefopam is contra-indicated in patients with a history of convulsive disorders. It should be used with caution in the elderly and in patients with glaucoma, urinary retention, or impaired hepatic or renal function.

Abuse. Abuse of parenteral nefopam has been reported in 3 patients with a history of chronic pain.[1] Psychostimulant-like symptoms such as agitation, impatience, and violence, were noted in 2 of the patients; antimuscarinic effects were also seen. All 3 patients were found to be psychologically dependent; in 2 who attempted to stop nefopam, withdrawal symptoms were noted.

1. Villier C, Mallaret MP. Nefopam abuse. *Ann Pharmacother* 2002; **36:** 1564–6.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were receiving nefopam, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with breast feeding.

Studies in 5 healthy nursing mothers given nefopam for post-episiotomy pain indicated that nefopam was present in human milk in an equivalent concentration to that in plasma.[2] It was calculated that on a body-weight basis a breast-fed infant would receive less than 3% of the maternal dose.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*: 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 10/10/06)

2. Liu DTY, *et al.* Nefopam excretion in human milk. *Br J Clin Pharmacol* 1987; **23:** 99–101.

Interactions

It has been recommended that nefopam should not be given to patients receiving MAOIs and should be used cautiously in those receiving tricyclic antidepressants. The adverse effects of nefopam may be additive to those of other drugs with antimuscarinic or sympathomimetic activity.

Pharmacokinetics

Nefopam is absorbed from the gastrointestinal tract. Peak plasma concentrations occur 1 to 3 hours after a dose by mouth and up to 1 hour after intramuscular injection. About 73% is bound to plasma proteins. Nefopam is distributed into breast milk. It has an elimination half-life of about 4 hours. It is extensively metabolised and excreted mainly in urine, in which less than 5% of a dose is excreted unchanged. About 8% of a dose is excreted via the faeces.

Uses and Administration

Nefopam hydrochloride is a non-opioid analgesic considered to act centrally, although its mechanism of action is unclear. It also has some antimuscarinic and sympathomimetic actions. Nefopam hydrochloride is used for the relief of moderate acute and chronic pain. The usual oral dose range is 30 to 90 mg three times daily; the recommended initial dose is 60 mg (or 30 mg in elderly patients) three times daily. Nefopam hydrochloride may also be given in doses of 20 mg by intramuscular injection, repeated every 6 hours if necessary; it has been recommended that the patient should always be lying down when receiving the injection and should remain so for 15 to 20 minutes afterwards. It has also been given by slow intravenous injection in doses of 20 mg every 4 hours up to a maximum of 120 mg daily.

Hiccup. In two case series[1,2] involving 10 patients in total, hiccups refractory to standard therapy stopped after treatment with intravenous nefopam. For the management of intractable hiccups see under Chlorpromazine, p.976.

1. Bilotta F, Rosa G. Nefopam for severe hiccups. *N Engl J Med* 2000; **343:** 1973–4.

2. Bilotta F, *et al.* Nefopam for refractory postoperative hiccups. *Anesth Analg* 2001; **93:** 1358–60.

Shivering. Nefopam is one of several drugs tried in the prevention of postoperative shivering (p.1779).

References.

1. Bilotta F, *et al.* Nefopam and tramadol for the prevention of shivering during neuraxial anesthesia. *Reg Anesth Pain Med* 2002; **27:** 380–4.

2. Piper SN, *et al.* A comparison of nefopam and clonidine for the prevention of postanaesthetic shivering: a comparative, double-blind and placebo-controlled dose-ranging study. *Anaesthesia* 2004; **59:** 559–64.

3. Bilotta F, *et al.* Nefopam or clonidine in the pharmacologic prevention of shivering in patients undergoing conscious sedation for interventional neuroradiology. *Anaesthesia* 2005; **60:** 124–8.

Preparations

Proprietary Preparations (details are given in Part 3)

Belg.: Acupan; ***Fr.:*** Acupan; ***Ger.:*** Ajan†; Silentan†; ***Irl.:*** Acupan; ***Ital.:*** Nefam†; Oxadol†; ***NZ:*** Acupan; ***Rus.:*** Oxadol (Оксадол); ***Switz.:*** Acupan†; ***UK:*** Acupan.

