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.

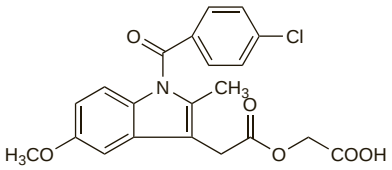
Ацеметацин

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

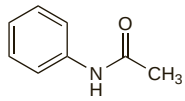
Acetanilide

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.

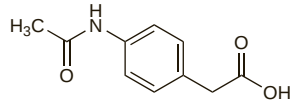
Actarit *(rINN)*

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.

Inflammatory bowel disease. Adalimumab is used in the management of Crohn's disease[1-4] (p.1697), including in patients who are intolerant of, or relapse on, infliximab treatment.[5-8] It has also been tried in the treatment of ulcerative colitis (p.1697).[9]

1. Hanauer SB, *et al.* Human anti-tumor necrosis factor monoclonal antibody (adalimumab) in Crohn's disease: the CLASSIC-I trial. *Gastroenterology* 2006; **130:** 323–33.
2. Sandborn WJ, *et al.* Adalimumab for maintenance treatment of Crohn's disease: results of the CLASSIC II trial. *Gut* 2007; **56:** 1232–9.
3. Colombel JF, *et al.* Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. *Gastroenterology* 2007; **132:** 52–65.
4. Plosker GL, Lyseng-Williamson KA. Adalimumab: in Crohn's disease. *BioDrugs* 2007; **21:** 125–32.
5. Sandborn WJ, *et al.* An open-label study of the human anti-TNF monoclonal antibody adalimumab in subjects with prior loss of response or intolerance to infliximab for Crohn's disease. *Am J Gastroenterol* 2004; **99:** 1984–9.
6. Papadakis KA, *et al.* Safety and efficacy of adalimumab (D2E7) in Crohn's disease patients with an attenuated response to infliximab. *Am J Gastroenterol* 2005; **100:** 75–9.
7. Peyrin-Biroulet L, *et al.* Adalimumab maintenance therapy for Crohn's disease with intolerance or lost response to infliximab: an open-label study. *Aliment Pharmacol Ther* 2007; **25:** 675–80.
8. Sandborn WJ, *et al.* Adalimumab induction therapy for Crohn disease previously treated with infliximab: a randomized trial. *Ann Intern Med* 2007; **146:** 829–38.
9. Peyrin-Biroulet L, *et al.* Adalimumab induction therapy for ulcerative colitis with intolerance or lost response to infliximab: an open-label study. *World J Gastroenterol* 2007; **13:** 2328–32.

Psoriasis. Adalimumab is used in the treatment of plaque psoriasis (p.1583).

References.

1. Gordon KB, *et al.* Clinical response to adalimumab treatment in patients with moderate to severe psoriasis: double-blind, randomized controlled trial and open-label extension study. *J Am Acad Dermatol* 2006; **55:** 598–606.
2. Papoutsaki M, *et al.* Adalimumab for severe psoriasis and psoriatic arthritis: an open-label study in 30 patients previously treated with other biologics. *J Am Acad Dermatol* 2007; **57:** 269–75.
3. Menter A, *et al.* Adalimumab therapy for moderate to severe psoriasis: a randomized, controlled phase III trial. *J Am Acad Dermatol* 2008; **58:** 106–15.
4. Revicki D, *et al.* Impact of adalimumab treatment on health-related quality of life and other patient-reported outcomes: results from a 16-week randomized controlled trial in patients with moderate to severe plaque psoriasis. *Br J Dermatol* 2008; **158:** 549–57.
5. Saurat J-H, *et al.* CHAMPION Study Investigators. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis. *Br J Dermatol* 2008; **158:** 558–66.
6. NICE. Adalimumab for the treatment of adults with psoriasis: Technology Appraisal Guidance 146 (issued June 2008). Available at: http://www.nice.org.uk/nicemedia/pdf/TA146Guidance.pdf (accessed 25/07/08)

Rheumatoid arthritis. References to the use of adalimumab in rheumatoid arthritis (p.11).

