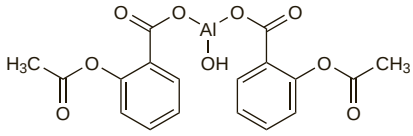
Aluminium Aspirin

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)

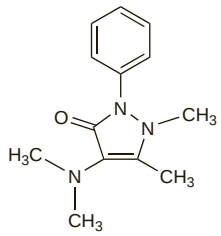
Multi-ingredient: ***Indon.:*** Remasal; ***S.Afr.:*** Analgen-SA†.

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)

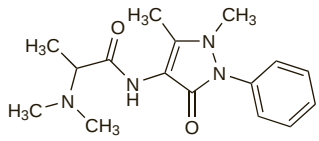
Multi-ingredient: ***Braz.:*** Gineburno†; ***Cz.:*** Diny†; Eunalgit†; ***Hung.:*** Antineuralgica; Demalgon; Demalgonil; Dolor; Germicid-C; Germicid†; Kefalgin; Meristin; ***Ital.:*** Virdex; ***Mex.:*** Flumil; ***Switz.:*** Thermocutan†; ***Venez.:*** Flexidone†.

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)

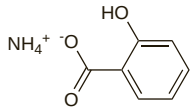
Multi-ingredient: ***Ital.:*** Vessiflex†.

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)

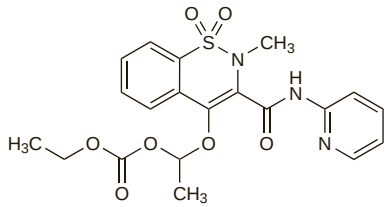
Multi-ingredient: ***Austral.:*** Radian-B†; ***Irl.:*** Radian-B†; ***UK:*** Radian-B.

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)

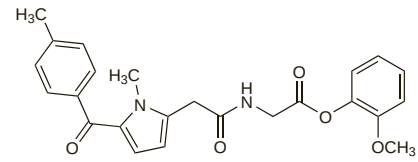
Jpn: Flucam†.

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)

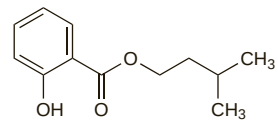
Ital.: Artricol; Artromed; Eufans.

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

(ANC <1500 cells/mm^3) is rare. Licensed product information recommends that neutrophil counts should be taken before starting anakinra and periodically throughout treatment. UK licensed information recommends monthly monitoring during the first 6 months and then quarterly thereafter; US licensed information requires monthly monitoring for the first 3 months and then quarterly monitoring for a period of up to 1 year. Anakinra should not be started in patients with neutropenia. Small reductions in the total white blood cell and platelets counts and a small increase in eosinophils have also been noted. Anakinra is also associated with an increased incidence of lymphoma in patients with rheumatoid arthritis.

For caution in patients with renal impairment see under Uses and Administration, below.

Effects on the cardiovascular system. A 29-year-old woman with refractory adult-onset Still's disease developed shortness of breath, which progressed to cardiorespiratory failure, 3 months after being started on anakinra;[1] although resuscitation was tried, the patient died. The authors considered that the role of anakinra in this event was unclear, particularly as the patient had shown some evidence of myocardial or pulmonary dysfunction before starting the drug.

1. Ruiz PJ, *et al.* Cardiac death in a patient with adult-onset Still's disease treated with the interleukin 1 receptor inhibitor anakinra. *Ann Rheum Dis* 2007; **66:** 422–3.

Effects on the skin. Inflammatory lesions at injection sites were reported in 5 patients after anakinra use.[1] The lesions were erythematous, oedematous, painful, and itchy plaques, and were seen within 16 days of starting treatment. Treatment with anakinra was completely stopped in 1 patient and interrupted in 2 other patients; when reintroduced, one patient developed abdominal pain, dyspnoea, and facial and abdominal erythema with pruritus.

1. Vila AT, *et al.* Adverse cutaneous reactions to anakinra in patients with rheumatoid arthritis: clinicopathological study of five patients. *Br J Dermatol* 2005; **153:** 417–23.

Interactions

Live vaccines should not be given with anakinra as its effect on vaccine efficacy or the risk of infection transmission is unknown.

The risk of serious infection and neutropenia is increased when anakinra and etanercept are used together (see under Infliximab, p.71); a similar effect may occur with other TNF antagonists. The use of anakinra with etanercept or other TNF inhibitors is not recommended.

Pharmacokinetics

After subcutaneous doses, peak plasma concentrations of anakinra are reached in 3 to 7 hours. Its terminal half-life is about 4 to 6 hours. Anakinra is excreted mainly in the urine.

Uses and Administration

Anakinra is a recombinant receptor antagonist of interleukin-1 (p.2325), an inflammatory mediator found in the plasma and synovial fluid of patients with rheumatoid arthritis.

Anakinra is used for the treatment of the signs and symptoms of moderate to severely active rheumatoid arthritis in patients who have had an inadequate response to methotrexate or another disease-modifying antirheumatic drug (DMARD) alone (but see below). In the UK, it is only licensed for use with methotrexate; however, in the USA, it may be given either alone or with another DMARD, although not one that inhibits TNF (see Interactions, above). The usual dose in adults is 100 mg once daily by subcutaneous injection. The dose should be given at about the same time each day.

