*Purdue Frederick, USA*); these increases were considered potentially lethal, even in opioid-tolerant patients.[1] Subsequently, this formulation was voluntarily withdrawn by the US manufacturer in July 2005.

1. Food and Drug Administration. FDA alert for healthcare professionals: alcohol-Palladone interaction (issued 13th July, 2005). Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/hydromorphoneHCP.pdf (accessed 26/06/08)

### Pharmacokinetics

Hydromorphone hydrochloride is rapidly but incompletely absorbed from the gastrointestinal tract after oral doses; peak plasma concentrations occur within 0.5 to 1 hour. Oral bioavailability is about 50% as it undergoes extensive first-pass metabolism. Hydromorphone is about 8 to 19% bound to plasma proteins. A plasma elimination half-life of about 2.5 hours has been reported after oral or intravenous doses. Hydromorphone appears to be widely distributed in the tissues; it crosses the placenta and is distributed into breast milk. It is extensively metabolised by glucuronidation in the liver and excreted in the urine mainly as conjugated hydromorphone, dihydroisomorphine, and dihydromorphine.

◊ References.

1. Vallner JJ, *et al.* Pharmacokinetics and bioavailability of hydromorphone following intravenous and oral administration to human subjects. *J Clin Pharmacol* 1981; **21:** 152–6.
2. Parab PV, *et al.* Pharmacokinetics of hydromorphone after intravenous, peroral and rectal administration to human subjects. *Biopharm Drug Dispos* 1988; **9:** 187–99.
3. Vashi V, *et al.* Clinical pharmacology and pharmacokinetics of once-daily hydromorphone hydrochloride extended-release capsules. *J Clin Pharmacol* 2005; **45:** 547–54.

### Uses and Administration

Hydromorphone hydrochloride, a phenanthrene derivative, is an opioid analgesic (p.104). It is related to morphine (p.89) but with a greater analgesic potency. Hydromorphone hydrochloride is used for the relief of moderate to severe pain and for the relief of non-productive cough.

In the treatment of **pain**, hydromorphone hydrochloride is a useful alternative to morphine for subcutaneous use since its greater solubility in water allows a smaller dose volume. After injection onset of action usually occurs within 15 minutes and analgesia is reported to last for more than 5 hours; after oral doses onset of analgesia is usually within 30 minutes. It is given by subcutaneous or intramuscular injection in initial doses of 1 to 2 mg every 4 to 6 hours as necessary. It may also be given by slow intravenous injection or by intravenous or subcutaneous infusion, with doses adjusted according to individual requirements. Higher parenteral doses may be given to opioid-tolerant patients using a highly concentrated solution containing 10 mg/mL that allows smaller dose volumes. In the UK, the initial oral dose is 1.3 mg every 4 hours; thereafter the dose may be increased as necessary. In the USA, initial oral doses of 2 mg may be given every 4 to 6 hours; doses may be increased to 4 mg or more for severe pain. Modified-release preparations are available for less frequent administration, but see Alcohol, under Interactions, above. By rectum, the usual dose is 3 mg every 6 to 8 hours.

For the relief of non-productive **cough** hydromorphone hydrochloride is given, as a syrup, in doses of 1 mg repeated every 3 to 4 hours.

◊ References.

1. Bruera E, *et al.* A randomized, double-blind, double-dummy, crossover trial comparing the safety and efficacy of oral sustained-release hydromorphone with immediate-release hydromorphone in patients with cancer pain. *J Clin Oncol* 1996; **14:** 1713–17.
2. Miller MG, *et al.* Continuous subcutaneous infusion of morphine vs. hydromorphone: a controlled trial. *J Pain Symptom Manage* 1999; **18:** 9–16.
3. Quigley C. Hydromorphone for acute and chronic pain. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 26/06/08).
4. Murray A, Hagen NA. Hydromorphone. *J Pain Symptom Manage* 2005; **29** (suppl): S57–S66.
5. Grosset AB, *et al.* Comparative efficacy of oral extended-release hydromorphone and immediate-release hydromorphone in patients with persistent moderate to severe pain: two randomized controlled trials. *J Pain Symptom Manage* 2005; **29:** 584–94.
6. Du Pen S, *et al.* Intrathecal hydromorphone for intractable nonmalignant pain: a retrospective study. *Pain Med* 2006; **7:** 10–15.
7. Chang AK, *et al.* Safety and efficacy of hydromorphone as an analgesic alternative to morphine in acute pain: a randomized clinical trial. *Ann Emerg Med* 2006; **48:** 164–72.

### Preparations

***USP 31:*** Hydromorphone Hydrochloride Injection; Hydromorphone Hydrochloride Tablets.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Dolonovag; ***Austral.:*** Dilaudid; ***Austria:*** Dilaudid; Hydal; ***Belg.:*** Palladone; ***Canad.:*** Dilaudid; Hydromorph; ***Cz.:*** Jurnista; Palladone; ***Denm.:*** Opidol†; Palladon; ***Fin.:*** Palladon; ***Fr.:*** Sophidone; ***Ger.:*** Dilaudid; Palladon; ***Hung.:*** Palladone; ***Irl.:*** Palladone; ***Israel:*** Palladone; ***Mex.:*** Liberaxim; ***Neth.:*** Palladon; ***Norw.:*** Palladon; ***NZ:*** Dilaudid†; ***Port.:*** Jurnista; Palladone; ***Swed.:*** Opidol†; Palladon; ***Switz.:*** Palladon; ***UK:*** Palladone; ***USA:*** Dilaudid; Palladone†.

**Multi-ingredient:** ***Swed.:*** Dilaudid-Atropin; ***Switz.:*** Dilaudid-Atropin†; ***USA:*** Dilaudid Cough.

---

## Ibuprofen *(BAN, USAN, rINN)*

Ibuprofeeni; Ibuprofén; Ibuprofenas; Ibuprofène; Ibuprofeno; Ibuprofenum; RD-13621; U-18573. 2-(4-Isobutylphenyl)propionic acid.

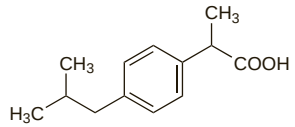
Ибупрофен

$C_{13}H_{18}O_2$ = 206.3.

*CAS — 15687-27-1.*

*ATC — C01EB16; G02CC01; M01AE01; M02AA13.*

*ATC Vet — QC01EB16; QG02CC01; QM01AE01; QM02AA13.*



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

**Ph. Eur. 6.2** (Ibuprofen). A white or almost white, crystalline powder or colourless crystals. M.p. 75° to 78°. Practically insoluble in water; freely soluble in acetone, in dichloromethane, and in methyl alcohol; it dissolves in dilute solutions of alkali hydroxides and carbonates.