1. den Broeder AA, *et al.* Long-term anti-tumour necrosis factor alpha monotherapy in rheumatoid arthritis: effect on radiological course and prognostic value of markers of cartilage turnover and endothelial activation. *Ann Rheum Dis* 2002; **61**: 311–18.
2. Rau R. Adalimumab (a fully human anti-tumour necrosis factor alpha monoclonal antibody) in the treatment of active rheumatoid arthritis: the initial results of five trials. *Ann Rheum Dis* 2002; **61** (suppl 2): 70–3.
3. Weinblatt ME, *et al.* Adalimumab, a fully human anti-tumor necrosis factor alpha monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate: the ARMADA trial. *Arthritis Rheum* 2003; **48:** 35–45.
4. Furst DE, *et al.* Adalimumab, a fully human anti tumor necrosis factor-alpha monoclonal antibody, and concomitant standard antirheumatic therapy for the treatment of rheumatoid arthritis: results of STAR (Safety Trial of Adalimumab in Rheumatoid Arthritis). *J Rheumatol* 2003; **30:** 2563–71.
5. van de Putte LB, *et al.* Efficacy and safety of adalimumab as monotherapy in patients with rheumatoid arthritis for whom previous disease modifying antirheumatic drug treatment has failed. *Ann Rheum Dis* 2004; **63:** 508–16.
6. Keystone EC, *et al.* Radiographic, clinical, and functional outcomes of treatment with adalimumab (a human anti-tumor necrosis factor monoclonal antibody) in patients with active rheumatoid arthritis receiving concomitant methotrexate therapy: a randomized, placebo-controlled, 52-week trial. *Arthritis Rheum* 2004; **50:** 1400–11.
7. Wick MC, *et al.* Adalimumab (Humira) restores clinical response in patients with secondary loss of efficacy from infliximab (Remicade) or etanercept (Enbrel): results from the STURE registry at Karolinska University Hospital. *Scand J Rheumatol* 2005; **34:** 353–8.
8. Navarro-Sarabia F, *et al.* Adalimumab for treating rheumatoid arthritis. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2005 (accessed 13/06/08).
9. Weinblatt ME, *et al.* Long term efficacy and safety of adalimumab plus methotrexate in patients with rheumatoid arthritis: ARMADA 4 year extended study. *Ann Rheum Dis* 2006; **65:** 753–9.
10. Breedveld FC, *et al.* The PREMIER study: a multicenter, randomized, double-blind clinical trial of combination therapy with adalimumab plus methotrexate versus methotrexate alone or adalimumab alone in patients with early, aggressive rheumatoid arthritis who had not had previous methotrexate treatment. *Arthritis Rheum* 2006; **54:** 26–37.
11. Heiberg MS, *et al.* Adalimumab and methotrexate is more effective than adalimumab alone in patients with established rheumatoid arthritis: results from a 6-month longitudinal, observational, multicentre study. *Ann Rheum Dis* 2006; **65:** 1379–83.
12. Cvetković RS, Scott LJ. Adalimumab: a review of its use in adult patients with rheumatoid arthritis. *BioDrugs* 2006; **20:** 293–311.
13. Burmester GR, *et al.* Adalimumab alone and in combination with disease-modifying antirheumatic drugs for the treatment of rheumatoid arthritis in clinical practice: the Research in Active Rheumatoid Arthritis (ReAct) trial. *Ann Rheum Dis* 2007; **66:** 732–9.
14. Bombardieri S, *et al.* Research in Active Rheumatoid Arthritis (ReAct) Study Group. Effectiveness of adalimumab for rheumatoid arthritis in patients with a history of TNF-antagonist therapy in clinical practice. *Rheumatology (Oxford)* 2007; **46:** 1191–9.
15. NICE. Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis: Technology Appraisal Guidance 130 (issued October 2007). Available at: http://www.nice.org.uk/nicemedia/pdf/TA130guidance.pdf (accessed 13/06/08)

Spondyloarthropathies. References to the use of adalimumab in ankylosing spondylitis and psoriatic arthritis (see Spondyloarthropathies, p.13).

