sia after caesarean section confirmed an additive analgesic effect for the combination, there was no demonstrable clinical benefit compared with fentanyl alone in this patient group who expect early mobilisation. However, the combination may be of greater benefit in patients for whom early ambulation is not routine.

Fentanyl has also been given by epidural injection to children for postoperative analgesia.[7]

Fentanyl has been tried by intrathecal injection for postoperative pain.[8]

As mentioned in Administration, Transdermal Route, above, an iontophoretic transdermal system for postoperative pain is also available.[9-11]

1. Mitchell RWD, Smith G. The control of acute postoperative pain. *Br J Anaesth* 1989; **63:** 147–58.
2. Morgan M. The rational use of intrathecal and extradural opioids. *Br J Anaesth* 1989; **63:** 165–88.
3. Grass JA, *et al*. A randomized, double-blind, dose-response comparison of epidural fentanyl versus sufentanil analgesia after cesarean section. *Anesth Analg* 1997; **85:** 365–71.
4. Swarm RA, *et al*. Pain treatment in the perioperative period. *Curr Probl Surg* 2001; **38:** 835–920.
5. Roussier M, *et al*. Patient-controlled cervical epidural fentanyl compared with patient-controlled i.v. fentanyl for pain after pharyngolaryngeal surgery. *Br J Anaesth* 2006; **96:** 492–6.
6. Cooper DW, *et al*. Patient-controlled extradural analgesia with bupivacaine, fentanyl, or a mixture of both, after caesarean section. *Br J Anaesth* 1996; **76:** 611–15.
7. Lejus C, *et al*. Postoperative extradural analgesia in children: comparison of morphine with fentanyl. *Br J Anaesth* 1994; **72:** 156–9.
8. Sudarshan G, *et al*. Intrathecal fentanyl for post-thoracotomy pain. *Br J Anaesth* 1995; **75:** 19–22.
9. Chelly JE. An iontophoretic, fentanyl HCl patient-controlled transdermal system for acute postoperative pain management. *Expert Opin Pharmacother* 2005; **6:** 1205–14.
10. Koo PJ. Postoperative pain management with a patient-controlled transdermal delivery system for fentanyl. *Am J Health-Syst Pharm* 2005; **62:** 1171–6.
11. Mayes S, Ferrone M. Fentanyl HCl patient-controlled iontophoretic transdermal system for the management of acute postoperative pain. *Ann Pharmacother* 2006; **40:** 2178–86.

Preparations

BP 2008: Fentanyl Injection;
USP 31: Fentanyl Citrate Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Durogesic; Fentax; Gray-F; Nafluvent; Sublimaze; Talnur; ***Austral.:*** Actiq; Durogesic; Sublimaze; ***Austria:*** Durogesic; ***Belg.:*** Durogesic; ***Braz.:*** Durogesic; Fentabbott; Fentanest; Fentatil; ***Canad.:*** Duragesic; ***Chile:*** Durogesic; ***Cz.:*** Durogesic; Fentagesic; Fentahexal; Fentalis; Ionsys; Matrifen; Wintanyl; ***Denm.:*** Actiq; Durogesic; Haldid; ***Fin.:*** Actiq; Durogesic; ***Fr.:*** Actiq; Durogesic; Ionsys; ***Ger.:*** Actiq; Durogesic; Fenta-Hameln†; ***Gr.:*** Actiq; Durogesic; Fentadur; Matrifen; ***Hong Kong:*** Durogesic; ***Hung.:*** Durogesic; Matrifen; Sedaton; ***India:*** Durogesic; Trofentyl; ***Indon.:*** Durogesic; ***Irl.:*** Actiq; Durogesic; Fental; Sublimaze; ***Israel:*** Durogesic; Tanyl; ***Ital.:*** Actiq; Durogesic; Fentanest; ***Jpn:*** Durotep; ***Malaysia:*** Durogesic; Talgesil; ***Mex.:*** Durogesic; Fenodid; Fentanest; ***Neth.:*** Actiq; Durogesic; ***Norw.:*** Actiq; Durogesic; Leptanal; ***NZ:*** Durogesic; Sublimaze; ***Philipp.:*** Durogesic; Sublimaze; ***Pol.:*** Durogesic; Fentahexal; ***Port.:*** Durogesic; Fentanest; Ionsys; Nilfene; ***Rus.:*** Durogesic (Дюрогезик); ***S.Afr.:*** Durogesic; Sublimaze; Tanyl; ***Singapore:*** Durogesic; ***Spain:*** Actiq; Durogesic; Fentanest; ***Swed.:*** Actiq; Durogesic; Leptanal; Matrifen; ***Switz.:*** Actiq; Durogesic; Sintenyl; ***Thai.:*** Durogesic; ***Turk.:*** Durogesic; ***UK:*** Actiq; Durogesic; Fentalis; Ionsys; Matrifen; Osmach; Sublimaze; Tilofyl; ***USA:*** Actiq; Duragesic; Fentora; Ionsys; Sublimaze; ***Venez.:*** Durogesic.