**USP 31** (Ibuprofen). A white to off-white crystalline powder having a slight characteristic odour. Practically insoluble in water; very soluble in alcohol, in acetone, in chloroform, and in methyl alcohol; slightly soluble in ethyl acetate. Store in airtight containers.

### Ibuprofen Lysine *(USAN)*

Ibuprofen Lysinate; Soluphene. Lysine 2-(4-isobutylphenyl)propionate.

Ибупрофен Лизин

$C_{19}H_{32}N_2O_4$ = 352.5.

*CAS — 57469-77-9.*

*ATC — C01EB16; G02CC01; M01AE01; M02AA13.*

*ATC Vet — QC01EB16; QG02CC01; QM01AE01; QM02AA13.*

**Stability.** Solutions of ibuprofen lysine in Water for Injections stored at room temperature were found to be most stable when protected from light.[1]

1. Volonté MG, *et al.* Stability of ibuprofen in injection solutions. *Am J Health-Syst Pharm* 2005; **62:** 630–3.

### Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96. Ibuprofen may be better tolerated than other NSAIDs.

Adverse effects that may be associated with the use of ibuprofen injection in premature **neonates** include intraventricular haemorrhage, periventricular leucomalacia, bronchopulmonary dysplasia, pulmonary haemorrhage, necrotising enterocolitis, intestinal perforation, oliguria, fluid retention, and haematuria; hypoxaemia and gastrointestinal haemorrhage have also been reported. In addition ibuprofen injection should not be given to neonates with life-threatening infection, with significant renal impairment, or with known or suspected necrotising enterocolitis. Infants who are bleeding (especially gastrointestinal bleeding or intracranial haemorrhage) or who have thrombocytopenia or coagulation defects should also not be given parenteral ibuprofen, and those given it should be monitored during treatment for signs of bleeding. Renal function should be monitored and if anuria or marked oliguria is evident at the time of a scheduled second or third dose, it should be delayed until renal function has returned to normal.

Symptoms of nausea, vomiting, and tinnitus have been reported after ibuprofen overdosage. More serious toxicity is uncommon, but gastric emptying followed by supportive measures is recommended if the quantity ingested within the previous hour exceeds 400 mg/kg.

**Breast feeding.** No adverse effects have been seen in breast-fed infants whose mothers were receiving ibuprofen, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with breast feeding. The *BNF* also considers the amount of ibuprofen distributed into breast milk to be too small to be harmful to a breast-fed infant. A study[2] estimated that a breast-fed infant would ingest about 0.0008% of the maternal dose. However, licensed product information for some preparations, including some topical preparations, recommends that breast feeding should be avoided during ibuprofen treatment.

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 07/11/07)
2. Walter K, Dilger C. Ibuprofen in human milk. *Br J Clin Pharmacol* 1997; **44:** 211–12.

**Children.** An analysis[1] of the outcome of treatment of 83 915 children found that the risk of hospitalisation for gastrointestinal bleeding, renal failure, or anaphylaxis was no greater in children given ibuprofen than in those given paracetamol.

1. Lesko SM, Mitchell AA. An assessment of the safety of pediatric ibuprofen. *JAMA* 1995; **273:** 929–33.

**Effects on the blood.** Blood disorders including agranulocytosis, aplastic anaemia,[1] pure white-cell aplasia,[2] and thrombocytopenia[3] have been reported in patients taking ibuprofen. Fatal haemolytic anaemia occurred in a man taking ibuprofen and oxazepam.[4]

1. Gryfe CI, Rubenzahl S. Agranulocytosis and aplastic anemia possibly due to ibuprofen. *Can Med Assoc J* 1976; **114:** 877.
2. Mamus SW, *et al.* Ibuprofen-associated pure white-cell aplasia. *N Engl J Med* 1986; **314:** 624–5.
3. Jain S. Ibuprofen-induced thrombocytopenia. *Br J Clin Pract* 1994; **48:** 51.
4. Guidry JB, *et al.* Fatal autoimmune hemolytic anemia associated with ibuprofen. *JAMA* 1979; **242:** 68–9.

**Effects on the cardiovascular system.** For a discussion of the cardiovascular effects of NSAIDs, including ibuprofen, see p.96.

**Effects on the CNS.** Aseptic meningitis has occurred in patients taking NSAIDs. A review[1] of NSAID-related CNS adverse effects summarised 23 literature reports of NSAID-associated aseptic meningitis; 17 reports involved ibuprofen, 4 sulindac, 1 naproxen, and 1 tolmetin. Of the 23 reports, 11 were in patients with a diagnosis of SLE. Typically the reaction is seen in patients who have just restarted NSAID therapy after a gap in their treatment. Within a few hours of restarting the NSAID the patient experiences fever, headache, and a stiff neck; abdominal pain may be present. The patient may become lethargic and eventually comatose. Symptoms resolve if the NSAID is stopped. It is believed to be a hypersensitivity reaction but there does not appear to be cross-reactivity between NSAIDs.

Similar conclusions have also been reported more recently.[2] After experience of 2 cases, a review of the literature identified 71 episodes of ibuprofen-induced aseptic meningitis in 36 patients; 22 patients had recurrent episodes after repeated ibuprofen use. An underlying auto-immune connective tissue disorder was noted in 22 patients of whom 14 had SLE, 6 had an undifferentiated or mixed disorder, 1 had rheumatoid arthritis , and 1 had Sjögren's syndrome. In most cases, symptoms developed within 24 hours of starting ibuprofen although 1 patient had been taking ibuprofen for 2 years before the onset of symptoms. Cross-reactivity was reported in only 1 patient who had also developed aseptic meningitis with both naproxen and rofecoxib.

1. Hoppmann RA, *et al.* Central nervous system side effects of nonsteroidal anti-inflammatory drugs: aseptic meningitis, psychosis, and cognitive dysfunction. *Arch Intern Med* 1991; **151:** 1309–13.
2. Rodríguez SC, *et al.* Characteristics of meningitis caused by ibuprofen: report of 2 cases with recurrent episodes and review of the literature. *Medicine* 2006; **85:** 214–20.

**Effects on electrolytes.** Hyponatraemia has been described in patients receiving ibuprofen;[1-3] other risk factors such as pre-existing renal impairment or use with desmopressin were generally present.

1. Blum M, Aviram A. Ibuprofen induced hyponatraemia. *Rheumatol Rehabil* 1980; **19:** 258–9.
2. Rault RM. Case report: hyponatremia associated with nonsteroidal antiinflammatory drugs. *Am J Med Sci* 1993; **305:** 318–20.
3. García EBG, *et al.* Hyponatraemic coma induced by desmopressin and ibuprofen in a woman with von Willebrand's disease. *Haemophilia* 2003; **9:** 232–4.

