The dosage of alfentanil used depends on whether the patient has spontaneous respiration or assisted ventilation and on the expected duration of anaesthesia. Doses are adjusted according to the needs of the patient. Children may require higher or more frequent doses than adults, whereas the elderly or debilitated patients may require lower or less frequent doses. Obese patients may require doses based on their ideal (lean) bodyweight.

When used as an adjunct in the **maintenance of general anaesthesia** the initial licensed dose in the UK is as follows:

- in patients with *spontaneous respiration*, up to 500 micrograms may be given slowly over about 30 seconds with supplementary doses of 250 micrograms
- *ventilated* patients may be given 30 to 50 micrograms/kg with supplements of 15 micrograms/kg. When given by infusion to ventilated patients there is an initial loading dose of 50 to 100 micrograms/kg given as a bolus or by infusion over 10 minutes, followed by infusion at a rate of 0.5 to 1 microgram/kg per minute

Typical doses that have been used in the USA are as follows:

- for *short surgical procedures of less than 1 hour* in patients with spontaneous respiration or assisted ventilation, the dose is 8 to 20 micrograms/kg; this may be followed by supplementary doses of 3 to 5 micrograms/kg every 5 to 20 minutes or an infusion of 0.5 to 1 microgram/kg per minute. Alternatively patients with assisted or controlled ventilation may be given an initial dose of 20 to 50 micrograms/kg, followed by supplementary doses of 5 to 15 micrograms/kg every 5 to 20 minutes
- in *general surgical procedures* in patients with assisted or controlled ventilation, an initial dose of 50 to 75 micrograms/kg may be followed by an infusion of 0.5 to 3 micrograms/kg per minute. If alfentanil has been given in anaesthetic doses (see below) for the induction of anaesthesia, infusion rates may need to be reduced by 30 to 50% during the first hour of maintenance

Maintenance infusions of alfentanil should be stopped 10 to 30 minutes before the anticipated end of surgery.

For details of doses in children, see below.

The dose for the **induction of anaesthesia** in patients with assisted ventilation undergoing procedures of at least 45 minutes is 130 to 245 micrograms/kg, followed by an inhalation anaesthetic or maintenance doses of alfentanil of 0.5 to 1.5 micrograms/kg per minute.

In the UK, *ventilated* patients in **intensive care** may be given alfentanil initially at an infusion rate of 2 mg/hour or a loading dose of 5 mg may be given in divided doses over 10 minutes or more slowly if hypotension or bradycardia occur. Thereafter a suitable rate of infusion should be determined for each patient (rates of 0.5 to 10 mg/hour have been used); patients should be carefully monitored and the duration of treatment should not generally exceed 4 days. During continuous infusion additional bolus injections of 0.5 to 1 mg may be given if required to provide analgesia for short painful procedures that may be carried out in intensive care.

Alfentanil is also used as an analgesic in patients with *spontaneous respiration* receiving monitored anaesthesia care; in the USA, an initial dose of 3 to 8 micrograms/kg may be followed by supplementary doses of 3 to 5 micrograms/kg every 5 to 20 minutes or an infusion of 0.25 to 1 microgram/kg per minute.

Administration. Alfentanil is usually given by intravenous injection or infusion, but has also been given intramuscularly,[1,2] intrathecally,[3] or epidurally (see Pain, below).

1. Arendt-Nielsen L, *et al.* Analgesic efficacy of im alfentanil. *Br J Anaesth* 1990; **65:** 164–8.
2. Virkkilä M, *et al.* Pharmacokinetics and effects of i.m. alfentanil as premedication for day-case ophthalmic surgery in elderly patients. *Br J Anaesth* 1993; **71:** 507–11.
3. Hughes DA, Hill DA. Intrathecal alfentanil with and without bupivacaine for analgesia in labour. *Anaesthesia* 2000; **55:** 1116–21.