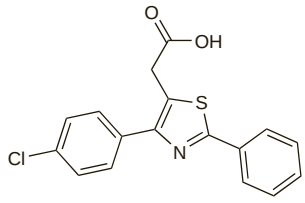
Multi-ingredient: *Arg.:* Disifelit; ***Austral.:*** Marcain with Fentanyl; Naropin with Fentanyl; ***Braz.:*** Nilperidol; ***Ital.:*** Leptofen; ***NZ:*** Bupafen; Marcain with Fentanyl; Naropin with Fentanyl.

Fentiazac *(BAN, USAN, rINN)*

BR-700; Fentiazaco; Fentiazacum; Wy-21894. [4-(4-Chlorophenyl)-2-phenylthiazol-5-yl]acetic acid.

Фентиазак

$C_{17}H_{12}ClNO_2S$ = 329.8.
CAS — 18046-21-4.
ATC — M01AB10; M02AA14.
ATC Vet — QM01AB10; QM02AA14.



Profile

Fentiazac is an NSAID (p.96) that has been used for the relief of pain and inflammation associated with musculoskeletal, joint, peri-articular, and soft-tissue disorders. It has also been used in the treatment of fever. Fentiazac has been given in usual oral doses of 200 mg once or twice daily. Fentiazac has also been applied topically and has been given rectally as the calcium salt.

Preparations

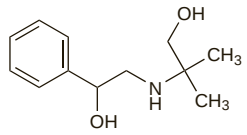
Proprietary Preparations (details are given in Part 3)
Ital.: O-Flam; ***Port.:*** Donorest†; IDR†; Norvedan†.

Fepradinol *(rINN)*

Fépradinol; Fepradinolum. (±)-α-{[(2-Hydroxy-1,1-dimethylethyl)amino]methyl}benzyl alcohol.

Фепрадинол

$C_{12}H_{19}NO_2$ = 209.3.
CAS — 63075-47-8.



Profile

Fepradinol is an NSAID (p.96) that has been used topically in a concentration of 6% for the relief of pain and inflammation. The hydrochloride has been used similarly.

Preparations

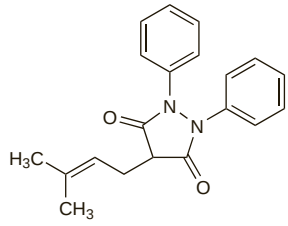
Proprietary Preparations (details are given in Part 3)
Chile: Sinalgia†; ***Mex.:*** Sinalgia; ***Spain:*** Dalgen; Flexidol†.

Feprazone *(BAN, rINN)*

DA-2370; Feprazona; Féprazone; Feprazonum; Phenylprenazone; Prenazone. 4-(3-Methylbut-2-enyl)-1,2-diphenylpyrazolidine-3,5-dione.

Фепразон

$C_{20}H_{20}N_2O_2$ = 320.4.
CAS — 30748-29-9 (feprazone); 57148-60-4 (feprazone piperazine salt 1:1).
ATC — M01AX18; M02AA16.
ATC Vet — QM01AX18; QM02AA16.



Profile

Feprazone, a phenylbutazone (p.117) derivative, is an NSAID (p.96). It has been given orally in the treatment of mild to moderate pain, fever, and inflammation associated with musculoskeletal and joint disorders. Feprazone has also been given rectally and used topically as a 5% cream.

Pinazone, the piperazine salt of feprazone, has been used similarly.