**Effects on the eyes.** Reversible amblyopia has been reported in patients receiving ibuprofen.[1,2] For reference to effects on the optic nerve associated with ibuprofen, see p.97.

1. Collum LMT, Bowen DI. Ocular side-effects of ibuprofen. *Br J Ophthalmol* 1971; **55:** 472–7.
2. Palmer CAL. Toxic amblyopia from ibuprofen. *BMJ* 1972; **3:** 765.

**Effects on the gastrointestinal tract.** Ibuprofen may be associated with a lower risk of upper gastrointestinal effects than some other NSAIDs, but nonetheless it can cause dyspepsia, nausea and vomiting, gastrointestinal bleeding, and peptic ulcers and perforation. Colitis and its exacerbation have occurred.[1,2]

1. Ravi S, *et al.* Colitis caused by non-steroidal anti-inflammatory drugs. *Postgrad Med J* 1986; **62:** 773–6.
2. Clements D, *et al.* Colitis associated with ibuprofen. *BMJ* 1990; **301:** 987.

**Effects on the kidneys.** Reports of adverse renal effects with ibuprofen include an increase in serum creatinine concentration,[1] acute renal failure,[2-6] and nephrotic syndrome.[7] Cystitis, haematuria, and interstitial nephritis may occur. Acute flank pain and reversible renal dysfunction has been reported in some patients treated with ibuprofen.[8,9] See also Effects on Electrolytes, above.

1. Whelton A, *et al.* Renal effects of ibuprofen, piroxicam, and sulindac in patients with asymptomatic renal failure: a prospective, randomized, crossover comparison. *Ann Intern Med* 1990; **112:** 568–76.
2. Brandstetter RD, Mar DD. Reversible oliguric renal failure associated with ibuprofen treatment. *BMJ* 1978; **2:** 1194–5.
3. Kimberly RP, *et al.* Apparent acute renal failure associated with therapeutic aspirin and ibuprofen administration. *Arthritis Rheum* 1979; **22:** 281–5.
4. Spierto RJ, *et al.* Acute renal failure associated with the use of over-the-counter ibuprofen. *Ann Pharmacother* 1992; **26:** 714.
5. Fernando AHN, *et al.* Renal failure after topical use of NSAIDs. *BMJ* 1994; **308:** 533.
6. Moghal NE, *et al.* Ibuprofen and acute renal failure in a toddler. *Arch Dis Child* 2004; **89:** 276–7.
7. Justiniani FR. Over-the-counter ibuprofen and nephrotic syndrome. *Ann Intern Med* 1986; **105:** 303.
8. McIntire SC, *et al.* Acute flank pain and reversible renal dysfunction associated with nonsteroidal anti-inflammatory drug use. *Pediatrics* 1993; **92:** 459–60.
9. Wattad A, *et al.* A unique complication of nonsteroidal anti-inflammatory drug use. *Pediatrics* 1994; **93:** 693.

**Effects on the liver.** Raised liver transaminase values were noted in 3 patients with chronic hepatitis C infection after taking ibuprofen.[1] Values returned to normal on stopping the drug; the effect recurred in one patient who was re-exposed. Other hepatic adverse effects reported with ibuprofen include hepatitis[2] and liver failure.[3].

See also Effects on the Skin, below.

1. Riley TR, Smith JP. Ibuprofen-induced hepatotoxicity in patients with chronic hepatitis C: a case series. *Am J Gastroenterol* 1998; **93:** 1563–5.
2. Borel I, *et al.* Hépatite aiguë sévère après prise d'ibuprofène. *Gastroenterol Clin Biol* 2001; **25:** 430–2.
3. Rodríguez-González FJ, *et al.* Orthotopic liver transplantation after subacute liver failure induced by therapeutic doses of ibuprofen. *Am J Gastroenterol* 2002; **97:** 2476–7.

**Effects on the skin.** Skin rashes may occur during hypersensitivity reactions although serious dermatological effects attributed to ibuprofen are rare. Reports of more serious effects have included Stevens-Johnson syndrome (often associated with hepatotoxicity),[1-4] photosensitivity,[5] and bullous leukocytoclastic vasculitis.[6]

1. Sternlieb P, Robinson RM. Stevens-Johnson syndrome plus toxic hepatitis due to ibuprofen. *N Y State J Med* 1978; **78:** 1239–43.
2. Srivastava M, *et al.* Drug-associated acute-onset vanishing bile duct and Stevens-Johnson syndromes in a child. *Gastroenterology* 1998; **115:** 743–6.
3. Health Canada. Ibuprofen: Stevens-Johnson syndrome. *Can Adverse React News* 2005; **15** (3): 3. Also available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/carn-bcei_v15n3-eng.pdf (accessed 29/08/08)
4. Taghian M, *et al.* Acute vanishing bile duct syndrome after ibuprofen therapy in a child. *J Pediatr* 2004; **145:** 273–6.
5. Bergner T, Przybilla B. Photosensitization caused by ibuprofen. *J Am Acad Dermatol* 1992; **26:** 114–16.
6. Davidson KA, *et al.* Ibuprofen-induced bullous leukocytoclastic vasculitis. *Cutis* 2001; **67:** 303–7.

**Hypersensitivity.** A fatal asthma attack occurred in a 65-year-old woman, with adult-onset asthma, 30 minutes after ingestion of ibuprofen 800 mg.[1]

For other hypersensitivity reactions or possible reactions see also Effects on the CNS and Effects on the Skin, above.

1. Ayres JG, *et al.* Asthma death due to ibuprofen. *Lancet* 1987; **i:** 1082.

**Meningitis.** For reports of aseptic meningitis after use of ibuprofen, see Effects on the CNS, above.

**Overdosage.** There was a substantial increase in the number of cases of ibuprofen overdose reported to the National Poisons Information Service of the UK in the 2 years after its introduction as an 'over-the-counter' medication.[1] However, no concurrent increase in severity of poisoning was found and in only 1 of 203 cases was ibuprofen thought to have caused serious problems. It was concluded that ibuprofen appeared to be much less toxic in acute overdose than either aspirin or paracetamol. Current advice is that doses below 100 mg/kg are unlikely to cause toxicity in *children*, whereas clinical features will occur in children who have ingested more than 400 mg/kg. In *adults* the dose-response effect is less clear cut, but those who have ingested less than 100 mg/kg are unlikely to require treatment.