Nepafenac *(USAN, rINN)*

AHR-9434; AL-6515; Népafénac; Nepafenaco; Nepafenacum. 2-(2-Amino-3-benzoylphenyl)acetamide.

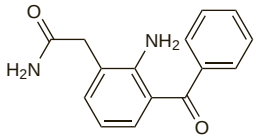
Непафенак

$C_{15}H_{14}N_2O_2$ = 254.3.

CAS — 78281-72-8.

ATC — S01BC10.

ATC Vet — QS01BC10.



Profile

Nepafenac, an NSAID (p.96), is a prodrug of amfenac. It is used in the treatment of pain and inflammation following cataract surgery. An ophthalmic suspension containing nepafenac 0.1% is instilled 3 times daily starting on the day before surgery and continuing for 2 weeks after surgery.

◊ References.

1. Colin J, Paquette B. Comparison of the analgesic efficacy and safety of nepafenac ophthalmic suspension compared with diclofenac ophthalmic solution for ocular pain and photophobia after excimer laser surgery: a phase II, randomized, double-masked trial. *Clin Ther* 2006; **28:** 527–36.
2. Lane SS. Nepafenac: a unique nonsteroidal prodrug. *Int Ophthalmol Clin* 2006; **46:** 13–20.
3. Lane SS, *et al.* Nepafenac ophthalmic suspension 0.1% for the prevention and treatment of ocular inflammation associated with cataract surgery. *J Cataract Refract Surg* 2007; **33:** 53–8. Correction. *ibid.*; 564.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Nevanac; ***Chile:*** Nevanac; ***Cz.:*** Nevanac; ***Port.:*** Nevanac; ***USA:*** Nevanac.

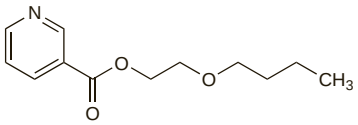
Nicoboxil *(rINN)*

Butoxyethyl Nicotinate; Nicoboxilo; Nicoboxilum. 2-Butoxyethyl nicotinate.

Никобоксил

$C_{12}H_{17}NO_3$ = 223.3.

CAS — 13912-80-6.



Profile

Nicoboxil is a nicotinate used in topical preparations as a rubefacient. It is also included in some topical preparations used for the treatment of acne vulgaris.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austral.:*** Finalgon; ***Austria:*** Finalgon; ***Canad.:*** Finalgon†; ***Ger.:*** Finalgon; ***Ital.:*** Anti-Acne; ***NZ:*** Finalgon†; ***Port.:*** Finalgon; ***Rus.:*** Betalgon (Беталгон); Betanicomylon (Бетаникомилон); Finalgon (Финалгон); ***Spain:*** Finalgon; ***UK:*** Actinac.

Nicomorphine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de nicomorfina; Nicomorphine, Chlorhydrate de; Nicomorphini Hydrochloridum. 3,6-Di-*O*-nicotinoylmorphine hydrochloride; (–)-(5*R*,6*S*)-4,5-Epoxy-9a-methylmorphin-7-en-3,6-diyl dinicotinate hydrochloride.

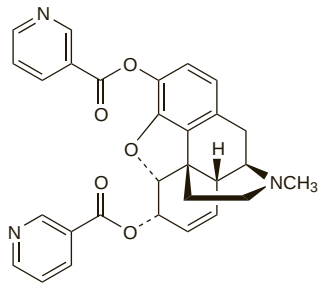
Никоморфина Гидрохлорид

$C_{29}H_{25}N_3O_5$,HCl = 532.0.

CAS — 639-48-5 (nicomorphine); 12040-41-4 (nicomorphine hydrochloride); 35055-78-8 (nicomorphine xHCl).

ATC — N02AA04.

ATC Vet — QN02AA04.



(nicomorphine)

Profile

Nicomorphine hydrochloride is an opioid analgesic (p.101) used in the treatment of moderate to severe pain. It is given in oral doses of 5 to 10 mg daily or by intramuscular, slow intravenous, or subcutaneous injection in doses of 10 to 20 mg; higher doses have also been used. It may also be given rectally in usual doses of 10 to 20 mg daily.