Preparations

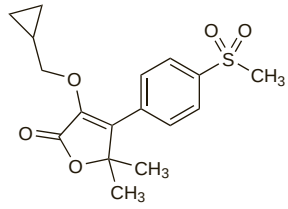
Proprietary Preparations (details are given in Part 3)
Ital.: Zepelin; ***Spain:*** Brotazona; ***Venez.:*** Vapesin.

Firocoxib *(USAN, rINN)*

Firocoxibum; ML-1785713. 3-(Cyclopropylmethoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]furan-2(5*H*)-one.

Фирококсиб

$C_{17}H_{20}O_5S$ = 336.4.
CAS — 189954-96-9.
ATC Vet — QM01AH90.



Profile

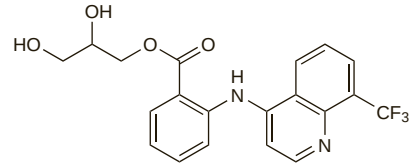
Firocoxib, a selective cyclo-oxygenase-2 (COX-2) inhibitor, is an NSAID used in veterinary medicine for the treatment of inflammation and pain associated with osteoarthritis in dogs.

Floctafenine *(BAN, USAN, rINN)*

Floctafenina; Floctafénine; Floctafeninum; R-4318; RU-15750. 2,3-Dihydroxypropyl *N*-(8-trifluoromethyl-4-quinolyl)anthranilate.

Флоктафенин

$C_{20}H_{17}F_3N_2O_4$ = 406.4.
CAS — 23779-99-9.
ATC — N02BG04.
ATC Vet — QN02BG04.



Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96.

Anaphylactic shock has been reported, and may be preceded by minor allergic manifestations; floctafenine should be stopped in any patient who develops signs suggestive of allergy (such as pruritus or urticaria). Reactions may also involve the liver. Floctafenine may cross-react with glafenine (p.62) and should not be given to patients who have had glafenine-associated reactions.

Porphyria. Floctafenine is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

Interactions

For interactions associated with NSAIDs, see p.99.

Pharmacokinetics

Floctafenine is absorbed from the gastrointestinal tract; peak plasma concentrations are obtained 1 to 2 hours after ingestion. Its plasma half-life is about 8 hours. It is metabolised in the liver to floctafenic acid. It is excreted mainly as glucuronide conjugates in the urine and bile.

Uses and Administration

Floctafenine, an anthranilic acid derivative related to glafenine (p.62), is an NSAID (p.99) used in oral doses of up to 1.2 g daily, in divided doses, for the short-term relief of pain.

Preparations

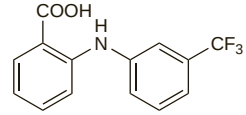
Proprietary Preparations (details are given in Part 3)
Canad.: Idarac†; ***Fr.:*** Idarac; ***Irl.:*** Idarac†; ***Thai.:*** Idarac.

Flufenamic Acid *(BAN, USAN, rINN)*

Acide Flufénamique; Ácido flufenámico; Acidum Flufenamicum; CI-440; CN-27554; Flufenaamihappo; Flufenamsyra; INF-1837; Kwas flufenamowy; NSC-82699. *N*-(ααα-Trifluoro-*m*-tolyl)anthranilic acid.

Флуфенамовая Кислота

$C_{14}H_{10}F_3NO_2$ = 281.2.
CAS — 530-78-9 (flufenamic acid); 61891-34-7 (flufenamate aluminium); 16449-54-0 (flufenamate aluminium).
ATC — M01AG03.
ATC Vet — QM01AG03.



Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96.

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

An early study[2] found that only very small amounts of flufenamic acid were excreted into breast milk after oral doses.

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 01/11/07)
2. Buchanan RA, *et al*. The breast milk excretion of flufenamic acid. *Curr Ther Res* 1969; **11:** 533–8.

Effects on the gastrointestinal tract. Acute proctocolitis associated with oral flufenamic acid in a patient.[1]

1. Ravi S, *et al*. Colitis caused by non-steroidal anti-inflammatory drugs. *Postgrad Med J* 1986; **62:** 773–6.

Porphyria. Flufenamic acid has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Uses and Administration
Flufenamic acid, an anthranilic acid derivative related to mefenamic acid (p.80), is an NSAID (p.99). Flufenamic acid is mainly used topically in a concentration of 3 or 3.5% for the relief of pain and inflammation associated with musculoskeletal, joint, and soft-tissue disorders. Flufenamic acid and its aluminium salt have also been given orally.

