Mex.: Betagranulos; ***S.Afr.:*** Brasivol; ***Singapore:*** Ionax Scrub; ***UK:*** Brasivol; ***USA:*** Ionax Scrub; ***Venez.:*** Betagranulos; Ionax Scrub.

Multi-ingredient: ***Canad.:*** Pernox; ***Indon.:*** Aludonna; ***Ital.:*** Gastrodue†; ***Malaysia:*** Belcid†; ***Mex.:*** Dermobras; Ionax Scrub; ***Philipp.:*** Ionax Scrub; ***S.Afr.:*** Pedimed; ***Switz.:*** Cliniderm; ***USA:*** Pernox; Zanfel; ***Venez.:*** Exfoliderm.

Acitretin *(BAN, USAN, rINN)*

Acitretina; Acitretinas; Acitrétine; Acitretinum; Asitretiini; Asitretin; Etretin; Ro-10-1670; Ro-10-1670/000. (*all-trans*)-9-(4-Methoxy-2,3,6-trimethylphenyl)-3,7-dimethyl-2,4,6,8-nonatetraenoic acid; (2*E*,4*E*,6*E*,8*E*)-9-(4-Methoxy-2,3,6-trimethylphenyl)-3,7-dimethylnona-2,4,6,8-tetraenoic acid.

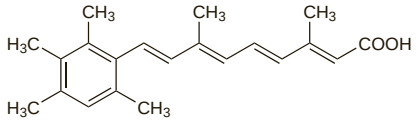
Ацитретин

$C_{21}H_{26}O_3$ = 326.4.

CAS — 55079-83-9.

ATC — D05BB02.

ATC Vet — QD05BB02.



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

Ph. Eur. 6.2 (Acitretin). A yellow or greenish-yellow, crystalline powder. Practically insoluble in water; slightly soluble in alcohol and in acetone; very slightly soluble in cyclohexane; sparingly soluble in tetrahydrofuran. It is sensitive to air, heat, and light, especially in solution. Store at 2° to 8° in airtight containers. Protect from light. It is recommended that the contents of an opened container be used as soon as possible and any unused part be protected by an atmosphere of inert gas.

USP 31 (Acitretin). A yellow or greenish, crystalline powder. Practically insoluble in water; slightly soluble in acetone and in alcohol; very slightly soluble in cyclohexane; sparingly soluble in tetrahydrofuran. Store in airtight containers at 20° to 25°, excursions permitted between 15° and 30°. Protect from light.

Adverse Effects and Precautions

As for Isotretinoin, p.1599.

Acitretin has a relatively short half-life, but etretinate, which has a very prolonged half-life, has been detected in the plasma of some patients receiving acitretin. Recommendations vary slightly in different countries but pregnancy should be avoided for at least 2 to 3 years after treatment has been withdrawn (see also Pregnancy, below) and patients should not donate blood for at least 1 to 3 years after stopping therapy. Female patients should avoid alcohol during treatment with acitretin and for 2 months after stopping treatment (see under Interactions, below).

Breast feeding. Acitretin was distributed into the breast milk of a woman treated with oral acitretin for psoriasis. Although the estimated amount of acitretin that would be consumed by a breast-fed infant was only 1.5% of the maternal dose, the authors considered that the toxic potential of acitretin to the infant justified its avoidance. In this case, the infant was not breast-fed during acitretin therapy.[1] Licensed product information also recommends that breast-feeding women should not be given acitretin. The American Academy of Pediatrics, however, has found no mention of clinical effect on the infant, and considers the maternal use of acitretin to be usually compatible with breast feeding.[2]

1. Rollman O, Pihl-Lundin I. Acitretin excretion into human breast milk. *Acta Derm Venereol (Stockh)* 1990; **70:** 487–90.
2. 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 27/09/07)

Capillary leak syndrome. There are rare reports of capillary leak syndrome associated with acitretin. In one case, generalised oedema and weight gain, haemorrhagic lesions, and evidence of rhabdomyolysis were seen.[1] In another, there was oedema and weight gain, dyspnoea, pulmonary infiltrates, pleural effusion, hypotension, and oliguria.[2] These reactions may be related to the retinoic acid syndrome that can occur with tretinoin (see p.1618). Generalised oedema has also been reported with etretinate (p.1597).

