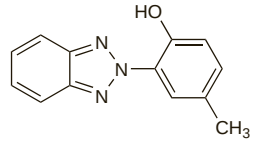
Drometrizole *(USAN, rINN)*

Drométrizol; Drometrizol; Drometrizolum. 2-(2*H*-Benzotriazol-2-yl)-*p*-cresol.

Дрометризол

$C_{13}H_{11}N_3O$ = 225.2.

CAS — 2440-22-4.



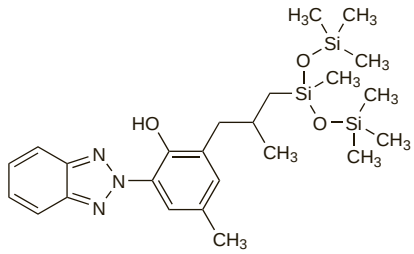
Drometrizole Trisiloxane

2-(2*H*-Benzotriazol-2-yl)-4-methyl-6-(2-methyl-3-{1,3,3,3-tetramethyl-1-[(trimethylsilyl)oxy]-1-disiloxanyl}propyl)phenol.

Дрометризола Трисилоксан

$C_{24}H_{39}N_3O_3Si_3$ = 501.8.

CAS — 155633-54-8.



NOTE. Mexoryl XL and Silatrizole are trade names that have been used for drometrizole trisiloxane.

Profile

Drometrizole trisiloxane is used as a sunscreen (p.1576). It is effective against UVA light (for definitions, see p.1580).

Preparations

Proprietary Preparations some preparations are listed in Part 3.

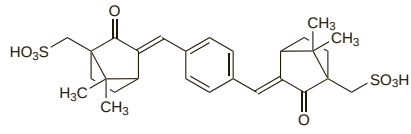
Ecamsule *(USAN, rINN)*

Ecamsul; Écamsule; Ecamsulum. (±)-(3*E*,3′*E*)-3,3′-(*p*-Phenylenedimethylidyne)bis[2-oxo-10-bornanesulfonic acid]; Terephthalylidene-3,3′-dicamphor-10,10′-disulfonic acid.

Экамсул

$C_{28}H_{34}O_8S_2$ = 562.7.

CAS — 92761-26-7.



NOTE. Mexoryl SX is a trade name that has been used for ecamsule.

Profile

Ecamsule, a camphorsulfonic acid derivative, is used as a sunscreen (p.1576). It is effective against UVA light (for definitions, see p.1580).

Preparations

Proprietary Preparations some preparations are listed in Part 3.

Efalizumab *(USAN, rINN)*

Anti-CD11a; Éfalizumab; Efalizumabum; Hu-1124. Immunoglobulin G1, anti-(human antigen CD11a)(human-mouse monoclonal hu1124 γ1-chain), disulfide with human-mouse monoclonal hu1124 light chain, dimer.

Эфализумаб

CAS — 214745-43-4.

ATC — L04AA21.

ATC Vet — QL04AA21.

Adverse Effects and Precautions

The most common adverse affects associated with efalizumab are flu-like symptoms including chills, fever, headache, myalgia, and nausea. These reactions are dose-related in both incidence and severity and usually occur within two days after the first two injections. Other adverse effects include acne, back pain, and an elevation in alkaline phosphatase concentrations. More serious adverse effects of efalizumab include arthritis, interstitial pneumonitis, hypersensitivity reactions, inflammatory polyradiculoneuropathy, and thrombocytopenia. Treatment should be stopped in patients who develop such reactions. Severe haemolytic anaemia, diagnosed 4 to 6 months after the start of efalizumab treatment, has been reported. Treatment should be stopped immediately if haemolytic anaemia occurs. Asymptomatic leucocytosis or lymphocytosis commonly occurs during treatment. Worsening of psoriasis or development of variant forms (pustular, erythrodermic, or guttate) have been reported during and after stopping efalizumab therapy.

As a result of immunosuppression, patients given efalizumab are at increased risk of infection, and might be at increased risk of developing malignancies. It should not be given to patients with pre-existing serious infection and should be used with care in patients with a history of recurring infection or malignancy. Response to vaccines may also be reduced and acellular, live, and live-attenuated vaccines should not be given during efalizumab treatment.