Preparations
Proprietary Preparations (details are given in Part 3)
Ger.: Dignodolin†; ***Jpn:*** Opyrin.

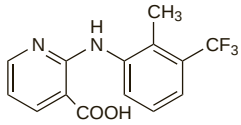
Multi-ingredient: ***Austria:*** Mobilisin; Mobilisin plus; Rheugesal; ***Belg.:*** Mobilisin; ***Braz.:*** Mobilisin Composto; ***Ger.:*** Algesalona†; ***Hung.:*** Mobilisin†; ***Ital.:*** Mobilisin; ***Port.:*** Latesil; Mobilisin; ***Spain:*** Movilisin; ***Switz.:*** Algesalona†; Assan; Assan thermo; Mobilisin.

Flunixin Meglumine *(BANM, USAN, rINNM)*
Fluniksiinimeglumiini; Flunixin megluminová sůl; Flunixine méglumine; Flunixini megluminum; Flunixinmeglumin; Flunixino meglumina; Flunixinum Megluminicum; Meglumini Flunixinum; Sch-14714 (flunixin). 2-{[2-Methyl-3-(trifluoromethyl)phenyl]amino}-3-pyridinecarboxylic acid compounded with 1-deoxy-1-(methylamino)-D-glucitol (1:1); 2-(α^3,α^3,α^3-Trifluoro-2,3,-xylidino)nicotinic acid compounded with 1-deoxy-1-(methylamino)-D-glucitol (1:1).

Меглумина Флуниксин

$C_{14}H_{11}F_3N_2O_2,C_7H_{17}NO_5$ = 491.5.

CAS — 38677-85-9 (flunixin); 42461-84-7 (flunixin meglumine).



(flunixin)

Pharmacopoeias. In *Eur.* (see p.vii) and *US* for veterinary use only.
Ph. Eur. 6.2 (Flunixin Meglumine for Veterinary Use; Flunixin Meglumine BP(Vet) 2008). A white to almost white crystalline powder. Freely soluble in water and in methyl alcohol; practically insoluble in acetone. A 5% solution in water has a pH of 7.0 to 9.0.
USP 31 (Flunixin Meglumine). A white to off-white crystalline powder. Soluble in water, in alcohol, and in methyl alcohol; practically insoluble in ethyl acetate. pH of a 5% solution in water is between 7.0 and 9.0. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Profile
Flunixin meglumine is an NSAID (p.96) used in veterinary medicine for the relief of pain and inflammation in acute and chronic disorders and as adjunctive therapy in the treatment of endotoxic or septic shock and mastitis.

Flupirtine Maleate *(BANM, USAN, rINNM)*
D-9998; Flupirtine, Maléate de; Flupirtini Maleas; Maleato de flupirtina; W-2964M. Ethyl 2-amino-6-(4-fluorobenzylamino)-3-pyridylcarbamate maleate.

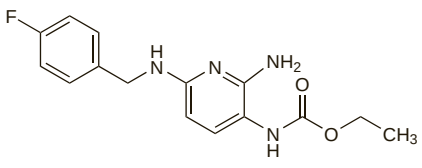
Флупиртина Малеат

$C_{15}H_{17}FN_4O_2,C_4H_4O_4$ = 420.4.

CAS — 56995-20-1 (flupirtine); 75507-68-5 (flupirtine maleate).

ATC — N02BG07.

ATC Vet — QN02BG07.



(flupirtine)

Profile
Flupirtine maleate is an analgesic that has been given for the relief of pain (see Choice of Analgesic, p.2) in usual doses of 100 mg three or four times daily by mouth, or 150 mg three or four times daily as a rectal suppository; daily doses of up to 600 mg by mouth or 900 mg rectally have been used where necessary. Flupirtine has also been given by intramuscular injection as the gluconate in the management of acute pain.

There has been some interest in the potential of flupirtine to treat prion diseases such as Creutzfeldt-Jakob disease (see below).

◊ References.
1. Friedel HA, Fitton A. Flupirtine: a review of its pharmacological properties, and therapeutic efficacy in pain states. *Drugs* 1993; **45:** 548–69.