1. Chew A-L, *et al.* Successful treatment of severe psoriasis and psoriatic arthritis with adalimumab. *Br J Dermatol* 2004; **151:** 492–6.
2. Mease PJ, *et al.* Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 2005; **52:** 3279–89.
3. van der Heijde D, *et al.* Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2006; **54:** 2136–46.
4. van der Heijde D, *et al.* ATLAS Study Group. Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2006; **54:** 2136–46.
5. Simpson D, Scott LJ. Adalimumab: in psoriatic arthritis. *Drugs* 2006; **66:** 1487–96.
6. Gladman DD, *et al.* Adalimumab improves joint-related and skin-related functional impairment in patients with psoriatic arthritis: patient-reported outcomes of the Adalimumab Effectiveness in Psoriatic Arthritis Trial. *Ann Rheum Dis* 2007; **66:** 163–8.
7. Gladman DD, *et al.* Adalimumab for long-term treatment of psoriatic arthritis: forty-eight week data from the adalimumab effectiveness in psoriatic arthritis trial. *Arthritis Rheum* 2007; **56:** 476–88.
8. Genovese MC, *et al.* M02-570 Study Group. Safety and efficacy of adalimumab in treatment of patients with psoriatic arthritis who had failed disease modifying antirheumatic drug therapy. *J Rheumatol* 2007; **34:** 1040–50. Correction. *ibid.*; 1439.
9. Davis JC, *et al.* Health-related quality of life outcomes in patients with active ankylosing spondylitis treated with adalimumab: results from a randomized controlled study. *Arthritis Rheum* 2007; **57:** 1050–7.
10. NICE. Adalimumab for the treatment of psoriatic arthritis: Technology Appraisal Guidance 125 (issued August 2007). Available at: http://www.nice.org.uk/nicemedia/pdf/TA125guidance.pdf (accessed 13/06/08)

Uveitis. Adalimumab has been tried with some success in the treatment of idiopathic uveitis (p.1515). Uveitis can also develop as a complication of other inflammatory disorders such as rheumatoid arthritis; treatment with adalimumab may improve ocular symptoms in addition to its effect on the primary disorder.

References.

1. Vazquez-Cobian LB, *et al.* Adalimumab therapy for childhood uveitis. *J Pediatr* 2006; **149:** 572–5.
2. Biester S, *et al.* Adalimumab in the therapy of uveitis in childhood. *Br J Ophthalmol* 2007; **91:** 319–24.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Humira; ***Austral.:*** Humira; ***Belg.:*** Humira; ***Braz.:*** Humira; ***Canad.:*** Humira; ***Chile:*** Humira; ***Cz.:*** Humira; ***Denm.:*** Humira; ***Fin.:*** Humira; ***Fr.:*** Humira; ***Ger.:*** Humira; ***Gr.:*** Humira; ***Hong Kong:*** Humira; ***Hung.:*** Humira; ***Irl.:*** Humira; ***Israel:*** Humira; ***Ital.:*** Humira; ***Malaysia:*** Humira; ***Mex.:*** Humira; ***Neth.:*** Humira; Trudexa; ***Norw.:*** Humira; ***NZ:*** Humira; ***Pol.:*** Humira; ***Port.:*** Humira; ***Singapore:*** Humira; ***Spain:*** Humira; ***Swed.:*** Humira; ***Switz.:*** Humira; ***UK:*** Humira; ***USA:*** Humira; ***Venez.:*** Humira.

Alfentanil Hydrochloride

(BANM, USAN, rINNM) ⊗

Alfentaniilihydrokloridi; Alfentanil, chlorhydrate d'; Alfentanil Hidroklorür; Alfentanil-hidroklorid; Alfentanil-hydrochlorid; Alfentanilhydroklorid; Alfentanili hydrochloridum; Alfentanilio hidrochloridas; Hidrocloruro de alfentanilo; R-39209. *N*-{1-[2-(4-Ethyl-5-oxo-2-tetrazolin-1-yl)ethyl]-4-(methoxymethyl)-4-piperidyl}propionanilide hydrochloride.

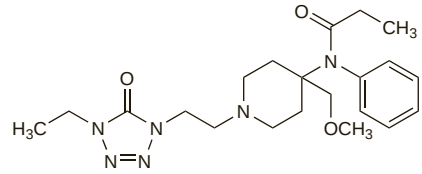
Альфентанила Гидрохлорид

$C_{21}H_{32}N_6O_3$,HCl = 453.0.

CAS — 71195-58-9 (alfentanil); 69049-06-5 (anhydrous alfentanil hydrochloride); 70879-28-6 (alfentanil hydrochloride monohydrate).