Assessment of the platelet count is advised before starting therapy and monthly during early treatment. Frequency of monitoring may be decreased with ongoing treatment.

Incidence of adverse effects. The safety data from 13 controlled and open-label studies of efalizumab in psoriasis have been analysed.[1] During the first 12 weeks of therapy the most common events in patients treated with efalizumab were headache, fever, chills, nausea, vomiting, or myalgia, starting within 48 hours of dosing. In 4 controlled studies that included 1620 patients treated with efalizumab and 715 with placebo, about a third of efalizumab-treated patients reported headache, while chills, nausea, and pain occurred in around 10%, and fever and myalgia in about 8%. These events usually occurred with the first 1 or 2 doses of efalizumab but by the third and subsequent doses the incidence was similar to that in the placebo group. Atypical or unusual worsening of psoriasis, and the development of variant forms, particularly guttate psoriasis, were reported in 3.2% of patients treated with efalizumab; other forms included psoriatic erythroderma, inverse psoriasis, palmoplantar psoriasis, and pustular psoriasis. In 5 studies of extended therapy for 13 to 60 weeks (1115 patients treated for 13 to 24 weeks and 228 for 60 weeks) the rate of adverse effects remained low, there was no new pattern of serious adverse effects, and there was no evidence of cumulative toxicity. An analysis of infection risk found similar rates of mild to moderate and serious infections in patients treated with either efalizumab or placebo. Nevertheless, efalizumab should not be used in patients with pre-existing serious infection. Anti-efalizumab antibodies were found in 67 of 1063 patients, but there was no apparent effect on efficacy, safety, or pharmacodynamics.

There have been infrequent reports of new onset or recurrent severe arthritis, including psoriatic arthritis, in patients treated with efalizumab. Separate analyses[1,2] of pooled study data both found that the incidence of arthropathy events was low (less than 4%) and similar for patients treated with either efalizumab or placebo. However, there was some suggestion[2] that patients with a history of arthropathy and those who have a poor clinical response to efalizumab may be at higher risk.

1. Papp KA, *et al.* Safety of efalizumab in patients with moderate to severe chronic plaque psoriasis: review of clinical data. *J Cutan Med Surg* 2005; **9:** 313–23.
2. Pincelli C, *et al.* The incidence of arthropathy adverse events in efalizumab-treated patients is low and similar to placebo and does not increase with long-term treatment: pooled analysis of data from phase III clinical trials of efalizumab. *Arch Dermatol Res* 2006; **298:** 329–38.

Carcinogenicity. Efalizumab is an immunosuppressant and as such might increase the risk of malignancy. An analysis[1] of pooled data from clinical studies that included 2980 patients given efalizumab found 51 patients (1.7%) with 67 malignancies. Most cases were of non-melanoma skin cancer (51 cases in 35 patients) and it was found that many had risk factors for skin cancer. Other cases included 3 lymphomas, 12 solid tumours at various sites, and 1 malignant melanoma. However, when compared with patients given placebo and data from 2 external cohorts of psoriasis patients (to allow for the increased risk of skin cancers seen in psoriasis patients compared with the general population) there was no evidence that efalizumab increased the risk of developing a malignancy. Nevertheless, further data are needed to determine whether efalizumab has any long-term effect on the development of malignancies.

1. Leonardi CL, *et al.* A review of malignancies observed during efalizumab (Raptiva) clinical trials for plaque psoriasis. *Dermatology* 2006; **213:** 204–14.

Effects on the blood. Thrombocytopenia has been described in 6 patients given efalizumab.[1] In 5 cases it started 8 to 12 weeks after starting weekly efalizumab. In all cases the platelet counts recovered quickly after efalizumab was stopped; in 5 cases corticosteroids were also given. In another case a woman presented with pancytopenia 4 weeks after starting efalizumab therapy.[2] Efalizumab was stopped and the patient treated with granulocyte colony-stimulating factor, normal immunoglobulin, oral prednisone, platelet transfusion, and darbepoetin alfa. Cell counts returned to normal limits within 4 weeks.

1. Warkentin TE, Kwon P. Immune thrombocytopenia associated with efalizumab therapy for psoriasis. *Ann Intern Med* 2005; **143:** 761–3.
2. Tom WL, *et al.* Efalizumab-induced autoimmune pancytopenia. *Br J Dermatol* 2006; **155:** 1045–7.