Creutzfeldt-Jakob disease. A double-blind placebo-controlled study[1] in 28 patients with Creutzfeldt-Jakob disease (CJD) found flupirtine to have beneficial effects on cognitive function. However, further studies are needed to establish any place in therapy.
1. Otto M, *et al.* Efficacy of flupirtine on cognitive function in patients with CJD: a double-blind study. *Neurology* 2004; **62:** 714–18.

Preparations
Proprietary Preparations (details are given in Part 3)
Braz.: Katadolon; ***Ger.:*** Katadolon; Trancopal Dolo; ***Port.:*** Metanor; Novocebrin; ***Rus.:*** Katadolon (Катадолон).

Flurbiprofen *(BAN, USAN, rINN)*
BTS-18322; Flurbiprofeeni; Flurbiprofén; Flurbiprofenas; Flurbiprofène; Flurbiprofeno; Flurbiprofenum; U-27182. 2-(2-Fluorobiphenyl-4-yl)propionic acid.

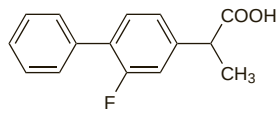
Флурбипрофен

$C_{15}H_{13}FO_2$ = 244.3.

CAS — 5104-49-4.

ATC — M01AE09; M02AA19; S01BC04.

ATC Vet — QM01AE09; QM02AA19; QS01BC04.



Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Flurbiprofen). A white or almost white crystalline powder. Practically insoluble in water; freely soluble in alcohol and in dichloromethane; dissolves in aqueous solutions of alkali hydroxides and carbonates.
USP 31 (Flurbiprofen). A white crystalline powder. Practically insoluble in water; freely soluble in dehydrated alcohol, in acetone, in ether, and in methyl alcohol; soluble in acetonitrile. Store in airtight containers.

Flurbiprofen Sodium *(BANM, rINNM)*
Flurbiprofène Sodique; Flurbiprofeno sódico; Natrii Flurbiprofenum. Sodium (±)-2-(2-fluoro-4-biphenylyl)propionate dihydrate.

Натрий Флурбипрофен

$C_{15}H_{12}FNaO_2,2H_2O$ = 302.3.

CAS — 56767-76-1.

Pharmacopoeias. In *Br.* and *US*.
BP 2008 (Flurbiprofen Sodium). A white to creamy-white, crystalline powder. Sparingly soluble in water; soluble in alcohol; practically insoluble in dichloromethane.

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

Minor symptoms of ocular irritation including transient burning and stinging have been reported on instillation of flurbiprofen sodium eye drops; there may be increased bleeding from ocular surgery and wound healing may be delayed. Local irritation has also followed rectal use, and local effects including a sensation of warming or burning in the mouth may be seen after using flurbiprofen lozenges.

Incidence of adverse effects. Reports from the manufacturers on the range and incidence of the adverse effects of flurbiprofen.[1,2]
1. Sheldrake FE, *et al.* A long-term assessment of flurbiprofen. *Curr Med Res Opin* 1977; **5:** 106–16.
2. Brooks CD, *et al.* Clinical safety of flurbiprofen. *J Clin Pharmacol* 1990; **30:** 342–51.

Effects on the CNS. A severe symmetrical parkinsonian syndrome developed in a 52-year-old man who had taken flurbiprofen for 7 days.[1]
1. Enevoldson TP, *et al.* Acute parkinsonism associated with flurbiprofen. *BMJ* 1990; **300:** 540–1.

Effects on the kidneys. Renal papillary necrosis has been described in a patient who had used flurbiprofen for many years.[1] Acute flank pain and reversible renal dysfunction has been reported in 2 patients treated with flurbiprofen.[2,3] Membranous nephropathy also developed in a patient who took flurbiprofen daily for 12 to 18 months.[4]
1. Nafría EC, *et al.* Renal papillary necrosis induced by flurbiprofen. *DICP Ann Pharmacother* 1991; **25:** 870–1.
2. Kaufhold J, *et al.* Flurbiprofen-associated tubulointerstitial nephritis. *Am J Nephrol* 1991; **11:** 144–6.
3. McIntire SC, *et al.* Acute flank pain and reversible renal dysfunction associated with nonsteroidal anti-inflammatory drug use. *Pediatrics* 1993; **92:** 459–60.
4. MacKay K. Membranous nephropathy associated with the use of flurbiprofen. *Clin Nephrol* 1997; **47:** 279–80.