1. Estival JL, *et al.* Capillary leak syndrome induced by acitretin. *Br J Dermatol* 2004; **150:** 150–2.
2. Vos LE, *et al.* Acitretin induces capillary leak syndrome in a patient with pustular psoriasis. *J Am Acad Dermatol* 2007; **56:** 339–42.

Effects on the blood. For reports of adverse effects on the blood by oral retinoids, including agranulocytosis associated with acitretin, see under Isotretinoin, p.1599.

Effects on the eyes. For reference to maculopathy occurring during therapy with acitretin, and the ocular effects of benign intracranial hypertension caused by retinoids, see under Isotretinoin, p.1600.

Effects on the musculoskeletal system. For reference to myopathy occurring during therapy with acitretin, and a discussion of hyperostosis and calcinosis that can occur with oral retinoid therapy, see under Isotretinoin, p.1600.

Effects on the skin. For mention of the exacerbation of erythroderma by acitretin, see under Isotretinoin, p.1601.

Pregnancy. The risks of spontaneous abortion and malformations similar to those associated with isotretinoin (p.1601) are high when acitretin or etretinate are given during pregnancy, particularly the first trimester.[1,2] Although the risks might be lower after stopping treatment, malformations have still been reported in infants and aborted fetuses conceived within 2 years of stopping acitretin[1,3] and up to 45 months after stopping etretinate.[1] In the UK licensed product information for acitretin recommends that pregnancy should be avoided during and for at least 2 years (3 years is recommended in the USA) after withdrawal of therapy because etretinate, which has a much longer half-life than acitretin, has been detected in the plasma of some patients given acitretin. It has been pointed out that plasma-etretinate concentrations are a poor indication of total body stores; a study[4] has indicated that there may be substantial concentrations of etretinate in the fatty tissues of women who have received acitretin.

For information on contraceptive choice in women taking oral retinoids, see under Isotretinoin, p.1601.

1. Geiger J-M, *et al.* Teratogenic risk with etretinate and acitretin treatment. *Dermatology* 1994; **189:** 109–16.
2. Barbero P, *et al.* Acitretin embryopathy: a case report. *Birth Defects Res A Clin Mol Teratol* 2004; **70:** 831–3.
3. Maradit H, Geiger J-M. Potential risk of birth defects after acitretin discontinuation. *Dermatology* 1999; **198:** 3–4.
4. Sturkenboom MCJM, *et al.* Inability to detect plasma etretinate and acitretin is a poor predictor of the absence of these teratogens in tissue after stopping acitretin treatment. *Br J Clin Pharmacol* 1994; **38:** 229–35.

Interactions

As for Isotretinoin, p.1602.

Etretinate has been detected in the plasma of some patients receiving acitretin and acitretin is also a metabolite of etretinate; therefore interactions associated with etretinate (see p.1597) may also apply to acitretin. Taking acitretin with alcohol has been associated with etretinate formation.

For discussion of the potential interactions of retinoids with hormonal contraceptives, and the effect this might have on contraceptive choice during retinoid treatment, see p.2068.

Alcohol. The consumption of alcohol has been associated with the formation of etretinate in patients taking acitretin.[1,2] One study[2] found a trend suggesting that a higher alcohol intake was associated with a higher risk of etretinate formation and higher etretinate concentrations. However, the presence of alcohol is not essential for this transformation to take place and etretinate has also been detected in a patient taking acitretin who did not drink alcohol.[3] Consequently, licensed product information warns that alcohol must not be consumed by female patients during acitretin therapy and for 2 months after stopping, to avoid the formation of etretinate and associated prolonged risks of teratogenicity (see Pregnancy, above).

