### Preparations

**Proprietary Preparations** (details are given in Part 3)

***Arg.:*** Berlofen; Bristaflam†; ***Austria:*** Beofenac†; ***Belg.:*** Air-Tal; Biofenac; ***Braz.:*** Aceflan†; Cecoflan†; Proflam; ***Chile:*** Airtal†; Bristaflam†; ***Denm.:*** Barcan; ***Fin.:*** Barcan; ***Fr.:*** Cartrex; ***Ger.:*** Beofenac; ***Gr.:*** Aceclonac; Arlina; Biofenac; Sovipan; ***Hung.:*** Aflamin; ***India:*** Aceclo; Arrestin; Movon; Zerodol; ***Ital.:*** Airtal; Gladio; Kafenac; ***Mex.:*** Bristaflam; ***Neth.:*** Biofenac; ***Norw.:*** Barcan; ***Philipp.:*** Clanza; ***Port.:*** Airtal; Biofenac; ***Rus.:*** Airtal (Аэртал); ***Spain:*** Airtal; Airtal Difucrem; Falcol; Gerbin; Sanein; ***Swed.:*** Barcan; ***Switz.:*** Locomin†; ***UAE:*** Aceclofar; ***UK:*** Preservex; ***Venez.:*** Airtal†; Bristaflam.

**Multi-ingredient:** ***India:*** Kinectine; Kinectine P; Kinectine-MR; Movon-MR; Movon-P†; Zerodol-MR; Zerodol-P.

## Acemetacin *(BAN, rINN)*

Acemetacina; Acémétacine; Acemetacinum; Asemetasin; Bay-f-4975; Indometasinin Glikolik Asit Esteri; TVX-1322. *O*-[(1-*p*-Chlorobenzoyl-5-methoxy-2-methylindol-3-yl)acetyl]glycolic acid.

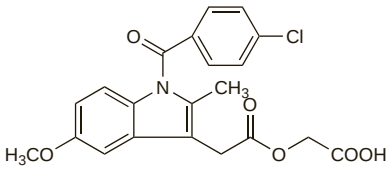
Ацеметацин

$C_{21}H_{18}ClNO_6$ = 415.8.

*CAS — 53164-05-9.*

*ATC — M01AB11.*

*ATC Vet — QM01AB11.*



**Pharmacopoeias.** In *Eur.* (see p.vii)

**Ph. Eur. 6.2** (Acemetacin). A yellow or greenish-yellow, crystalline powder. It exhibits polymorphism. Practically insoluble in water; slightly soluble in anhydrous alcohol; soluble in acetone. Protect from light.

### Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96.

### Interactions

For interactions associated with NSAIDs, see p.99.

### Pharmacokinetics

Acemetacin is well absorbed after oral dosage. Its major metabolite is indometacin (p.66) which, after repeated doses, is present at higher concentrations than those of acemetacin. Acemetacin is bound to plasma proteins to a slightly lesser extent than indometacin. It is eliminated via both the liver and the kidneys.

### Uses and Administration

Acemetacin, a glycolic acid ester of indometacin, is an NSAID (p.99). Its pharmacological activity is due to both acemetacin and its major metabolite, indometacin (p.66). Acemetacin is used in rheumatoid arthritis, osteoarthritis, and low back pain, and for postoperative pain and inflammation. Usual oral doses are 120 to 180 mg daily in divided doses. Acemetacin is eliminated by both hepatic and renal routes, although pharmacokinetics are not affected by moderate renal or hepatic impairment and appear to be unchanged in the elderly.

◊ References.


1. Jones RW, *et al*. Comparative pharmacokinetics of acemetacin in young subjects and elderly patients. *Br J Clin Pharmacol* 1991; **31:** 543–5.
2. Hazleman B, Bernstein RM. Acemetacin in the long-term therapy of rheumatoid arthritis. *Curr Med Res Opin* 1993; **13:** 119–26.
3. Chou CT, Tsai YY. A double-blind, randomized, controlled parallel group study evaluating the efficacy and safety of acemetacin for the management of osteoarthritis. *Int J Clin Pharmacol Res* 2002; **22:** 1–6.
4. Leeb BF, *et al*. Behandlung der Gonarthrose: Wirksamkeit und Verträglichkeit von retardiertem Acemetacin im Vergleich zu Celecoxib. *Orthopade* 2004; **33:** 1032–41.


### Preparations

**Proprietary Preparations** (details are given in Part 3)

***Austria:*** Rheutrop; ***Cz.:*** Rantudil; ***Ger.:*** Acemetadoc; Acephlogont†; Rantudil; ***Gr.:*** Gamespir†; Rantutal; ***Hung.:*** Rantudil; ***Ital.:*** Acemix; Solart†; ***Jpn:*** Rantudil; ***Mex.:*** Rantudil; ***Philipp.:*** Rantudil; ***Pol.:*** Rantudil; ***Port.:*** Rantudil; ***Spain:*** Espledol; Oldan; ***Switz.:*** Tilur; ***Turk.:*** Rantudil; ***UK:*** Emflex; ***Venez.:*** Mostanol†; Pranex.

**Multi-ingredient:** ***Arg.:*** Rucaten Forte; Rucaten Prednisolona.

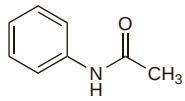
## Acetanilide

Acetanilida; Antifebrin. *N*-Phenylacetamide.

Антифебрин; Ацетанилид

$C_8H_9NO$ = 135.2.

*CAS — 103-84-4.*



**Pharmacopoeias.** In *Fr.*

### Profile

Acetanilide, a para-aminophenol derivative related to paracetamol (p.108), has analgesic and antipyretic properties. It was replaced by safer analgesics.