Administration in children. Alfentanil is licensed in the UK for use in ventilated children during surgical procedures as an analgesic and adjunct to general anaesthetics or as a primary anaesthetic. When used as an adjunct in the **maintenance of general anaesthesia** licensed product information states that ventilated children may be given the usual intravenous *injection* doses as for ventilated adults (see above). However, the *BNFC* suggests that neonates may be given 5 to 20 micrograms/kg initially and children aged from 1 month to 18 years, 10 to 20 micrograms/kg initially; supplementary doses of up to 10 micrograms/kg may be given. When given by *infusion* the *BNF* states that ventilated children may be given the usual doses as for ventilated adults (see above); the *BNFC* suggests that usual adult doses may be given to those aged as young as 1 month. The *BNFC* also suggests that neonates may be given an initial loading dose of 10 to 50 micrograms/kg over 10 minutes followed by infusion at a rate of 0.5 to 1 microgram/kg per minute.

Anaesthesia. Alfentanil, like fentanyl (p.59), appears to produce fewer circulatory changes than morphine and may be preferred for anaesthetic use, especially in cardiovascular surgery. It is generally considered to have a shorter duration of action than fentanyl. It has been used with propofol to facilitate intubation, and for total intravenous anaesthesia.

For a discussion of the drugs used to facilitate intubation and of opioids such as alfentanil used to control the pressor response and the rise of intra-ocular pressure associated with intubation, see Anaesthesia, p.1900. For reference to a study indicating that pretreatment with alfentanil can reduce the pain associated with injection of propofol, see p.1791.

CAESAREAN SECTION. UK licensed product information contraindicates the use of alfentanil before clamping the cord during caesarean section because of the risk of respiratory depression in the neonate. A study of alfentanil 30 micrograms/kg in women undergoing caesarean section was abandoned after massive respiratory depression had occurred in 4 of 5 neonates.[1] Another study[2] in patients undergoing elective caesarean section found that although maternal haemodynamic responses to intubation were minimised when alfentanil 10 micrograms/kg was given intravenously immediately before induction, neonates in the alfentanil group had lower Apgar scores compared with those in the placebo group.

However, alfentanil has been used successfully to minimise haemodynamic responses to intubation and surgery in patients with severe cardiovascular disorders undergoing caesarean section.[3,4] A baby delivered after the successful use of alfentanil 35 micrograms/kg in a mother with severe aortic stenosis[3] was apnoeic and unresponsive with poor muscle tone; the baby responded rapidly to naloxone. Alfentanil 10 micrograms/kg immediately before induction attenuated the cardiovascular response to intubation in patients with severe pregnancy-induced hypertension[4] and was considered a suitable alternative to fentanyl 2.5 micrograms/kg; no effect on neonatal mortality could be attributed to anaesthetic technique. However, it has been suggested that the use of smaller doses of alfentanil of 7.5 micrograms/kg with magnesium sulfate 30 mg/kg may provide better cardiovascular control.[5]

1. Leuwer M, *et al.* Pharmacokinetics and pharmacodynamics of an equipotent fentanyl and alfentanil dose in mother and infant during caesarean section. *Br J Anaesth* 1990; **64:** 398P–9P.
2. Gin T, *et al.* Alfentanil given immediately before the induction of anesthesia for elective cesarean delivery. *Anesth Analg* 2000; **90:** 1167–72.
3. Redfern N, *et al.* Alfentanil for caesarean section complicated by severe aortic stenosis: a case report. *Br J Anaesth* 1987; **59:** 1309–12.
4. Rout CC, Rocke DA. Effects of alfentanil and fentanyl on induction of anaesthesia in patients with severe pregnancy-induced hypertension. *Br J Anaesth* 1990; **65:** 468–74.
5. Ashton WB, *et al.* Attenuation of the pressor response to tracheal intubation by magnesium sulphate with and without alfentanil in hypertensive proteinuric patients undergoing caesarean section. *Br J Anaesth* 1991; **67:** 741–7.