Nonetheless, reports illustrate the complexity of major overdosage with ibuprofen. A syndrome of coma, hyperkalaemia with cardiac arrhythmias, metabolic acidosis, pyrexia, and respiratory and renal failure was reported[2] in a 17-year-old man after major overdosage with ibuprofen and minor overdosage with doxepin. Hyperkalaemia was not evident until 14 hours after hospital admission and was thought to be due to a combination of potassium replacement for initial hypokalaemia, acidosis, muscle damage, and ibuprofen-induced renal failure. A 6-year-old child developed[3] shock, coma, and metabolic acidosis after ingestion of a dose of ibuprofen equivalent to 300 mg/kg. Treatment consisting of intubation, mechanical ventilation, fluid resuscitation, gastric lavage, and activated charcoal proved successful. In another report,[4] in which a 21-month-old child had ingested the equivalent of 500 mg/kg of ibuprofen, the presenting symptoms were acute renal failure with severe metabolic acidosis. The child developed tonic-clonic seizures 46 hours after ingestion, with significant hypocalcaemia and hypomagnesaemia, which may have been exacerbated by use of sodium polystyrene sulfonate and furosemide. The seizures, which could not be controlled with diazepam, phenytoin, and phenobarbital, ceased on correction of electrolyte balance.

1. Perry SJ, *et al.* Ibuprofen overdose: the first two years of over–the–counter sales. *Hum Toxicol* 1987; **6:** 173–8.
2. Menzies DG, *et al.* Fulminant hyperkalaemia and multiple complications following ibuprofen overdose. *Med Toxicol Adverse Drug Exp* 1989; **4:** 468–71.
3. Zuckerman GB, Uy CC. Shock, metabolic acidosis, and coma following ibuprofen overdose in a child. *Ann Pharmacother* 1995; **29:** 869–71.
4. Al-Harbi NN, *et al.* Hypocalcemia and hypomagnesemia after ibuprofen overdose. *Ann Pharmacother* 1997; **31:** 432–4.

## Interactions

For interactions associated with NSAIDs, see p.99.

**Antineoplastics.** For the effect of ibuprofen on the metabolism of *pemetrexed*, see p.762.

**Aspirin.** It has been suggested that ibuprofen may reduce the cardioprotective effect of aspirin but see NSAIDS under Interactions of Aspirin, p.23.

**Lipid regulating drugs.** For a report of rhabdomyolysis and renal failure attributed to an interaction between ibuprofen and *ciprofibrate*, see p.1233.

**Muscle relaxants.** *Baclofen* toxicity may develop after starting ibuprofen; for further details, see p.1888.

## Pharmacokinetics

Ibuprofen is absorbed from the gastrointestinal tract and peak plasma concentrations occur about 1 to 2 hours after ingestion. Ibuprofen is also absorbed on rectal use. It is partially absorbed after topical application to the skin; some licensed product information states that percutaneous absorption from topical gel is about 5% of that from an oral dose form. Ibuprofen is 90 to 99% bound to plasma proteins and has a plasma half-life of about 2 hours. It is rapidly excreted in the urine mainly as metabolites and their conjugates. About 1% is excreted in urine as unchanged ibuprofen and about 14% as conjugated ibuprofen. There appears to be little if any distribution into breast milk.

The above figures refer to racemic ibuprofen. However, ibuprofen's disposition is stereoselective and there is some metabolic conversion of the inactive *R*-(−)-enantiomer to the active *S*-(+)-enantiomer, dexibuprofen (p.39).

◊ References.

1. Davies NM. Clinical pharmacokinetics of ibuprofen: the first 30 years. *Clin Pharmacokinet* 1998; **34:** 101–54.
2. Sharma PK, *et al.* Pharmacokinetics of oral ibuprofen in premature infants. *J Clin Pharmacol* 2003; **43:** 968–73.
3. Gregoire N, *et al.* Population pharmacokinetics of ibuprofen enantiomers in very premature neonates. *J Clin Pharmacol* 2004; **44:** 1114–24.
4. Han EE, *et al.* Pharmacokinetics of ibuprofen in children with cystic fibrosis. *Clin Pharmacokinet* 2004; **43:** 145–56.
5. Hao H, *et al.* Enantioselective pharmacokinetics of ibuprofen and involved mechanisms. *Drug Metab Rev* 2005; **37:** 215—34.
6. Kyllonen M, *et al.* Perioperative pharmacokinetics of ibuprofen enantiomers after rectal administration. *Paediatr Anaesth* 2005; **15:** 566–73.

## Uses and Administration

Ibuprofen, a propionic acid derivative, is an NSAID (p.99). Its anti-inflammatory properties may be weaker than those of some other NSAIDs.

Ibuprofen is used in the management of mild to moderate pain and inflammation in conditions such as dysmenorrhoea, headache including migraine, postoperative pain, dental pain, musculoskeletal and joint disorders such as ankylosing spondylitis, osteoarthritis, and rheumatoid arthritis including juvenile idiopathic arthritis, peri-articular disorders such as bursitis and tenosynovitis, and soft-tissue disorders such as sprains and strains. It is also used to reduce fever.

Ibuprofen is also used as an alternative to indometacin in the treatment of patent ductus arteriosus.

The usual **oral** dose for painful conditions is 1.2 to 1.8 g daily in divided doses although maintenance doses of 600 mg to 1.2 g daily may be effective in some patients. If necessary the dose may be increased; in the UK the maximum recommended dose is 2.4 g daily whereas in the USA it is 3.2 g daily. Modified-release preparations of ibuprofen are available for once- or twice-daily dosing, although actual dosages vary with different preparations. Patients with rheumatoid arthritis generally require higher doses of ibuprofen than those with osteoarthritis. The recommended dose for fever reduction is 200 to 400 mg every 4 to 6 hours to a maximum of 1.2 g daily. For oral doses in children, see Administration in Children, below.

Ibuprofen may be given **parenterally** in the treatment of patent ductus arteriosus in preterm infants; for details of doses, see below.

Ibuprofen is applied **topically** as a 5% cream, foam, gel, or spray solution; a 10% gel is also available. It is also used topically as a dressing containing 500 micrograms/cm$^2$ of ibuprofen for the management of ulcers and superficial wounds.

Ibuprofen is usually given as the base but **derivatives**, including various salts, esters, and other complexes, have also been used. These include lysine (see Patent Ductus Arteriosus, below) and sodium salts, guaiacol and pyridoxine esters, and mabuprofen (ibuprofen aminoethanol), isobutanolammonium, and meglumine derivatives.

Ibuprofen is usually given as a racemic mixture but preparations containing only the *S*-(+)-isomer dexibuprofen (p.39) are available in some countries.

