Nepafenac *(USAN, rINN)*

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

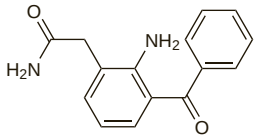
Непафенак

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

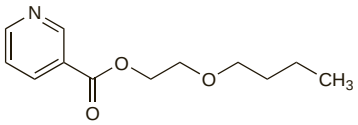
Nicoboxil *(rINN)*

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.

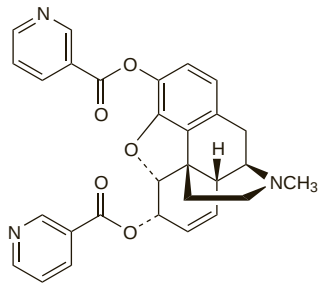
Никоморфина Гидрохлорид

$C_{29}H_{25}N_3O_5$,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.

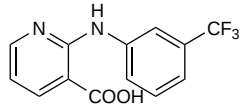
Нифлумовая Кислота

$C_{13}H_9F_3N_2O_2$ = 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.

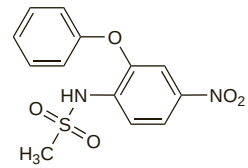
Нимесулид

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