PHAEOCHROMOCYTOMA. Alfentanil does not release histamine and was of value in the anaesthetic management of patients with phaeochromocytoma.[1] It has a very rapid onset of action, good vasodilating properties, and a relatively short elimination half-life. These patients are often very somnolent for the first 48 hours after surgery and postoperative opioid dosage requirements may be less than expected. Alfentanil infusion continued into the postoperative period allows careful titration of dosage.

1. Hull CJ. Phaeochromocytoma: diagnosis, preoperative preparation and anaesthetic management. *Br J Anaesth* 1986; **58:** 1453–68.

Pain. ***POSTOPERATIVE ANALGESIA.*** Continuous on-demand epidural infusions of alfentanil 200 micrograms/hour or fentanyl 20 micrograms/hour provided comparable analgesia to morphine 200 micrograms/hour in the early postoperative period;[1] alfentanil (16 minutes) and fentanyl (13 minutes) had the advantage of more rapid onset of analgesia than morphine (44 minutes). However, some considered that there was no overall advantage of epidural over intravenous alfentanil either as patient-controlled analgesia[2] or by continuous infusion.[3]

1. Chrubasik J, *et al.* Relative analgesic potency of epidural fentanyl, alfentanil, and morphine in treatment of postoperative pain. *Anesthesiology* 1988; **68:** 929–33.
2. Chauvin M, *et al.* Equivalence of postoperative analgesia with patient-controlled intravenous or epidural alfentanil. *Anesth Analg* 1993; **76:** 1251–8.
3. van den Nieuwenhuyzen MCO, *et al.* Epidural vs intravenous infusion of alfentanil in the management of postoperative pain following laparotomies. *Acta Anaesthesiol Scand* 1996; **40:** 1112–18.

Preparations

USP 31: Alfentanil Injection.

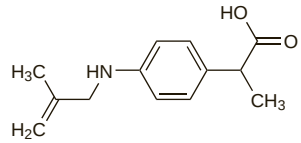
Proprietary Preparations (details are given in Part 3)
Arg.: Brevafen; ***Austral.:*** Rapifen; ***Austria:*** Rapifen; ***Belg.:*** Rapifen; ***Braz.:*** Alfast; Rapifen; ***Canad.:*** Alfenta; ***Chile:*** Rapifen; ***Cz.:*** Rapifen; ***Denm.:*** Rapifen; ***Fin.:*** Rapifen; ***Fr.:*** Rapifen; ***Ger.:*** Rapifen; ***Gr.:*** Rapifen; ***Hong Kong:*** Rapifen; ***Hung.:*** Rapifen; ***Irl.:*** Rapifen; ***Israel:*** Rapifen; ***Ital.:*** Fentalim; ***Malaysia:*** Rapifen†; ***Mex.:*** Rapifen; ***Neth.:*** Rapifen; ***Norw.:*** Rapifen; ***NZ:*** Rapifen; ***S.Afr.:*** Rapifen; ***Spain:*** Fanaxal; Limifen; ***Swed.:*** Rapifen; ***Switz.:*** Rapifen; ***Turk.:*** Rapifen; ***UK:*** Rapifen; ***USA:*** Alfenta; ***Venez.:*** Rapifen.

Alminoprofen *(rINN)*

Alminoprofène; Alminoprofeno; Alminoprofenum. 4-[(2-Methylallyl)amino]hydratropic acid.

Альминопрофен

$C_{13}H_{17}NO_2$ = 219.3.
CAS — 39718-89-3.
ATC — M01AE16.
ATC Vet — QM01AE16.



Profile
Alminoprofen, a propionic acid derivative related to ibuprofen (p.64), is an NSAID (p.96). It has been used in inflammatory and rheumatic disorders in oral doses of up to 900 mg daily.