**Administration in children.** In the UK, the following oral doses of ibuprofen, given according to age, are recommended by the *BNFC* for the treatment of **pain**, **inflammation**, or **fever** in children:

- 1 to 3 months: 5 mg/kg 3 or 4 times daily
- 3 to 6 months: 50 mg 3 times daily
- 6 to 12 months: 50 mg 3 or 4 times daily
- 1 to 4 years: 100 mg 3 times daily
- 4 to 7 years: 150 mg 3 times daily
- 7 to 10 years: 200 mg 3 times daily
- 10 to 12 years: 300 mg 3 times daily
- 12 to 18 years: 200 to 400 mg 3 or 4 times daily increased, if necessary, to a maximum of 2.4 g daily
- in *severe* conditions in children aged between 3 months and 12 years, a dose of 30 mg/kg daily in 3 or 4 divided doses may be given

In the USA, suggested doses for children aged 6 months and over are: for fever, 5 to 10 mg/kg (depending on the severity of the fever) and for pain, 10 mg/kg; doses may be given every 6 to 8 hours up to a maximum daily dose of 40 mg/kg.

In the treatment of **rheumatic disease** including juvenile idiopathic arthritis, the *BNFC* recommends a dose of 10 mg/kg 3 or 4 times daily (maximum 2.4 g daily) in children aged 3 months and over; if necessary up to 60 mg/kg daily in 4 to 6 divided doses (maximum 2.4 g daily) may be given in systemic juvenile idiopathic arthritis.

Similar dosage regimens are also suggested by UK licensed product information; however, ibuprofen use is not generally recommended in children weighing less than 5 kg and some suggest a maximum daily dose of 500 mg in those weighing less than 30 kg. A usual daily dose in the USA for juvenile idiopathic arthritis is 30 to 40 mg/kg in divided doses.

For **post-immunisation pyrexia**, a dose of 50 mg has been recommended; a second dose may be given after 6 hours. If the pyrexia persists after the second dose, medical advice should be sought. Infants aged 2 to 3 months may also be given a 50-mg dose of ibuprofen for post-immunisation pyrexia on the advice of a doctor.

Ibuprofen or its lysine salt are also used in the treatment of **patent ductus arteriosus** in preterm infants; dosage details for this indication are given below.

**Cachexia.** For reference to the use of ibuprofen with megestrol to treat cancer cachexia, see p.2115.

**Cystic fibrosis.** In patients with cystic fibrosis (see p.166), the inflammatory response to chronic pulmonary infection with *Pseudomonas* organisms contributes to lung destruction. NSAIDs have been studied in patients with cystic fibrosis as an alternative to corticosteroids to reduce pulmonary inflammation. A systematic review[1] found evidence in support of using high-dose NSAIDs, most notably ibuprofen, to slow the progression of lung damage in patients with cystic fibrosis. However, there are limited data about the long-term safety of high doses[1] and some consider that this may have limited such use of NSAIDs;[2] others remain to be convinced that a benefit has been demonstrated.[3] The reviewers did consider that there were sufficient data to recommend that NSAIDs be temporarily stopped when intravenous aminoglycosides or other nephrotoxic drugs are used.[1]


1. Lands LC, Stanojevic S. Oral non-steroidal anti-inflammatory drug therapy for cystic fibrosis. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2007 (accessed 07/11/07).
2. Fennel PB, *et al*. Use of high-dose ibuprofen in a pediatric cystic fibrosis center. *J Cyst Fibros* 2007; **6:** 153–8.
3. Bush A, Davies J. Non! to non-steroidal anti-inflammatory therapy for inflammatory lung disease in cystic fibrosis (at least at the moment). *J Pediatr* 2007; **151:** 228–30.


**Pain.** Findings from a long-term study[1] in 585 patients (mean age of 64 years) with knee pain suggested that oral and topical ibuprofen had an equivalent analgesic effect although the former was associated with more minor adverse effects; there was no difference in the rate of major adverse effects.


1. Underwood M, *et al*. Topical or oral ibuprofen for chronic knee pain in older people: the TOIB study. *Health Technol Assess* 2008; **12:** 1–176.


**Patent ductus arteriosus.** Ibuprofen or its lysine salt may be given **parenterally** for the treatment of patent ductus arteriosus (p.68) in preterm infants of less than 34 weeks' gestation; doses are expressed in terms of ibuprofen. Three intravenous doses (infused over 15 minutes) are given at 24-hour intervals; the initial dose is equivalent to 10 mg/kg of ibuprofen followed by two further doses of 5 mg/kg. If, 48 hours after this course of therapy the ductus remains open, a second course may be given, but if this produces no response surgery may be necessary. Ibuprofen injection, *when given as the base*, should be used undiluted, but if necessary it may be reconstituted with sodium chloride 0.9% or glucose 5% for injection. *When given as the lysine salt*, it should be diluted with sodium chloride 0.9% or glucose 5%.

For a suggestion that ibuprofen might be a better choice than indometacin for the treatment of patent ductus arteriosus, see p.68.