Anakinra has been tried in septic shock and graft-versus-host disease in transplant recipients, but results were disappointing.

Administration in renal impairment. Caution may be advisable if anakinra is used in patients with renal impairment. A study[1] in patients with varying degrees of renal function indicated that no dosage adjustment was needed for anakinra in patients with mild or moderate renal impairment but dosage on alternate days appeared advisable in those with severe renal impairment. US licensed product information also recommends alternate-day dosing in patients with severe impairment or end-stage disease (creatinine clearance less than 30 mL/minute). However, in the UK, licensed product information contra-indicates use in those with this degree of impairment.

Dialysis does not affect anakinra concentrations to any significant degree.

1. Yang B-B, *et al.* Pharmacokinetics of anakinra in subjects with different levels of renal function. *Clin Pharmacol Ther* 2003; **74:** 85–94.

Familial Mediterranean fever. For mention of anakinra having been tried in familial Mediterranean fever, see p.557.

Rheumatoid arthritis. In the UK, anakinra is licensed for the treatment of rheumatoid arthritis (p.11) in patients with an inadequate response to methotrexate alone; however, NICE does not recommend its use except in the context of a controlled, long-term clinical study.

References.

1. Bresnihan B, *et al.* Treatment of rheumatoid arthritis with recombinant human interleukin-1 receptor antagonist. *Arthritis Rheum* 1998; **41:** 2196–2204.
2. Cohen S, *et al.* Treatment of rheumatoid arthritis with anakinra, a recombinant human interleukin-1 receptor antagonist, in combination with methotrexate: results of a twenty-four-week, multicenter, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2002; **46:** 614–24.
3. Nuki G, *et al.* Long-term safety and maintenance of clinical improvement following treatment with anakinra (recombinant human interleukin-1 receptor antagonist) in patients with rheumatoid arthritis: extension phase of a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2002; **46:** 2838–46.
4. Fleischmann RM, *et al.* Anakinra, a recombinant human interleukin-1 receptor antagonist (r-metHuIL-1ra), in patients with rheumatoid arthritis: a large, international, multicenter, placebo-controlled trial. *Arthritis Rheum* 2003; **48:** 927–34.
5. NICE. Anakinra for rheumatoid arthritis: Technology Appraisal Guidance 72 (issued November 2003). Available at: http://www.nice.org.uk/nicemedia/pdf/TA072guidance.pdf (accessed 22/06/07)
6. Schiff MH. Durability and rapidity of response to anakinra in patients with rheumatoid arthritis. *Drugs* 2004; **64:** 2493–2501.
7. Waugh J, Perry CM. Anakinra: a review of its use in the management of rheumatoid arthritis. *BioDrugs* 2005; **19:** 189–202.
8. Reiff A. The use of anakinra in juvenile arthritis. *Curr Rheumatol Rep* 2005; **7:** 434–40.
9. den Broeder AA, *et al.* Observational study on efficacy, safety, and drug survival of anakinra in rheumatoid arthritis patients in clinical practice. *Ann Rheum Dis* 2006; **65:** 760–2.
10. Burger D, *et al.* Is IL-1 a good therapeutic target in the treatment of arthritis? *Best Pract Res Clin Rheumatol* 2006; **20:** 879–96.

Preparations

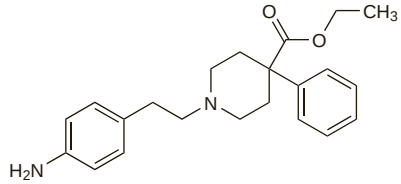
Proprietary Preparations (details are given in Part 3)
Austral.: Kineret; ***Canad.:*** Kineret; ***Cz.:*** Kineret; ***Denm.:*** Kineret; ***Fin.:*** Kineret; ***Fr.:*** Kineret; ***Ger.:*** Kineret; ***Gr.:*** Kineret; ***Irl.:*** Kineret; ***Ital.:*** Kineret; ***Neth.:*** Kineret; ***Norw.:*** Kineret; ***Pol.:*** Kineret; ***Port.:*** Kineret; ***Spain:*** Kineret; ***Swed.:*** Kineret; ***UK:*** Kineret; ***USA:*** Kineret.

Anileridine *(BAN, rINN)*

Anileridiini; Anileridin; Anileridina; Anilé ridine; Anileridinum. Ethyl 1-(4-aminophenethyl)-4-phenylpiperidine-4-carboxylate.

Анилеридин

$C_{22}H_{28}N_2O_2$ = 352.5.
CAS — 144-14-9.
ATC — N01AH05.
ATC Vet — QN01AH05.



Pharmacopoeias. In *US.*
USP 31 (Anileridine). A white to yellowish-white, odourless or practically odourless, crystalline powder. When exposed to light and air it oxidises and darkens in colour. It exhibits polymorphism, and of two crystalline forms observed, one melts at about 80° and the other at about 89°. Very slightly soluble in water; soluble 1 in 2 of alcohol and 1 in 1 of chloroform; soluble in ether but solutions may be turbid. Store in airtight containers. Protect from light.