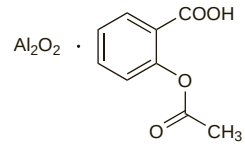
Preparations
Proprietary Preparations (details are given in Part 3)
Fr.: Minalfene.

Aloxiprin *(BAN, rINN)*

Acetilsalicilato de polioxoaluminio; Aloksipriini; Aloxiprina; Aloxiprine; Aloxiprinum.

Алоксиприн

CAS — 9014-67-9.
ATC — B01AC15; N02BA02.
ATC Vet — QB01AC15; QN02BA02.



Pharmacopoeias. In *Br.*
BP 2008 (Aloxiprin). A polymeric condensation product of aluminium oxide and aspirin. A fine, white or slightly pink powder, odourless or almost odourless. It contains not less than 7.5% and not more than 8.5% of aluminium and not less than 79.0% and not more than 87.4% of total salicylates, calculated as aspirin, $C_9H_8O_4$, both calculated with reference to the dried substance. Practically insoluble in water, in alcohol, and in ether; slightly soluble in chloroform.

Profile
Aloxiprin, a polymeric condensation product of aluminium oxide and aspirin, has actions similar to those of aspirin (p.20); aloxiprin 600 mg is equivalent to about 500 mg of aspirin. Aloxiprin has been used as an analgesic and anti-inflammatory in musculoskeletal and joint disorders. It has also been used in the treatment and prevention of thromboembolic disorders.

Preparations
BP 2008: Aloxiprin Tablets.

Proprietary Preparations (details are given in Part 3)
Cz.: Superpyrin.

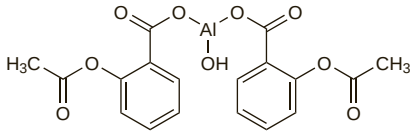
Multi-ingredient: ***UK:*** Askit.

Aluminium Aspirin

Acetilsalicilato de aluminio; Aluminum Acetylsalicylate; Aluminum Aspirin; Aluminum Bis(acetylsalicylate); Aspirin Aluminium. Bis(2-acetoxybenzoato-*O*′)hydroxyaluminium.

Алюминий Аспирина; Аспирин Алюминий

$C_{18}H_{15}AlO_9$ = 402.3.
CAS — 23413-80-1.



Pharmacopoeias. In *Jpn.*

Profile

Aluminium aspirin is a salicylic acid derivative (see Aspirin, p.20) that has been given orally in the management of fever, pain, and musculoskeletal and joint disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

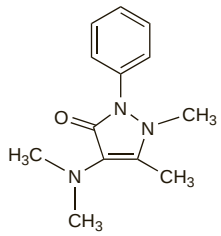
Multi-ingredient: ***Indon.:*** Remasal; ***S.Afr.:*** Analgen-SA†.

Aminophenazone *(rINN)*

Amidazofen; Amidopyrine; Amidopyrine-Pyramidon; Aminofenatsoni; Aminofenazon; Aminofenazona; Aminophénazone; Aminophenazonum; Aminopyrine; Dimethylaminoantipyrine; Dimethylaminophenazone. 4-Dimethylamino-1,5-dimethyl-2-phenyl-4-pyrazolin-3-one.

Аминофеназон

$C_{13}H_{17}N_3O$ = 231.3.
CAS — 58-15-1.
ATC — N02BB03.
ATC Vet — QN02BB03.



Pharmacopoeias. In *It.*

Profile

Aminophenazone, a pyrazolone derivative, is an NSAID (p.96), but the risk of agranulocytosis is sufficiently great to render it unsuitable for systemic use. Onset of agranulocytosis may be sudden and unpredictable. Aminophenazone has been used as salts or complexes, including topically as the salicylate.

Precautions. ***CARCINOGENICITY.*** Some[1] consider that aminophenazone should be regarded as a potential carcinogen because it reacted readily with nitrous acid to form dimethylnitrosamine. The reaction was catalysed by thiocyanate present in the saliva particularly in smokers.