1. Larsen FG, *et al.* Conversion of acitretin to etretinate in psoriatic patients is influenced by ethanol. *J Invest Dermatol* 1993; **100:** 623–7.
2. Larsen FG, *et al.* Acitretin is converted to etretinate only during concomitant alcohol intake. *Br J Dermatol* 2000; **143:** 1164–9.
3. Maier H, Hönigsmann H. Concentration of etretinate in plasma and subcutaneous fat after long-term acitretin. *Lancet* 1996; **348:** 1107.

Pharmacokinetics

Acitretin is absorbed from the gastrointestinal tract and peak plasma concentrations have been obtained 1 to 5 hours after oral doses. Bioavailability after a single dose is about 60 to 70%, but this can vary considerably; bioavailability may be increased by dosage with food. Acitretin is highly bound to plasma proteins. It is metabolised to 13-*cis*-acitretin. Etretinate (p.1597) has also been detected in the plasma of some patients after doses of acitretin. The elimination half-life of acitretin is about 2 days but account should always be taken of the fact that the half-life of etretinate is much longer, being about 120 days. Acitretin is excreted as metabolites in bile and urine, and is distributed into breast milk.

◊ General references.

1. Larsen FG, *et al.* Pharmacokinetics and therapeutic efficacy of retinoids in skin diseases. *Clin Pharmacokinet* 1992; **23:** 42–61.
2. Larsen FG. Pharmacokinetics of etretinate and acitretin with special reference to treatment of psoriasis. *Acta Derm Venereol (Stockh)* 1994; **190** (suppl): 1–33.
3. Wiegand UW, Chou RC. Pharmacokinetics of acitretin and etretinate. *J Am Acad Dermatol* 1998; **39** (suppl): S25–S33.

Renal impairment. The pharmacokinetics of acitretin are reported to be altered in patients with chronic renal failure but neither acitretin nor its 13-*cis* metabolite are removed by haemodialysis.[1]

1. Stuck AE, *et al.* Pharmacokinetics of acitretin and its 13-cis metabolite in patients on haemodialysis. *Br J Clin Pharmacol* 1989; **27:** 301–4.

Uses and Administration

Acitretin is a retinoid and is a metabolite of etretinate (p.1597). It is used orally in the treatment of severe psoriasis resistant to other forms of therapy, palmoplantar pustular psoriasis, severe congenital ichthyosis and Darier's disease (keratosis follicularis), and in severe lichen planus.

In the UK, acitretin is given in an initial daily dose of 25 or 30 mg with food for 2 to 4 weeks; in the USA (where it is licensed only for use in psoriasis) initial doses up to 50 mg daily are permitted. The daily dosage is adjusted thereafter according to clinical response and adverse effects; optimal results are usually obtained with 25 to 50 mg given daily for a further 6 to 8 weeks but some patients may require up to 75 mg daily. For the treatment of Darier's disease a starting dose of 10 mg may be appropriate, adjusted thereafter according to response. In Darier's disease and congenital ichthyosis treatment may be required for more than 3 months but a daily dosage of 50 mg should not be exceeded. In the UK, licensed product information recommends that continuous treatment should not last longer than 6 months for any indication because of limited clinical data. For lichen planus, doses are similar to those used in the UK (see above).

For doses in children, see below.

Administration in children. Acitretin is not generally considered suitable for use in children. However, a review of its use in 29 children with severe inherited disorders of keratinisation[1] reported that acitretin was an effective and safe treatment provided that the minimal effective dose was used and that adverse effects were carefully monitored. UK licensed product information contra-indicates acitretin use in children unless the benefits significantly outweigh the risks, particularly premature epiphyseal closure and other skeletal effects associated with retinoids. However, if deemed necessary an oral dose of 500 micrograms/kg once daily (occasionally up to 1 mg/kg daily for limited periods) has been suggested, but the maximum daily dose should not exceed 35 mg. The *BNFC* suggests that these doses may be used under expert supervision for children aged 1 month to 12 years for the treatment of severe extensive psoriasis resistant to other forms of therapy, palmo-plantar pustular psoriasis, severe congenital ichthyosis, and Darier's disease. The adult dose (see above) is considered suitable for children from 12 years of age. The *BNFC* also includes a dose of 500 micrograms/kg daily (occasionally up to 1 mg/kg daily) for the management of harlequin ichthyosis in neonates.