### Preparations

***BP 2008:*** Ibuprofen Cream; Ibuprofen Gel; Ibuprofen Oral Suspension; Ibuprofen Tablets;
***USP 31:*** Ibuprofen and Pseudoephedrine Hydrochloride Tablets; Ibuprofen Oral Suspension; Ibuprofen Tablets.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Actron; Acuilfem; Afebril; Algioprofen†; Atomo Desinflamante Ibu; Bistryl†; Brunal†; Butidiona; Causalon Ibu; Copiron; Dolocox†; Dolorsyn; Druisel; Fabogesic; Febratic; Fontol; Ibu; Ibu Evanol; Ibu-Lady†; Ibu-Novalgina; Ibubenitol; Ibucalmin; Ibucler; Ibufabra; Ibufix; Ibulam; Ibumar; Ibumultin; Ibup; Ibupirac; Ibupiretas; Ibuprofenix; Ibuprofex; Ibusi; Ibusol; Ibusumal; Ibutenk; Ibuxim; Ibuzidine; Kesan†; Matrix; Motrax†; Novo Geniol; Oxibut; Pakurat; Paraflex Crema†; Ponstil Mujer; Ponstin; Ponstinetas; Salivia; Sindol; Teprix; Tonal; Vefren; ***Austral.:*** ACT-3; Actiprofen; Advil; Brufen; Bugesic†; Dimetapp Pain & Fever Relief; Hexal Compufen†; Nurofen; Proven; Rafen; Tri-Profen; ***Austria:*** Advil; Aktren; Avallone; Brufen; Dismenol Neu; Dolgit; Dolibu; Dolofort; Duafen; Ibu; Ibudol; Ibufem; Ibugel; Ibumetin; Ibupron; Iburem†; Ibutop; Imbun; Kratalgin; Momento; Nurofen; ratioDolor; Tabcin; Urem†; ***Belg.:*** Adulfen Lysine; Advil Mono; Brufen; Buprophar; Dolofin; Epsilon; Extrapan; Ibu-Slow†; Ibumed; Ibutop; Junifen; Malafene; Nurofebryl; Nurofen; Optalidon Nieuwe Formule; Perdofemina; Perdophen; Perviam; Provenol; Siprofen†; Spidifen; ***Braz.:*** Actiprofen; Advil; Algiflex; Algy-Flanderil†; Alivium; Artril; Dalsy; Doraplax†; Doretrim†; Dorigren; Frenador†; Ib-Profeno†; Ibufran; Ibupril; Ibuprofan; Lombalgina; Motrin; Parartrin; Spidufen; Uniprofen; ***Canad.:*** Advil; Motrin; Novo-Profen; ***Chile:*** Actron; Advil†; Bediatil; Bladex†; Deucodol; Dolorub; Fenpic†; Fortapal; Ibu; Ibu-4†; Ibu-6†; Ibupirac; Ipson; Kin; Motrin; Niofen; Pediaprofen; Pironal; Pyriped; Tifen†; ***Cz.:*** Advil; Baroc; Brufen; Dolgit; Ibalgin; Ibumax; Irfen†; Nurofen; Nurofen Advance; Nurofen Stopgrip; Pabiprofen; Panafen; Pedea; Solpaflex; Tomaflex; Urgo; ***Denm.:*** Apain; Brufen; Ibumetin; Ibureumin; Ibutop; Ipren; Pedea; Solpaflex†; ***Fin.:*** Brufen; Burana; Ibumax; Ibumetin; Ibusal; Ibuxin; ***Fr.:*** Advil; Anadvil; Antarene; Brufen; Dolgit; Doltaque; Ergix; Expanfen; Gelufene; Hemagene Tailleur; Ibualgic†; Ibutop; Intralgis; Nureflex; Nurofen; Nurofentabs; Nuroflash; Pedea; Solufen; Spedifen; Spifen; Upfen; ***Ger.:*** Advel; Aktren; Contraneural; Dismenol N; Dolgit; Dolo Sanol; Dolo-Puren; Dolodoc; Dolormin; Esprenit; Eudorlin Extra; Eudorlin Migrane; Gyno-Neuralgin; Gynofug†; Ibu; Ibu Benuron; ibu-Attritin; Ibu-ratiopharm; Ibubeta; Ibudolor; Ibuflam; Ibuhexal; Ibumerck; Ibuphlogont†; Ibuprof†; Ibutad; Ibutop; Ilvico grippal†; Imbun; Jenaprofen; Kontagripp; Mensoton; Migranin Ibuprofen; Novogent†; Nurofen; Optalidon; Opturem; Parsal; Pedea; Pfeil†; Phamoprofen†; ratioDolor†; Schmerz-Dolgit; Spalt; Tabalon; Tempi†; Tispol Ibu-DD; Togal Akut Ibuprofen; Trauma-Dolgit; Urem; ***Gr.:*** Advil; Algofren; Brufen; Buscofem; Nurofen; Rozovin†; ***Hong Kong:*** Advil; Bifen; Brufen†; Bupogesic; Dolo-Spedifen†; Ibufac; Ibupen; Neutropain; Nurofen; Perofen; Profen; Rupan†; Schufen; Spedifen; ***Hung.:*** Advil; Algoflex; Dolgit; Huma-Profen; Ibulos†; Ibumax; Ibutop; Melfen; Nurofen; Solpaflex; Spedifen; ***India:*** Brufen; Butafen†; Cipgesic; Emflam; Ibugesic; Ibupal; ***Indon.:*** Anafen; Arthrifen; Bufect; Dofen; Dolofen-F; Febryn; Fenris; Iprox; Lexaprofen; Nofena; Ostarin; Prifen; Profen; Proris; Rhelafen; Ribunal; Shelrofen; Spedifen; Yariven; ***Irl.:*** Advil; Brufen; Bufigen; Fenopine; Ibugel; Melfen; Nurofen; Phorpain; Proflex; Solfen†; ***Israel:*** Adex; Advil; Artofen; Ibufen; Ibuleve; Nurofen; ***Ital.:*** Algofen; Antalfebal; Antalfort; Antalgil; Antalisin; Arfen; Benflogin; Brufen; Buscofen; Calmine; Cibalgina Due Fast; Dolocyl; Dolofast; Edenil; Faspic; Ganaprofene†; Gineflor; Ginenorm; Moment; Nureflex; Nurofast; Nurofen; Nurosolv; Pedea; Subitene; Zafen†; ***Malaysia:*** Bifen; Brugesic†; Ibufac; Ibufen†; Nurofen; Perofen; Rupan†; Spedifen; ***Mex.:*** ABKI; Actron; Adivon; Advil; Aflusil; Ainex; Aldofen; Algidol; Bestafen; Carone; Citalgan; Dadicil; Days; Dibufen; Dipofen; Diprodol; Dolprin; Dolprofen; Dolval; Dolver; Eufenil; Febratic; Fidoin-Q; Flexafen; Gelidol; Gobrosan; Ibuflam; Ibuflex; Ifentil; Inpained; Maxifen; Medifen; Mejorultra†; Motrin; Natiken†; Novartril†; Offeno†; Pro-XB; Proartinal; Probuxil; Quadrax; Realdrax; Ribufen; Tabalon; ***Neth.:*** Advil; Brufen; Femapirin; Ibosure; Ibulgan†; Nurofen; Pedea; Roco; Sarixell; Spidifen; Zafen; ***Norw.:*** Brufen; Ibumetin; Ibuprox; Ibux; ***NZ:*** ACT-3; Brufen; Fenapaed; Ibucare; Nurofen; Panafen; ***Philipp.:*** Advil; Brufen; Dolan; Idyl; Medicol; Midol; Skelan; ***Pol.:*** Bolinet; Deep Relief†; Dolgit; Ibufen; Ibum; Ibupar; Ibuprom; Nurofen; Pedea; ***Port.:*** Anadvil; Arfen; Baroc; Brufen; Calbrun; Dolocyl; Dolomate; Dolormin; Faspic; Frenidor; Ibupax†; Junifen; Moment; Motrin†; Norvectan; Nupriland†; Nurofen; Ozonol; Pedea; Plusofen; Seclodin; Solufen; Solvium; Spidifen; Sporfen; Trifene; Zafen; Zip-A-Dol; ***Rus.:*** Aldospray (Альдоспрей); Burana (Бурана); Dolgit (Долгит); Ibufen (Ибуфен); Nurofen (Нурофен); Solpaflex (Солпафлекс); ***S.Afr.:*** Advil; Antiflam†; Betagesic; Betaprofen; Brufen; Brugesic†; Iboflam; Ibugesic; Ibuleve; Ibumax; Ibumed; Inza; Lenafen†; Norflam Ti; Nurofen; Painil†; Ranfen; ***Singapore:*** Ampifen†; Bifen; Ibufen; Ibuloid†; Nurofen; ***Spain:*** Advil; Aldospray Analgesico; Algiasdin; Algidrin; Alogesia; Altior; Babypiril; Bexistar; Calmafher†; Dadosel; Dalsy; Diltix; Doctril; Dolbufen; Dolorac; Dorival; Espidifen; Factopan; Feminalin; Fiedosin; Frenatermin; Gelofeno; Ibubex; Ibufen; Ibumac; Ibuprox; Inadol†; Isdibudol†; Isdol†; Junifen; Narfen; Neobrufen; Nodolfen; Norvectan; Nurofen; Oberdol; Oltyl†; Optajun; Paidofebril; Pedea; Pirexin; Pocyl†; Ratiodol; Remidol†; Saetil; Solvium; Takigrip†; Tedifebrin; ***Swed.:*** Alindrin; Brufen; Ibumetin; Ipren; ***Switz.:*** Algifor; Artofen; Brufen; Dismenol; Dolo-Dismenol; Dolo-Spedifen; Dolocyl; Ecoprofen; Grefen; Ibufen-L; Ibusifar; Iproben; Iprogel†; Irfen; Melabon; Nurofen; Optifen; Perskindol Ibuprofen acute; Saridon N; Sinedol Ibuprofen; Spedifen; Treupel Dolo Ibuprofen; ***Thai.:*** Ambufen; Anbifen; Aprofen; Babefen Sus†; Borafen; Borakid; Brufen; Brumed†; Bruprin; Brusil; Bumed; Cefen; Cenbufen; Duran†; Faspic; G-Fen; Gesica; Greatofen; Heidi; Ibrofen; Ibu; Ibufac; Ibugan; Ibulan; Iburen†; Junifen†; Mano-Bruzone; Nurofen; Ostofen†; P-Fen; Perofen†; Pippen; Probue; Probufen; Profena†; Profeno; Rheumanox; Rumasian; Rumatifen; Rupan†; Schufen; Skelan IB; Tofen; Trofen; Umafen; ***Turk.:*** Advil; Artril; Bebol; Biophen; Brufen; Dolgit; Dolven; Gerofen; Ibu-600; Ibufen; Nurofen; Pedifen; Profen; Repozal; Rofen; Siyafen; Suprafen; Temsofen; Ultrafen; Upren; ***UAE:*** Profinal; ***UK:*** Advil; Anadin Ibuprofen; Anadin Joint Pain; Anadin Ultra; Arthrofen; Biatain-Ibu; Brufen; Calprofen; Cuprofen; Ebufac; Fenbid; Fenpaed; Feverfen; Galprofen; Hedex Ibuprofen; Ibrufhalal; Ibufem; Ibugel; Ibuleve; Ibumousse; Ibuspray; Ibutop Cuprofen; Ibutop Ralgex; Librofem; Mandafen; Manorfen; Mentholatum Ibuprofen; Migrafen; Motrin†; Novaprin; Nurofen; Nurofen Migraine; Obifen; Orbifen; Pacifene; Pedea; Phor Pain; Proflex; Radian-B Ibuprofen; Relcofen; Rimafen; ***USA:*** Advil; Anadar; Genpril†; Haltran†; Ibu; Ibu-Tab; Ibu-4, -6, -8; Ibutab; Menadol; Midol Cramp & Body Aches; Motrin; NeoProfen; Nuprin†; Saleto-200; ***Venez.:*** Advil; Brugesic; Bupriten†; Buprodol; Butilene†; Dologesic; Femicaps; Femmex Plus; Ibucaps; Ibufen; Ibufenac†; Iburin; Iburox†; Ibutan; Lumbax; Max; Maydol; Mestral; Motrin; Pedibu.