◊ References.

1. Koopman-Kimenai PM, *et al.* Pharmacokinetics of intravenously administered nicomorphine and its metabolites in man. *Eur J Anaesthesiol* 1993; **10:** 125–32.
2. Koopman-Kimenai PM, *et al.* Rectal administration of nicomorphine in patients improves biological availability of morphine and its glucuronide conjugates. *Pharm World Sci* 1994; **16:** 248–53.
3. Koopman-Kimenai PM, *et al.* The bioavailability of intramuscularly administered nicomorphine (Vilan) with its metabolites and their glucuronide conjugates in surgical patients. *Int J Clin Pharmacol Ther* 1995; **33:** 442–8.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Vilan; ***Denm.:*** Vilan; ***Neth.:*** MorZet; Vilan†; ***Switz.:*** Vilan.

Niflumic Acid *(rINN)*

Acide niflumique; Ácido niflúmico; Acidum niflumicum; UP-83. 2-(ααα-Trifluoro-*m*-toluidino)nicotinic acid.

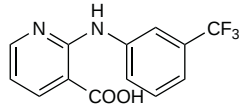
Нифлумовая Кислота

$C_{13}H_9F_3N_2O_2$ = 282.2.

CAS — 4394-00-7.

ATC — M01AX02; M02AA17.

ATC Vet — QM01AX02; QM02AA17.



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

Ph. Eur. 6.2 (Niflumic Acid). A pale yellow, crystalline powder. Practically insoluble in water; soluble in alcohol and in methyl alcohol; freely soluble in acetone.

Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96.

Fluoride-associated osteosis has been reported with prolonged use. Niflumic acid should be stopped if hypersensitivity skin reactions appear.

Effects on the skin. From a case-control study[1] of children admitted to a hospital emergency department in Italy it was calculated that the odds-ratio of users of niflumic acid, or its derivative morniflumate, developing serious cutaneous reactions was 4.9. Given this figure and the fact that safer drugs were available the authors considered that there was no indication for which niflumic acid was required in children. However, a large cohort study[2] involving 193 727 children aged between 0 and 14 years found that niflumic acid was not associated with a higher risk of mucocutaneous reactions when compared with other NSAIDs or paracetamol. The authors of the later study suggested that the conclusions of the original study may have been confounded because there was no adjustment for age or indication.

1. Menniti-Ippolito F, *et al.* Niflumic acid and cutaneous reactions in children. *Arch Dis Child* 2001; **84:** 430–1.
2. Sturkenboom M, *et al.* Incidence of mucocutaneous reactions in children treated with niflumic acid, other nonsteroidal antiinflammatory drugs, or nonopioid analgesics. Abstract: *Pediatrics* 2005; **116:** 212. Full version: http://pediatrics.aappublications.org/cgi/content/full/116/1/e26 (accessed 08/11/07)

Uses and Administration

Niflumic acid, a nicotinic acid derivative, is an NSAID (p.99). It has been used in inflammatory and musculoskeletal and joint disorders in usual oral doses of about 250 mg three or four times daily; up to 1500 mg daily has been used in severe disorders. It has also been used topically as a 3% cream or ointment or 2.5% gel. The morpholinoethyl ester, morniflumate (p.86), has similar uses.

Niflumic acid glycinamide has been used topically in inflammatory mouth disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Flogovital; ***Belg.:*** Niflugel; Nifluril; ***Cz.:*** Niflugel; Nifluril; ***Fr.:*** Flunir†; Niflugel; Nifluril; ***Gr.:*** Niflamol; Novopone†; ***Hung.:*** Donalgin; ***Ital.:*** Niflam; ***Port.:*** Nifluril; ***Rus.:*** Donalgin (Доналгин); ***Spain:*** Niflactol.

Multi-ingredient: ***Arg.:*** Flogodisten.

Nimesulide *(BAN, rINN)*

Nimesulid; Nimesulida; Nimesulidas; Nimésulide; Nimesulidi; Nimesulidinum; Nimesulidum; Nimeszulid; R-805. 4′-Nitro-2′-phenoxymethanesulphonanilide.