ATC — N01AH02.

ATC Vet — QN01AH02.



(alfentanil)

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

Ph. Eur. 6.2 (Alfentanil Hydrochloride). A white or almost white powder. Freely soluble in water, in alcohol, and in methyl alcohol. Protect from light.

USP 31 (Alfentanil Hydrochloride). A white to almost white powder. Soluble in water; freely soluble in alcohol, in chloroform, and in methyl alcohol; sparingly soluble in acetone. Store in airtight containers.

Dependence and Withdrawal

As for Opioid Analgesics, p.101.

Adverse Effects and Treatment

As for Opioid Analgesics in general, p.102, and for Fentanyl, p.56.

Effects on the cardiovascular system. Sinus arrest had occurred[1] during intubation in 2 patients given alfentanil 30 micrograms/kg.

1. Maryniak JK, Bishop VA. Sinus arrest after alfentanil. *Br J Anaesth* 1987; **59:** 390–1.

Effects on mental function. Like fentanyl, alfentanil 7.5 or 15 micrograms/kg intravenously had no effect on memory in healthy subjects.[1] In another study impairment of memory for new facts did occur 2 hours after operation in patients anaesthetised with alfentanil 7.5 micrograms/kg, but not in those given fentanyl;[2] methohexital might have contributed to the impairment.

1. Scamman FL, *et al.* Ventilatory and mental effects of alfentanil and fentanyl. *Acta Anaesthesiol Scand* 1984; **28:** 63–7.
2. Kennedy DJ, Ogg TW. Alfentanil and memory function: a comparison with fentanyl for day case termination of pregnancy. *Anaesthesia* 1985; **40:** 537–40.

Effects on the respiratory system. Alfentanil, like other opioid agonists, causes dose-related respiratory depression; it is significant with doses of more than 1 mg. Recovery has been reported to be faster after alfentanil than after fentanyl (see p.56),[1,2] possibly reflecting the shorter elimination half-life of alfentanil. Even so, accumulation of alfentanil is possible with large doses over a prolonged period. Profound analgesia is accompanied by marked respiratory depression which may persist or recur postoperatively.

Sudden respiratory arrest usually within an hour after the end of alfentanil infusion has been reported in patients who initially appeared to have made a rapid recovery from anaesthesia;[3-5] all responded to treatment with naloxone. Close monitoring of respiration in the initial postoperative period was recommended and this was reinforced by the manufacturers;[6] factors such as hyperventilation and the use of opioid premedication might enhance or prolong the respiratory depressant effects of alfentanil.

1. Andrews CJH, *et al.* Ventilatory effects during and after continuous infusion of fentanyl or alfentanil. *Br J Anaesth* 1983; **55:** 211S–16S.
2. Scamman FL, *et al.* Ventilatory and mental effects of alfentanil and fentanyl. *Acta Anaesthesiol Scand* 1984; **28:** 63–7.
3. Sebel PS, *et al.* Respiratory depression after alfentanil infusion. *BMJ* 1984; **289:** 1581–2.
4. Krane BD, *et al.* Alfentanil and delayed respiratory depression: cases studies and review. *Anesth Analg* 1990; **70:** 557–61.
5. Sternlo JEG, Sandin RH. Recurrent respiratory depression after total intravenous anaesthesia with propofol and alfentanil. *Anaesthesia* 1998; **53:** 378–81.
6. Waldron HA, Cookson RF. Respiratory depression after alfentanil infusion. *BMJ* 1985; **290:** 319.

Precautions

As for Opioid Analgesics in general, p.103.

Children. Alfentanil given to preterm infants undergoing paralysis and mechanical ventilation for respiratory distress syndrome resulted in a rapid and significant fall in heart rate and blood pressure, emphasising that proper evaluation of the pharmacological and clinical effects was necessary.[1]

The *BNFC* states that the half-life of alfentanil is prolonged in neonates and accumulation is likely with prolonged use; muscle rigidity may occur and the use of muscle relaxants may be required.

1. Marlow N, *et al.* Hazards of analgesia for newborn infants. *Arch Dis Child* 1988; **63:** 1293.

The elderly. EEG changes suggested that elderly patients had increased brain sensitivity to alfentanil,[1] and that lower doses might be indicated in older patients for pharmacodynamic rather