1. Lacour M, *et al.* An appraisal of acitretin therapy in children with inherited disorders of keratinization. *Br J Dermatol* 1996; **134:** 1023–9.

Eye disorders. A case report indicated that acitretin, given for psoriasis at an initial dose of 30 mg daily for one month and then reduced to 20 mg daily, improved corneal opacities in a patient with chronic tuberculosis-related interstitial keratitis.[1]

1. Labetoulle M, *et al.* Rapid improvement of chronic interstitial keratitis with acitretin. *Br J Ophthalmol* 2002; **86:** 1445–6.

Malignant neoplasms. Acitretin may be useful in preventing the development of skin neoplasms in high-risk individuals, such as solid organ transplant recipients.[1,2] However, long-term therapy is needed to maintain the effect and adverse effects can limit its use[2] (see also Malignant Neoplasms under Isotretinoin, p.1603). Gradual dose escalation may help to minimise mucocutaneous effects, and one proposed schedule for oral acitretin starts with 10 mg on alternate days for 2 weeks, 10 mg daily for the next 2 weeks, then 20 mg daily for a month; the dose is then adjusted as tolerated. Maintenance regimens of 25 mg daily, or alternating daily doses of 10 mg and 20 mg, have been used.[3]

1. Chen K, *et al.* Oral retinoids for the prevention of skin cancers in solid organ transplant recipients: a systematic review of randomized controlled trials. *Br J Dermatol* 2005; **152:** 518–23.
2. Kovach BT, *et al.* Systemic strategies for chemoprevention of skin cancers in transplant recipients. *Clin Transplant* 2005; **19:** 726–34.
3. Otley CC, *et al.* Chemoprevention of nonmelanoma skin cancer with systemic retinoids: practical dosing and management of adverse effects. *Dermatol Surg* 2006; **32:** 562–8.

Skin disorders. Acitretin is used alone or with PUVA (a psoralen with UVA irradiation) or UVB in psoriasis[1-4] (p.1583). Studies have shown that use with PUVA or UVB light may increase efficacy and allow a reduction in the exposure to radiation required. It is also used in keratinisation disorders such as severe forms of ichthyosis[1,5-7] (p.1580) and Darier's disease (keratosis follicularis)[1,8] (p.1578). Benefit has been reported in various other skin disorders including lichen planus (p.1580), lichen sclerosus (p.1580), and cutaneous lupus erythematosus (p.1513).[1]

1. Berbis P. Acitretin. *Ann Dermatol Venereol* 2001; **128:** 737–45.
2. Lebwohl M, *et al.* Consensus conference: acitretin in combination with UVB or PUVA in the treatment of psoriasis. *J Am Acad Dermatol* 2001; **45:** 544–53.
3. Lee CS, Koo J. A review of acitretin, a systemic retinoid for the treatment of psoriasis. *Expert Opin Pharmacother* 2005; **6:** 1725–34.
4. British Association of Dermatologists. Psoriasis guideline 2006. Available at: http://www.bad.org.uk/healthcare/guidelines/psoriasis_guideline_(Final_update)_280906.pdf (accessed 27/09/07)
5. Bruckner-Tuderman L, *et al.* Acitretin in the symptomatic therapy for severe recessive X-linked ichthyosis. *Arch Dermatol* 1988; **124:** 529–32.
6. Steijlen PM, *et al.* Acitretin in the treatment of lamellar ichthyosis. *Br J Dermatol* 1994; **130:** 211–14.
7. Katugampola RP, Finlay AY. Oral retinoid therapy for disorders of keratinization: single-centre retrospective 25 years' experience on 23 patients. *Br J Dermatol* 2006; **154:** 267–76.
8. van Dooren-Greebe RJ, *et al.* Acitretin monotherapy in Darier's disease. *Br J Dermatol* 1989; **121:** 375–9.

Preparations

USP 31: Acitretin Capsules.