Anileridine Hydrochloride *(BANM, rINNM)*

Anilé ridine, Chlorhydrate d'; Anileridini Hydrochloridum; Hidrocloruro de anileridina.

Анилеридина Гидрохлорид

$C_{22}H_{28}N_2O_2$,2HCl = 425.4.
CAS — 126-12-5.

Pharmacopoeias. In *US.*
USP 31 (Anileridine Hydrochloride). A white or nearly white odourless crystalline powder. Soluble 1 in 5 of water and 1 in 80 of alcohol; practically insoluble in chloroform and in ether. pH of a 5% solution in water is 2.5 to 3.0. Store in airtight containers. Protect from light.

Anileridine Phosphate *(BANM, rINNM)*

Anilé ridine, Phosphate d'; Anileridini Phosphas; Fosfato de anileridina.

Анилеридина Фосфат

$C_{22}H_{28}N_2O_2$,H_3PO_4 = 450.5.
CAS — 4268-37-5.

Profile

Anileridine, a phenylpiperidine derivative, is an opioid analgesic (p.101) chemically related to pethidine (p.113) and with similar actions. It has been used as the hydrochloride in the management of moderate to severe pain. Anileridine has also been given by injection as the phosphate.

Preparations

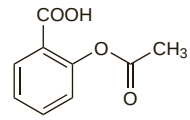
USP 31: Anileridine Hydrochloride Tablets; Anileridine Injection.

Aspirin *(BAN)*

Acetilsalicílico, ácido; Acetilsalicilo rūgštis; Acetilszalicilsav; Acetylsal. Acid; Acetylsalicylic Acid; Acetylsalicylsyra; Acide acétylsalicylique; Acidum acetylsalicylicum; Asetilsalisilik Asit; Asetyylisalisyylihappo; Kwas acetylosalicylowy; Kyselina acetylsalicylová; Polopiryna; Salicylic Acid Acetate. *O*-Acetylsalicylic acid; 2-Acetoxybenzoic acid.

Аспирин

$C_9H_8O_4$ = 180.2.
CAS — 50-78-2.
ATC — A01AD05; B01AC06; N02BA01.
ATC Vet — QA01AD05; QB01AC06; QN02BA01.



NOTE. The use of the name Aspirin is limited; in some countries it is a trade-mark.
Compounded preparations of aspirin may be represented by the following names:

- Co-codaprin (*BAN*)—aspirin 50 parts and codeine phosphate 1 part (w/w)
- Co-codaprin (*PEN*)—aspirin and codeine phosphate.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*
Ph. Eur. 6.2 (Acetylsalicylic Acid; Aspirin BP 2008). White or almost white, crystalline powder or colourless crystals. Slightly soluble in water; freely soluble in alcohol. Store in airtight containers.
USP 31 (Aspirin). White crystals, commonly tubular or needle-like, or white crystalline powder; odourless or has a faint odour. Is stable in dry air; in moist air it gradually hydrolyses to salicylic and acetic acids. Soluble 1 in 300 of water, 1 in 5 of alcohol, 1 in 17 of chloroform, and 1 in 10 to 15 of ether; sparingly soluble in absolute ether. Store in airtight containers.

Adverse Effects and Treatment

Aspirin has many properties in common with the non-aspirin NSAIDs, the adverse effects of which are described on p.96.

The most common adverse effects of therapeutic doses of aspirin are gastrointestinal disturbances such as nausea, dyspepsia, and vomiting. Gastrointestinal symptoms may be minimised by giving aspirin with food. Irritation of the gastric mucosa with erosion, ulceration, haematemesis, and melaena may occur. Histamine H_2-antagonists, proton pump inhibitors, and prostaglandin analogues such as misoprostol may be used in the management of NSAID-induced ulceration (see Peptic Ulcer Disease, p.1702), including that caused by aspirin. Slight blood loss, which is often asymptomatic, may occur in about 70% of patients; it is not usually of clinical significance but may, in a few patients, cause iron-deficiency anaemia during long-term therapy. Such occult blood loss is not affected by giving aspirin with food but may be reduced by use of enteric-coated or other modified-release tablets, H_2-antagonists, or high doses of antacids. Major upper gastrointestinal bleeding occurs rarely.

Some persons, especially those with asthma, chronic urticaria, or chronic rhinitis, exhibit notable hypersensitivity to aspirin (see also below), which may provoke reactions including urticaria and other skin eruptions, angioedema, rhinitis, and severe, even fatal, paroxysmal bronchospasm and dyspnoea. Persons sensitive to aspirin often exhibit cross-sensitivity to other NSAIDs.

Aspirin increases bleeding time, decreases platelet adhesiveness, and, in large doses, can cause hypoprothrombinaemia. It may cause other blood disorders, including thrombocytopenia.

Aspirin and other salicylates may cause hepatotoxicity, particularly in patients with juvenile idiopathic arthritis or other connective tissue disorders. In children the use of aspirin has been implicated in some cases of Reye's syndrome, leading to severe restrictions on the indications for aspirin therapy in children. For further details see under Reye's Syndrome, below.