1. Boyland E, Walker SA. Catalysis of the reaction of aminopyrine and nitrite by thiocyanate. *Arzneimittelforschung* 1974; **24:** 1181–4.

PORPHYRIA. Aminophenazone has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Preparations

Proprietary Preparations (details are given in Part 3)

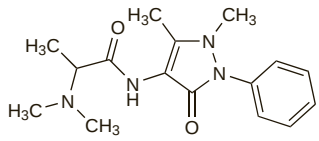
Multi-ingredient: ***Braz.:*** Gineburno†; ***Cz.:*** Diny†; Eunalgit†; ***Hung.:*** Antineuralgica; Demalgon; Demalgonil; Dolor; Germicid-C; Germicid†; Kefalgin; Meristin; ***Ital.:*** Virdex; ***Mex.:*** Flumil; ***Switz.:*** Thermocutan†; ***Venez.:*** Flexidone†.

Aminopropylone

Aminopropilona; Aminopropylon. *N*-(2,3-Dihydro-1,5-dimethyl-3-oxo-2-phenyl-1*H*-pyrazol-4-yl)-2-(dimethylamino)propanamide.

Аминопропилон

$C_{16}H_{22}N_4O_2$ = 302.4.
CAS — 3690-04-8.



Profile

Aminopropylone is an NSAID (p.96) that has been used in topical preparations, for the local treatment of pain and inflammatory conditions. The hydrochloride has been used similarly.

Preparations

Proprietary Preparations (details are given in Part 3)

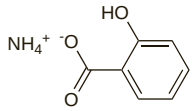
Multi-ingredient: ***Ital.:*** Vessiflex†.

Ammonium Salicylate

Salicilato de amonio.

Аммоний Салицилат

$C_7H_9NO_3$ = 155.2.
CAS — 528-94-9.



Profile

Ammonium salicylate is a salicylic acid derivative used topically in rubefacient preparations similarly to methyl salicylate (p.85) for the relief of pain in musculoskeletal and joint disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

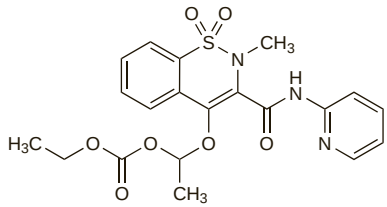
Multi-ingredient: ***Austral.:*** Radian-B†; ***Irl.:*** Radian-B†; ***UK:*** Radian-B.

Ampiroxicam *(BAN, rINN)*

Ampiroxicamum; CP-65703. 4-[1-(Ethoxycarbonyloxy)ethoxy]-2-methyl-*N*^{2}-pyridyl-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide.

Ампироксикам

$C_{20}H_{21}N_3O_7S$ = 447.5.
CAS — 99464-64-9.



Profile

Ampiroxicam is an NSAID (p.96) that is reported to be metabolised to piroxicam (p.117). It has been given orally for the relief of pain and inflammation particularly in musculoskeletal disorders such as rheumatoid arthritis and osteoarthritis.

Adverse effects. Photosensitivity reactions have occurred during ampiroxicam treatment.[1-3]

1. Kurumaji Y. Ampiroxicam-induced photosensitivity. *Contact Dermatitis* 1996; **34:** 298–9.
2. Toyohara A, *et al.* Ampiroxicam-induced photosensitivity. *Contact Dermatitis* 1996; **35:** 101–2.
3. Chishiki M, *et al.* Photosensitivity due to ampiroxicam. *Dermatology* 1997; **195:** 409–10.

Preparations

Proprietary Preparations (details are given in Part 3)

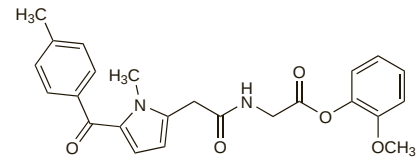
Jpn: Flucam†.