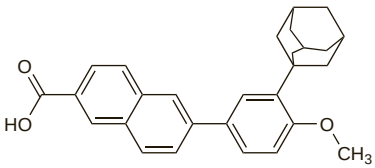
Proprietary Preparations (details are given in Part 3)
Arg.: Neotigason; ***Austral.:*** Neotigason; ***Austria:*** Neotigason; ***Belg.:*** Neotigason; ***Braz.:*** Neotigason; ***Canad.:*** Soriatane; ***Chile:*** Neotigason; ***Cz.:*** Neotigason; ***Denm.:*** Neotigason; ***Fin.:*** Neotigason; ***Fr.:*** Soriatane; ***Ger.:*** Neotigason; ***Gr.:*** Neotigason; ***Hong Kong:*** Neotigason†; ***Hung.:*** Neotigason; ***Irl.:*** Neotigason; ***Israel:*** Neotigason; ***Ital.:*** Neotigason; ***Malaysia:*** Neotigason; ***Mex.:*** Neotigason; ***Neth.:*** Neotigason; ***Norw.:*** Neotigason; ***NZ:*** Neotigason; ***Philipp.:*** Neotigason; ***Pol.:*** Neotigason; ***Port.:*** Neotigason; ***S.Afr.:*** Neotigason; ***Singapore:*** Neotigason†; ***Spain:*** Neotigason; ***Swed.:*** Neotigason; ***Switz.:*** Neotigason; ***Thai.:*** Neotigason; ***Turk.:*** Neotigason; ***UK:*** Neotigason; ***USA:*** Soriatane; ***Venez.:*** Neotigason.

Adapalene *(BAN, USAN, rINN)*

Adapaleeni; Adapalen; Adapalène; Adapaleno; Adapalenum; CD-271. 6-[3-(1-Adamantyl)-4-methoxyphenyl]-2-naphthoic acid.

Адапален

$C_{28}H_{28}O_3$ = 412.5.
CAS — 106685-40-9.
ATC — D10AD03.
ATC Vet — QD10AD03.



Adverse Effects and Precautions

As for Tretinoin, p.1618.

Pregnancy. Anophthalmia and agenesis of the optic chiasma were found in a fetus after termination of pregnancy in a woman who had applied adapalene 0.1% topically from the month before pregnancy until 13 weeks of gestation.[1]

1. Autret E, *et al.* Anophthalmia and agenesis of optic chiasma associated with adapalene gel in early pregnancy. *Lancet* 1997; **350:** 339.

Uses and Administration

Adapalene is a naphthoic acid derivative and retinoid analogue with actions similar to those of tretinoin (p.1619). Adapalene is used in topical treatment of mild to moderate acne (p.1577) where comedones, papules, and pustules predominate.

Adapalene is usually applied once daily at night as a 0.1% solution, cream, or gel to skin that has been cleansed and dried; a 0.3% gel is also available. Some patients may require less frequent applications. Other topical preparations that may cause irritation should not be used concurrently. If treatment with topical antibacterials or benzoyl peroxide is required, these should be applied in the morning and adapalene applied at night.

There may be apparent exacerbations of the acne during early treatment and a consistent therapeutic response may not be evident for at least 8 weeks. However, if there is no response after 12 weeks, therapy should be reassessed.

For use in young children, see below.

◊ References.

1. Brogden RN, Goa KL. Adapalene: a review of its pharmacological properties and clinical potential in the management of mild to moderate acne. *Drugs* 1997; **53:** 511–19.
2. Waugh J, *et al.* Adapalene: a review of its use in the treatment of acne vulgaris. *Drugs* 2004; **64:** 1465–78.
3. Pariser DM, *et al.* Adapalene Study Group. The efficacy and safety of adapalene gel 0.3% in the treatment of acne vulgaris: a randomized, multicenter, investigator-blinded, controlled comparison study versus adapalene gel 0.1% and vehicle. *Cutis* 2005; **76:** 145–51.
4. Thiboutot D, *et al.* Adapalene Study Group. Adapalene gel 0.3% for the treatment of acne vulgaris: a multicenter, randomized, double-blind, controlled, phase III trial. *J Am Acad Dermatol* 2006; **54:** 242–50.
5. Thiboutot DM, *et al.* Adapalene gel, 0.1%, as maintenance therapy for acne vulgaris: a randomized, controlled, investigator-blind follow-up of a recent combination study. *Arch Dermatol* 2006; **142:** 597–602.