Interactions

For a warning concerning the use of live vaccines in patients receiving efalizumab see Adverse Effects and Precautions, above.

Pharmacokinetics

Peak plasma concentrations of efalizumab are reached about 1 to 2 days after subcutaneous injection, with a bioavailability of about 50%. Steady state is reached at week 4 of weekly dosing. Efalizumab is metabolised by intracellular degradation. It is cleared by non-linear saturable elimination and the time to elimination after the last dose is about 25 days.

◊ References.

1. Mortensen DL, *et al.* Pharmacokinetics and pharmacodynamics of multiple weekly subcutaneous efalizumab doses in patients with plaque psoriasis. *J Clin Pharmacol* 2005; **45:** 286–98.
2. Sun Y-N, *et al.* Population pharmacokinetics of efalizumab (humanized monoclonal anti-CD11a antibody) following long-term subcutaneous weekly dosing in psoriasis subjects. *J Clin Pharmacol* 2005; **45:** 468–76.
3. Joshi A, *et al.* An overview of the pharmacokinetics and pharmacodynamics of efalizumab: a monoclonal antibody approved for use in psoriasis. *J Clin Pharmacol* 2006; **46:** 10–20.

Uses and Administration

Efalizumab is a humanised monoclonal antibody that binds to human CD11a on leucocytes to inhibit the activation of T-lymphocytes. It is used for the treatment of chronic moderate to severe plaque psoriasis (p.1583) in patients aged 18 years and over. Efalizumab is given by subcutaneous injection. The initial dose is 700 micrograms/kg, followed by a weekly dose of 1 mg/kg; a single dose should not exceed 200 mg. Treatment is given for 12 weeks, then continued in those who have responded.

◊ References.

1. Lebwohl M, *et al.* A novel targeted T-cell modulator, efalizumab, for plaque psoriasis. *N Engl J Med* 2003; **349:** 2004–13.
2. Gordon KB, *et al.* Efalizumab for patients with moderate to severe plaque psoriasis: a randomized controlled trial. *JAMA* 2003; **290:** 3073–80. Correction. *ibid.* 2004; **291:** 1070.
3. Menter A, *et al.* Efficacy and safety observed during 24 weeks of efalizumab therapy in patients with moderate to severe plaque psoriasis. *Arch Dermatol* 2005; **141:** 31–8.
4. Leonardi CL, *et al.* Extended efalizumab therapy improves chronic plaque psoriasis: results from a randomized phase III trial. *J Am Acad Dermatol* 2005; **52:** 425–33.
5. Wellington K, Perry CM. Efalizumab. *Am J Clin Dermatol* 2005; **6:** 113–20.
6. Jordan JK. Efalizumab for the treatment of moderate to severe plaque psoriasis. *Ann Pharmacother* 2005; **39:** 1476–82.
7. Menter A, *et al.* Long-term management of plaque psoriasis with continuous efalizumab therapy. *J Am Acad Dermatol* 2006; **54** (suppl 1): S182–S188.
8. Dubertret L, *et al.* Clinical experience acquired with the efalizumab (Raptiva) (CLEAR) trial in patients with moderate-to-severe plaque psoriasis: results from a phase III international randomized, placebo-controlled trial. *Br J Dermatol* 2006; **155:** 170–81.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Raptiva; ***Austral.:*** Raptiva; ***Braz.:*** Raptiva; ***Canad.:*** Raptiva; ***Cz.:*** Raptiva; ***Denm.:*** Raptiva; ***Fin.:*** Raptiva; ***Fr.:*** Raptiva; ***Ger.:*** Raptiva; ***Gr.:*** Raptiva; ***Hong Kong:*** Raptiva; ***Irl.:*** Raptiva; ***Ital.:*** Raptiva; ***Malaysia:*** Raptiva; ***Mex.:*** Raptiva; ***Neth.:*** Raptiva; ***Norw.:*** Raptiva; ***NZ:*** Raptiva; ***Port.:*** Raptiva; ***Singapore:*** Raptiva; ***Spain:*** Raptiva; ***Swed.:*** Raptiva; ***Switz.:*** Raptiva; ***UK:*** Raptiva; ***USA:*** Raptiva.