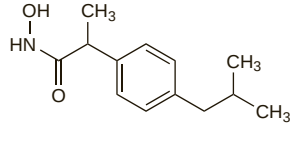
**Multi-ingredient:** ***Arg.:*** Aliviagrip; Bioneural B12†; Buscapina Fem; Butidiona†; Causalon Gesic†; Deep Relief†; Dexprofeno; Espasmo Ibupirac†; Espasmo Motrax†; Espasmofin; Ibu Evanol Plus; Ibu-Buscapina†; Ibu-Tetralgin; Ibudolofrix; Ibudristan; Ibumar Migra†; Ibunastizol; Ibupirac Fem; Ibupirac Flex; Ibupirac Migra; Mensalgin; Migral II; Novo Wilpan†; Roveril; Supragesic; ***Austral.:*** Dimetapp Headcold & Flu; Nurofen Cold & Flu; Nurofen Plus; Panafen Plus; Sudafed Sinus & Anti-inflammatory Pain Relief; Tri-Profen Cold & Flu†; ***Austria:*** Advil Cold; Ardinex; ***Belg.:*** Adulfen Codeine; ***Braz.:*** Algi-Itamanil†; Algi-Reumatril; Algifen†; Fymnal†; Reuplex; ***Canad.:*** Advil Cold & Sinus; Advil Cold & Sinus Plus; Childrens Advil Cold; Dristan Sinus†; Robax Platinum; Sudafed Sinus Advance; Vicks DayQuil Sinus & Pain Relief; ***Chile:*** Adona; Artritapsin; Butartrol; Deucodol Plus; Dioran†; Dolnix; Dolo Winasorb; Dolo-Niofen; Dolo-Octirona; Dolonase; Gedol†; Ibupirac Compuesto; Ibupirac Flu; Ipson-D; Midol†; Neo Butartrol; Niofen Flu; Predual DI†; Silartrin†; Termo-Niofen; ***Cz.:*** Advil Cold; Ardinex†; Ibu-Hepa; Ibufein†; Modafen; ***Fin.:*** Ardinex; Burana-C; ***Fr.:*** Anadvil Rhume; Cliptol; Nurofen Rhume; Rhinadvil; Rhinathiol Rhume†; Rhinureflex; Vicks Rhume†; ***Gr.:*** Nurofen CF; Vicks; ***Hung.:*** Advil Cold; Algoflex-M; Deep Relief; Nurofen Cold & Flu; Rhinathiol Cold; ***India:*** Acks; Anaflam; Answell; Bruace; Cipgesic Plus; Combiflam; Duoflam; Duoflam Plus; Emflam Plus; Flexon; Flexon-MR; Ibu-Proxyvon; Ibuflamar-P; Ibugesic Plus; Ibugesic-M; Reactine Forte; Reducin-A†; Robiflam; Somaflam; ***Indon.:*** Aknil; Axalan; Iremax; Limasip; Neo Rheumacyl; Neuralgin; Shelrod-Plus; ***Irl.:*** Advil Cold & Flu; Codafen Continus†; Nurofen Cold & Flu; Nurofen Plus; ***Israel:*** Nurofen Cold & Flu; ***Ital.:*** Solviflu; Vicks Flu-Action; ***Jpn:*** Colgen Kowa IB Toumei; ***Mex.:*** Algitrin; Bipasmin Compuesto NF†; Carbager-Plus; Dualgos; Sinutab Advance; ***NZ:*** Nurofen Cold & Flu; Nurofen Plus; ***Philipp.:*** Alaxan; Anoflam; Brustan; Flexigesic; Muskelax; Restolax; Selxan; ***Pol.:*** Ardinex; Dip Rilif; Ibalgin Sport; Ibuprom Zatoki; Metafen; Modafen; Nurofen Antigrip; Nurofen Plus; ***Rus.:*** Brustan (Брустан); Ibuclin (Ибуклин); Novigan (Новиган); Nurofen Plus (Нурофен Плюс); ***S.Afr.:*** Advil CS; Dentopain; Gen-Payne; Ibucod; Ibumol; Ibupain; Ibupain Forte; Lotem; Mybucod; Mybulen; Mypaid; Myprodol; Nurofen Cold & Flu; Sinumax IB; ***Spain:*** Nurofen Complex; Salvarina; ***Swed.:*** Ardinex; ***Switz.:*** Ibufen-L; ***Thai.:*** Alaxan Pl; Brustan; Cetan; Dologen; Kintal†; Rumatifen-Plus; Skelan; ***Turk.:*** Nurofen Cold & Flu; ***UAE:*** Profinal Cold & Sinus; Profinal FM; Profinal XP; ***UK:*** Codafen Continus†; Cuprofen Plus; Deep Relief; Lemsip Flu 12Hr; Lemsip Pharmacy Powercaps; Non-Drowsy Sudafed Dual Relief Max; Nurofen Cold & Flu; Nurofen Plus; Nurofen Sinus; Orbifen Cold & Flu; Solpadeine Migraine; Solpaflex; ***USA:*** Advil Allergy Sinus; Advil Cold & Sinus; Advil PM; Anadar Cold & Flu; Childrens Advil Cold; Childrens Ibuprofen Cold; Childrens Motrin Cold; Combunox; Dimetapp Childrens Cold & Fever; Dimetapp Sinus; Dristan Sinus; Ibudone; Motrin IB Sinus; Reprexain; Sine-Aid IB; Vicoprofen; ***Venez.:*** Brudol; Brugesina; Colfene; Femmexultra; Ibucoden.