Administration in children. Although not licensed for young children in the UK the *BNFC* includes adapalene 0.1% cream and gel, applied thinly once daily at night, for neonatal and infantile acne.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Adapne; Differin; Panalene; Sinac; ***Austral.:*** Differin; ***Austria:*** Differin; ***Belg.:*** Differin; ***Braz.:*** Dalap; Differin; ***Canad.:*** Differin; ***Chile:*** Adiamil; Differin; ***Cz.:*** Differine; ***Denm.:*** Redap; ***Fin.:*** Differin; ***Fr.:*** Differine; ***Ger.:*** Differin; ***Gr.:*** Adaferin; ***Hong Kong:*** Differin; ***Hung.:*** Differin; ***India:*** Aclene; Adaferin; Adiff; Deriva; ***Indon.:*** Evalen; ***Irl.:*** Differin; ***Israel:*** Adaferin; ***Ital.:*** Differin; ***Malaysia:*** Differin; ***Mex.:*** Adaferin; ***Neth.:*** Differin; ***Norw.:*** Differin; ***NZ:*** Differin; ***Philipp.:*** Differin; Klenzit; ***Pol.:*** Differin; ***Port.:*** Differin; ***Rus.:*** Differin (Дифферин); ***S.Afr.:*** Differin; ***Singapore:*** Differin; ***Spain:*** Differine; ***Swed.:*** Differin; ***Switz.:*** Differin; ***Thai.:*** Differin; ***Turk.:*** Differin; ***UK:*** Differin; ***USA:*** Differin; ***Venez.:*** Differin.

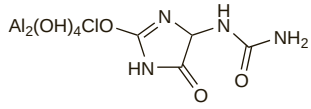
Multi-ingredient: ***Fr.:*** Epiduo; ***India:*** Deriva-C.

Alcloxa *(USAN, rINN)*

ALCA; Alcloxum; Aluminium Chlorhydroxyallantoinate; RC-173. Chlorotetrahydroxy[(2-hydroxy-5-oxo-2-imidazolin-4-yl)ureato]-dialuminium.

Алькло́кса

$C_4H_9Al_2ClN_4O_7$ = 314.6.
CAS — 1317-25-5.



Profile

Alcloxa is an astringent and keratolytic related to allantoin (below). It is present in multi-ingredient preparations intended for various skin and gastrointestinal disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Babysan Powder.

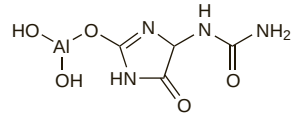
Multi-ingredient: ***Hong Kong:*** Pilelife; ***Malaysia:*** Neo-Medrol; ***NZ:*** Acnederm†; ***Singapore:*** Neo-Medrol; ***Thai.:*** Neo-Medrol; ***UK:*** Dermidex.

Aldioxa *(USAN, rINN)*

ALDA; Aldioxum; Aluminium Dihydroxyallantoinate; Dihydroxyaluminum Allantoinate; RC-172. Dihydroxy[(2-hydroxy-5-oxo-2-imidazolin-4-yl)ureato]aluminium.

Альдиокса

$C_4H_7AlN_4O_5$ = 218.1.
CAS — 5579-81-7.



Pharmacopoeias. In *Jpn.*

Profile

Aldioxa is an astringent and keratolytic related to allantoin (below). It is present in multi-ingredient preparations intended for various skin and gastrointestinal disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** ZeaSorb; ***Austral.:*** ZeaSorb; ***Canad.:*** ZeaSorb; ***Chile:*** ZeaSorb†; ***Fr.:*** ZeaSorb; ***Indon.:*** ZeaSorb; ***Irl.:*** ZeaSorb; ***Israel:*** Aronal Forte; ***Ital.:*** Rikospray; ***Malaysia:*** ZeaSorb†; ***Mex.:*** Dentsiblen; ***Philipp.:*** ZeaSorb; ***S.Afr.:*** ZeaSorb; ***Singapore:*** ZeaSorb; ***Thai.:*** ZeaSorb; ***UK:*** Cetanorm; ZeaSorb.