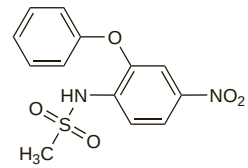
Нимесулид

$C_{13}H_{12}N_2O_5S$ = 308.3.

CAS — 51803-78-2.

ATC — M01AX17.

ATC Vet — QM01AX17.



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

Ph. Eur. 6.2 (Nimesulide). A yellowish crystalline powder. It exhibits polymorphism. Practically insoluble in water; slightly soluble in dehydrated alcohol; freely soluble in acetone.

Profile

Nimesulide is an NSAID (p.96) reported to be a selective inhibitor of cyclo-oxygenase-2 (COX-2). It may be given in oral doses of up to 100 mg twice daily for inflammatory conditions, fever, pain, and dysmenorrhoea; use in the EU is limited to a maximum of 15 days due to reports of hepatotoxicity (see Adverse Effects, below). It has also been given rectally in a dose of 200 mg twice daily or applied topically as a 3% gel. Nimesulide betadex (nimesulide betacyclodextrin complex) has been used similarly.

◊ References.

1. Bennett A, *et al.* Nimesulide: a multifactorial therapeutic approach to the inflammatory process? a 7-year clinical experience. *Drugs* 1993; **46:** (suppl 1): 1–283.
2. Senna GE, *et al.* Nimesulide in the treatment of patients intolerant of aspirin and other NSAIDs. *Drug Safety* 1996; **14:** 94–103.
3. Vizzardi M, *et al.* Nimesulide beta cyclodextrin (nimesulide-betadex) versus nimesulide in the treatment of pain after arthroscopic surgery. *Curr Ther Res* 1998; **59:** 162–71.
4. Bernareggi A. Clinical pharmacokinetics of nimesulide. *Clin Pharmacokinet* 1998; **35:** 247–74.
5. Shah AA, *et al.* Selective inhibition of COX-2 in humans is associated with less gastrointestinal injury: a comparison of nimesulide and naproxen. *Gut* 2001; **48:** 339–46.
6. Nüing RM, *et al.* Pathogenetic role of cyclooxygenase-2 in hyperprostaglandin E syndrome/antenatal Bartter syndrome: therapeutic use of the cyclooxygenase-2 inhibitor nimesulide. *Clin Pharmacol Ther* 2001; **70:** 384–90.

Adverse effects. Although *thrombocytopenia* is a common feature in patients infected with HIV, a group of workers considered that thrombocytopenia in one of their patients was related to the use of nimesulide.[1]

There have been reports[2-4] of *hepatotoxicity* after treatment with nimesulide. Data from spontaneous reports has also suggested that nimesulide may be associated with a higher risk of hepatotoxicity than other NSAIDs.[4] A cohort study[5] involving about 400 000 users of NSAIDs in one region of Italy between 1997 and 2001 found that those taking nimesulide were 1.3 times more likely to develop hepatotoxicity than users of other NSAIDs and 1.9 times more likely to suffer severe liver injury. In May 2007 the Irish regulatory authority withdrew nimesulide from the Irish market after concerns about hepatotoxicity.[6] Since being licensed in 1995, nimesulide had generated 53 adverse reaction reports involving liver toxicity, including 9 cases of liver failure, 3 of which resulted in death and 6 in liver transplantation; there had also been 1 other liver-related fatality. The EMEA[7] subsequently recommended that treatment with nimesulide should be limited to 15 days.

There have been reports[8,9] of *toxic pustuloderma* (acute generalised exanthematous pustulosis) after receiving oral nimesulide. *Fixed drug eruptions* have also been seen.[10]

An infant developed hypotension and hypothermia after inadvertently taking an *overdose* of 8 times the recommended daily dose of nimesulide.[11] The patient recovered after gastric lavage with activated charcoal and supportive therapy.

1. Pasticci MB, *et al.* Nimesulide, thrombocytopenic purpura, and human immunodeficiency virus (HIV) infection. *Ann Intern Med* 1990; **112:** 233–4.