Amtolmetin Guacil *(rINN)*

Amtolmetina guacilo; Amtolmétine Guacil; Amtolmetinum Guacilum; MED-15; ST-679. *N*-[(1-Methyl-5-*p*-toluoylpyrrol-2-yl)acetyl]glycine *o*-methoxyphenyl ester.

Амтолметин Гуацил

$C_{24}H_{24}N_2O_5$ = 420.5.
CAS — 87344-06-7.



Profile

Amtolmetin guacil is an NSAID (p.96) that is an ester prodrug of tolmetin (p.130). It is used in painful and inflammatory disorders in oral doses of 600 to 1200 mg daily.

◊ References.

1. Biasi G, Marcolongo R. Efficacia e tollerabilità dell'amtolmetina guacil nel trattamento dell'artrosi in fase di riacutizzazione. *Minerva Med* 2001; **92:** 315–24.
2. Jajic Z, *et al.* Gastrointestinal safety of amtolmetin guacyl in comparison with celecoxib in patients with rheumatoid arthritis. *Clin Exp Rheumatol* 2005; **23:** 809–18.

Preparations

Proprietary Preparations (details are given in Part 3)

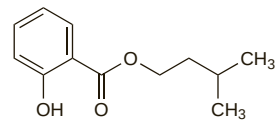
Ital.: Artricol; Artromed; Eufans.

Amyl Salicylate

Isoamyl Salicylate; Isopentyl Salicylate; Salicilato de isoamilo; Salicilato de isopentilo. 3-Methylbutyl 2-hydroxybenzoate.

Амилсалицилат

$C_{12}H_{16}O_3$ = 208.3.
CAS — 87-20-7.



Pharmacopoeias. In *Fr.*

Profile

Amyl salicylate is a salicylic acid derivative used topically in rubefacient preparations similarly to methyl salicylate (p.85) for its analgesic and anti-inflammatory actions. It has also been used in perfumery.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Atomo Desinflamante; Atomo Desinflamante C; Atomo Desinflamante Familiar; Rati Salil Crema; ***Fr.:*** Sedartryl†; ***Spain:*** Linimento Klar†.

Anakinra *(BAN, USAN, rINN)*

Anakinrum; rhIL-1ra; r-metHuIL-1ra. *N*^{2}-L-methionylinterleukin 1 receptor antagonist (human isoform x reduced).

Анакинра

CAS — 143090-92-0.
ATC — L04AC03.
ATC Vet — QL04AC03.

M
RPSGRKSSKM QAFRIWDVNQ KTFYLRNNQL VAGYLQGPNV NLEEKIDVVP
IEPHALFLGI HGGKMCLSCV KSGDETRLQL EAVNITDLSE NRKQDKRFAF
IRSDSGPTTS FESAACPGWF LCTAMEADQP VSLTNMPDEG VMVTKFYFQE
DE

Adverse Effects and Precautions

Mild to moderate injection site reactions with symptoms of erythema, bruising, swelling, and pain are common with anakinra particularly in the first month of treatment. Other common reactions include headache, nausea, diarrhoea, and abdominal pain. Antibodies to anakinra may develop. Allergic reactions such as rashes have been reported rarely; if a severe allergic reaction occurs, anakinra should be stopped and appropriate treatment given.

Serious infections have been reported with anakinra, particularly in patients with asthma. These infections are mainly bacterial, such as cellulitis, pneumonia, and bone and joint infections. More rarely, opportunistic infections involving fungal, mycobacterial, and viral pathogens have also been seen. Anakinra should be stopped in those who develop a serious infection. In addition, therapy should not be started in patients with active infections, including chronic or localised infections; caution is recommended in those with a history of recurrent infections or with underlying conditions that may predispose to infections.

A small decrease in absolute neutrophil count (ANC) is commonly seen with anakinra treatment; however, true neutropenia