Alefacept *(BAN, USAN, rINN)*

Aléfacept; Alefaceptum; BG-9273; BG-9712; LFA3TIP; Recombinant Human LFA-3/1gG$_1$ Fusion Protein. A dimer of 1-92 antigen LFA-3 (human) fusion protein with human immunoglobulin G1 (hinge-C_H2-C_H3 γ1-chain).

Алефацепт

CAS — 222535-22-0.
ATC — L04AA15.
ATC Vet — QL04AA15.

Adverse Effects and Precautions

Chills are common on intravenous dosage of alefacept. Other adverse effects are cough, dizziness, headache, injection site pain and inflammation, myalgia, nausea, pharyngitis, and pruritus. More serious adverse reactions are cardiovascular events (including coronary artery disorder and myocardial infarction), hypersensitivity reactions, lymphopenia, and serious infections requiring hospitalisation. Cases of hepatotoxicity including asymptomatic transaminase elevation, fatty infiltration of the liver, hepatitis, and acute liver failure have occurred. Like other drugs with immunosuppressant actions, alefacept may increase the risk of malignancies, particularly basal or squamous cell cancers of the skin. It should not be given to patients with a history of malignancy.

Alefacept should also not be given to patients with pre-existing serious infections, and should be stopped if these develop. Its use should be considered carefully in patients with chronic infections or a history of recurrent infection.

Alefacept induces a dose-dependent reduction in circulating CD4+ and CD8+ T-lymphocyte counts. It is therefore also contra-indicated in patients with HIV infection as the reduction in CD4+ T-lymphocytes could accelerate disease progression or increase complications of HIV infection. CD4+ T-lymphocyte counts should be monitored before starting alefacept therapy and then every 2 weeks during the 12-week treatment period. Treatment should not be started in patients with a CD4+ T-lymphocyte count below normal. Doses should be withheld and weekly monitoring started if the counts fall below 250 cells/microlitre, and treatment stopped if the counts remain below this level for one month.

Therapy should be stopped immediately, and appropriate treatment given, in patients who experience anaphylaxis or serious hypersensitivity; it should not be restarted.

◊ References.

1. Goffe B, *et al.* An integrated analysis of thirteen trials summarizing the long-term safety of alefacept in psoriasis patients who have received up to nine courses of therapy. *Clin Ther* 2005; **27:** 1912–21.

Pharmacokinetics

Alefacept has a bioavailability of about 63% after intramuscular injection. After an intravenous dose it has an elimination half-life of about 11 to 12 days.

◊ References.

1. Vaishnaw AK, TenHoor CN. Pharmacokinetics, biologic activity, and tolerability of alefacept by intravenous and intramuscular administration. *J Pharmacokinet Pharmacodyn* 2002; **29:** 415–26.

Uses and Administration

Alefacept is a recombinant human fusion protein that binds to CD2 on memory T-lymphocytes, preventing their activation and reducing their number. It is used in the management of moderate to severe chronic plaque psoriasis (p.1583) and is given in a dose of 7.5 mg once weekly by intravenous injection, or 15 mg once weekly by intramuscular injection, for 12 weeks. A second 12-week course may be given if necessary, starting not less than 12 weeks after the completion of the first.

◊ General references.

1. Ellis CN, Krueger GG. Treatment of chronic plaque psoriasis by selective targeting of memory effector T lymphocytes. *N Engl J Med* 2001; **345:** 248–55.
2. Krueger GG, *et al.* A randomized, double-blind, placebo-controlled phase III study evaluating efficacy and tolerability of 2 courses of alefacept in patients with chronic plaque psoriasis. *J Am Acad Dermatol* 2002; **47:** 821–33.
3. Krueger GG, Ellis CN. Alefacept therapy produces remission for patients with chronic plaque psoriasis. *Br J Dermatol* 2003; **148:** 784–8.