## Ibuproxam *(rINN)*

Ibuproxamum. 4-Isobutylhydratropohydroxamic acid.

Ибупроксам

$C_{13}H_{19}NO_2$ = 221.3.
*CAS — 53648-05-8.*
*ATC — M01AE13.*
*ATC Vet — QM01AE13.*



### Profile

Ibuproxam is an NSAID (p.96) that has been used topically as a 5% ointment in musculoskeletal, joint, and soft-tissue disorders.

### Preparations

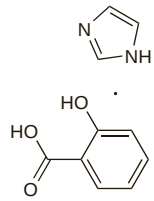
**Proprietary Preparations** (details are given in Part 3)
***Ital.:*** Ibudros†; ***Spain:*** Nialen.

## Imidazole Salicylate *(rINN)*

Imidazole, Salicylate d'; Imidazoli Salicylas; Salicilato de imidazol. Imidazole compounded with salicylic acid.

Имидазола Салицилат

$C_{10}H_{10}N_2O_3$ = 206.2.
*CAS — 36364-49-5.*
*ATC — N02BA16.*
*ATC Vet — QN02BA16.*



### Profile

Imidazole salicylate is a salicylic acid derivative (see Aspirin, p.20) that has been used in the treatment of fever and inflammatory respiratory-tract and otorhinolaryngeal disorders. Imidazole salicylate has been given in oral doses of up to 2.25 g daily in divided doses. It has also been given as a rectal suppository and has been applied topically as a 5% gel for the relief of muscular and rheumatic pain.

### Preparations

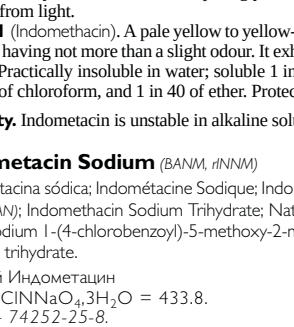
**Proprietary Preparations** (details are given in Part 3)
***Ital.:*** Selezen.

# Indometacin *(BAN, rINN)*

Indometacina; Indometacinas; Indométacine; Indometacinum; Indometacyna; Indometasiini; Indometasin; Indomethacin *(USAN)*. [1-(4-Chlorobenzoyl)-5-methoxy-2-methylindol-3-yl]acetic acid.

Индометацин

$C_{19}H_{16}ClNO_4$ = 357.8.
*CAS — 53-86-1.*
*ATC — C01EB03; M01AB01; M02AA23; S01BC01.*
*ATC Vet — QC01EB03; QM01AB01; QM02AA23; QS01BC01.*



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

**Ph. Eur. 6.2** (Indometacin). A white or yellow, crystalline powder. Practically insoluble in water; sparingly soluble in alcohol. Protect from light.

**USP 31** (Indomethacin). A pale yellow to yellow-tan, crystalline powder having not more than a slight odour. It exhibits polymorphism. Practically insoluble in water; soluble 1 in 50 of alcohol, 1 in 30 of chloroform, and 1 in 40 of ether. Protect from light.

**Stability.** Indometacin is unstable in alkaline solution.

## Indometacin Sodium *(BANM, rINNM)*

Indometacina sódica; Indométacine Sodique; Indomethacin Sodium *(USAN)*; Indomethacin Sodium Trihydrate; Natrii Indometacinum. Sodium 1-(4-chlorobenzoyl)-5-methoxy-2-methylindole-3-acetate, trihydrate.

Натрий Индометацин

$C_{19}H_{15}ClNNaO_4,3H_2O$ = 433.8.
*CAS — 74252-25-8.*

**Pharmacopoeias.** In *US*.

**USP 31** (Indomethacin Sodium). Protect from light.

**Incompatibility.** Indometacin sodium injection is reconstituted with preservative-free sodium chloride for injection 0.9% or preservative-free water for injection. Preparations containing glucose should not be used; reconstitution at a pH below 6 may