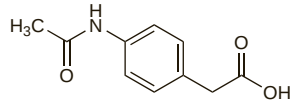
## Actarit *(rINN)*

Actaritum; MS-932. (*p*-Acetamidophenyl)acetic acid.

Актарит

$C_{10}H_{11}NO_3$ = 193.2.

*CAS — 18699-02-0.*



### Profile

Actarit is reported to be a disease-modifying antirheumatic drug. It has been given in the treatment of rheumatoid arthritis in a usual oral dose of 100 mg three times daily.

**Adverse effects.** A photosensitivity reaction developed in a 52-year-old woman one month after starting actarit and doxycycline.[1] Photopatch tests for both drugs were only positive for the patches containing actarit.


1. Kawada A, *et al*. Photosensitivity due to actarit. *Contact Dermatitis* 1997; **36:** 175–6.


**Use.** References.


1. Nakamura H, *et al*. Clinical effects of actarit in rheumatoid arthritis: improvement of early disease activity mediated by reduction of serum concentrations of nitric oxide. *Clin Exp Rheumatol* 2000; **18:** 445–50.


### Preparations

**Proprietary Preparations** (details are given in Part 3)

***Jpn:*** Mover†; Orcl.

# Adalimumab *(BAN, USAN, rINN)*

Adalimumabum; D2E7; LU-200134. Immunoglobulin G1 (human monoclonal D2E7 heavy chain anti-human tumor necrosis factor), disulfide with human monoclonal D2E7κ-chain, dimer.

Адалимумаб

*CAS — 331731-18-1.*

*ATC — L04AB04.*

*ATC Vet — QL04AB04.*

### Adverse Effects and Precautions

As for Infliximab, p.69.

Injection site reactions including erythema, itching, pain, and swelling are the most common adverse reactions with adalimumab; however, most reactions are mild and do not result in drug withdrawal. Other common reactions include headache, rashes, back pain, hypertension, paraesthesias, increased alkaline phosphate levels, and cough.

Autoantibodies to adalimumab have been detected.

### Interactions

As for Infliximab, p.71.

Methotrexate is reported to reduce the clearance of adalimumab by up to 44% but licensed product information for the latter states that dosage adjustment for either drug does not appear to be necessary.

### Pharmacokinetics

Adalimumab is reported to have linear pharmacokinetics at usual dosages. After subcutaneous injection peak concentrations are reached in about 3 to 8 days and bioavailability is estimated to be 64%. The mean terminal half-life is about 2 weeks.

◊ References.


1. Nestorov I. Clinical pharmacokinetics of tumor necrosis factor antagonists. *J Rheumatol* 2005; **74** (suppl): 13–18.


### Uses and Administration

Adalimumab is a recombinant human monoclonal tumour necrosis factor (TNF) antibody that binds specifically to TNF-α and blocks its interaction with endogenous cell-surface TNF receptors. It also modulates biological responses that are induced or regulated by TNF. Elevated levels of TNF have been found in the affected tissues and fluids of patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, and Crohn's disease.

Adalimumab is used in the treatment of moderate to severe, active **rheumatoid arthritis** and active and progressive **psoriatic arthritis** to delay structural damage and improve physical function. In the UK, it is licensed for use in patients who have had an inadequate response to standard disease-modifying antirheumatic drugs (DMARDs), although in severe progressive rheumatoid arthritis it may be used in patients not previously treated with methotrexate; in the USA, it may be used to reduce the signs and symptoms of early disease. Adalimumab is also used in the treatment of active **ankylosing spondylitis**: UK licensed product information recommends that it should only be used in patients with severe disease who have had an inadequate response to conventional treatment; however, in the USA it may be used to reduce signs and symptoms in early disease. For all the above indications, it is given by subcutaneous injection in a dose of 40 mg every other week. In the treatment of rheumatoid arthritis, UK licensed product information recommends that adalimumab should be given with methotrexate, although monotherapy may be used where treatment with methotrexate would be inappropriate. When used as monotherapy in rheumatoid arthritis, some patients may benefit from increasing the dose to 40 mg every week. Clinical response is usually achieved within 12 weeks of treatment.

Adalimumab is also used in the treatment of moderate to severe, active **Crohn's disease** unresponsive to conventional treatment; it may also be used in patients who have relapsed while taking infliximab. Patients may be given an initial dose of 160 mg on day 1 (given as four 40-mg injections in one day or two 40-mg injections daily for 2 consecutive days), followed by 80 mg two weeks later (day 15). After a further two weeks (day 29), a maintenance dose of 40 mg every other week may be started. Alternatively, UK licensed product information advises that patients at risk of adverse effects may be given 80 mg initially, followed by 40 mg 2 weeks later; thereafter, usual maintenance doses may be given. A clinical response is usually seen within 12 weeks of starting treatment; those patients who relapse while on adalimumab may benefit from increasing the maintenance dose to 40 mg every week.

In the treatment of moderate to severe chronic **plaque psoriasis** in patients unresponsive to, or intolerant of, conventional systemic therapy including phototherapy, the recommended initial dose of adalimumab is 80 mg subcutaneously; this may be followed by a maintenance dose of 40 mg subcutaneously on alternate weeks, starting 1 week after the initial dose. A clinical response is usually seen within 16 weeks of starting treatment.

For the uses of adalimumab in children, and recommended doses, see below.

**Administration in children.** In the USA, adalimumab is licensed in the treatment of moderate to severe, active juvenile idiopathic arthritis in children aged 4 years and above: it may be used alone or with methotrexate. The dose is calculated according to weight and is given subcutaneously: those weighing 15 kg to less than 30 kg should be given 20 mg every other week, while heavier children may receive 40 mg every other week.