Effects on the liver. A case of cholestatic jaundice probably due to flurbiprofen has been reported.[1]
1. Kotowski KE, Grayson MF. Side effects of non-steroidal anti-inflammatory drugs. *BMJ* 1982; **285:** 377.

Effects on the skin. Cutaneous vasculitis apparently due to flurbiprofen occurred in a 59-year-old woman with long-standing rheumatoid arthritis.[1] Contact dermatitis has also been seen in a 22-year-old woman who applied a poultice containing flurbiprofen to her wrist.[2]
1. Wei N. Flurbiprofen and cutaneous vasculitis. *Ann Intern Med* 1990; **112:** 550–1.
2. Kawada A, *et al.* Contact dermatitis due to flurbiprofen. *Contact Dermatitis* 2000; **42:** 167–8.

Hypersensitivity. A diffuse, pruritic, maculopapular rash developed in a patient 48 hours after taking a second dose of flurbiprofen.[1] Two days later, the rash had become urticarial, and angioedema and hypotension were also noted. Patch testing with flurbiprofen powder was positive.

See also Effects on the Skin, above.
1. Romano A, Pietrantonio F. Delayed hypersensitivity to flurbiprofen. *J Intern Med* 1997; **241:** 81–3.

Precautions
As for NSAIDs in general, p.98.

Breast feeding. Flurbiprofen is distributed into breast milk; however, the *BNF* and licensed product information consider the amount to be too small to be harmful to a breast-fed infant.

Herpes simplex keratitis. Whether flurbiprofen can exacerbate infection when used to treat ocular herpes simplex is unclear from *animal* studies,[1,2] but licensed product information for flurbiprofen sodium eye drops recommends that they should not be used in patients with active epithelial herpes simplex keratitis. Patients with a history of herpes simplex keratitis should also be monitored closely when undergoing treatment with these eye drops.
1. Trousdale MD, *et al.* Effect of flurbiprofen on herpes simplex keratitis in rabbits. *Invest Ophthalmol Vis Sci* 1980; **19:** 267–70.
2. Hendricks RL, *et al.* The effect of flurbiprofen on herpes simplex virus type 1 stromal keratitis in mice. *Invest Ophthalmol Vis Sci* 1990; **31:** 1503–11.

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

Parasympathomimetics. Licensed product information for acetylcholine chloride ophthalmic preparations and for flurbiprofen sodium eye drops states that there have been reports that *acetylcholine* and *carbachol* have been ineffective when used in patients treated with topical (ophthalmic) NSAIDs.

Pharmacokinetics
Flurbiprofen is readily absorbed from the gastrointestinal tract after oral doses with peak plasma concentrations occurring about 1 to 2 hours after ingestion. Absorption after rectal doses may be more rapid. It is about 99% bound to plasma proteins and has a plasma half-life of about 3 to 6 hours. It is metabolised mainly by hydroxylation (via the cytochrome P450 isoenzyme CYP2C9) and conjugation in the liver and excreted in urine. Flurbiprofen is distributed into breast milk.

Flurbiprofen is a chiral compound given as the racemate and the above pharmacokinetic characteristics refer to the racemic mixture. Allowance may have to be made for the different activities of the enantiomers.

◊ References.
1. Aarons L, *et al.* Plasma and synovial fluid kinetics of flurbiprofen in rheumatoid arthritis. *Br J Clin Pharmacol* 1986; **21:** 155–63.
2. Smith IJ, *et al.* Flurbiprofen in post-partum women: plasma and breast milk disposition. *J Clin Pharmacol* 1989; **29:** 174–84.
3. Kean WF, *et al.* The pharmacokinetics of flurbiprofen in younger and elderly patients with rheumatoid arthritis. *J Clin Pharmacol* 1992; **32:** 41–8.
4. Davies NM. Clinical pharmacokinetics of flurbiprofen and its enantiomers. *Clin Pharmacokinet* 1995; **28:** 100–14.

Uses and Administration
Flurbiprofen, a propionic acid derivative, is an NSAID (p.99). It is used in musculoskeletal and joint disorders such as ankylosing spondylitis, osteoarthritis, and rheumatoid arthritis, in soft-tissue disorders such as sprains and strains, for postoperative pain, and in mild to moderate pain including dysmenorrhoea and migraine. Flurbiprofen is also used as lozenges in the