

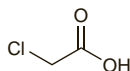
Monochloroacetic Acid

Chloroacetic Acid; Kwas chlorooctowy; Monochloroacético, ácido.

Монохлоруксусная Кислота

$C_2H_3O_2Cl = 94.5$.

CAS — 79-11-8.

**Profile**

Preparations containing 50% of monochloroacetic acid are used as a caustic for the removal of plantar warts (p.1584).

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Warzenmittel. **Ger.:** Acetocautin; **Switz.:** Acetocaustine.

Multi-ingredient: **Turk.:** IL-33.

Motretinide (USAN, rINN)

Motretinid; Motretinida; Motrétinide; Motretinidi; Motretinidum; Ro-11-1430. (*all-trans*)-N-Ethyl-9-(4-methoxy-2,3,6-trimethylphenyl)-3,7-dimethyl-2,4,6,8-nonatetraenamide.

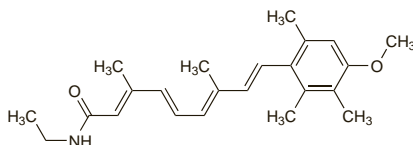
Мотретинид

$C_{23}H_{31}NO_2 = 353.5$.

CAS — 56281-36-8.

ATC — D10AD05.

ATC Vet — QD10AD05.

**Profile**

Motretinide is a retinoid structurally related to acitretin (p.1586). Motretinide is used topically in the treatment of acne (p.1577). It is applied in preparations containing 0.1%.

Preparations

Proprietary Preparations (details are given in Part 3)

Switz.: Tasmaderm.

Naphthalan Liquid

Naftalan; Naphthalenic Oil; Naphthalanum Liquidum.

Нафталановое Масло

CAS — 37229-16-6.

Profile

Naphthalan liquid is an oil-like complex mixture of naphthene hydrocarbons and tars obtained from the oil fields of Azerbaijan and Croatia. It has analgesic, anti-inflammatory, and emollient properties and is used in the treatment of conditions such as psoriasis and in various musculoskeletal disorders. It is usually applied locally in the form of the oil or as an ointment or alternatively patients may bath in the oil.

References.

1. Vržogić P, *et al.* Naphthalan – a natural medicinal product. *Acta Dermatovenol Croat* 2003; **11**: 178–84.

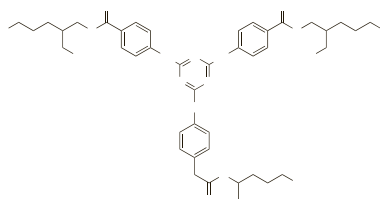
Octil Triazone

Ociltirazona; Octyl Triazone. 2,4,6-Trianiino-*p*-(carbo-2'-ethylhexyl-1'-oxy)-1,3,5-triazine.

ОКТИЛТРИАЗОН

$C_{48}H_{66}N_6O_6 = 823.1$.

CAS — 88122-99-0.



NOTE. Uvinul T 150 is a trade name that has been used for octil triazone.

Profile

Octil triazone is used as a sunscreen (p.1576). It is effective against UVB light (for definitions, see p.1580).

Preparations

Proprietary Preparations some preparations are listed in Part 3.

Octinoxate (USAN, rINN)

Octinoxato; Octinoxatum; Octyl methoxycinnamate. 2-Ethylhexyl-*p*-methoxycinnamate; 3-(4-Methoxyphenyl)-2-propenoic acid 2-ethylhexyl ester.

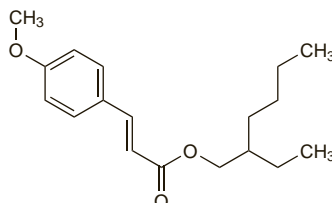
ОЦИНОКСАТ

$C_{18}H_{26}O_3 = 290.4$.

CAS — 5466-77-3.

ATC — D02BA02.

ATC Vet — QD02BA02.



NOTE. Escalol 557, Eusolex 2292, Neo-Heliopan AV, Parsol MCX, Tinosorb OMC, Uvinul MC 80, and Uvinul MC 80 N are trade names that have been used for octinoxate.

Pharmacopoeias. In *US*.

USP 31 (Octinoxate). Pale yellow oil. Insoluble in water. Store in airtight containers at a temperature of 8° to 15°.

Profile

Octinoxate, a substituted cinnamate, is used by topical application as a sunscreen (p.1576). Cinnamate sunscreens effectively absorb light throughout the UVB range but absorb little or no UVA light (for definitions, see p.1580). Cinnamate sunscreens may therefore be used to prevent sunburn but are unlikely to prevent drug-related or other photosensitivity reactions associated with UVA light; combination with a benzophenone may give some added protection against such photosensitivity. Cinnamates may occasionally produce photosensitivity reactions.

Preparations

Proprietary Preparations numerous preparations are listed in Part 3.

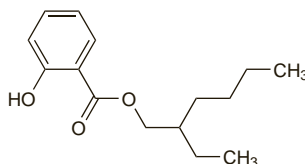
Octisalate (USAN, rINN)

Octisalato; Octisalatum; Octyl Salicylate. 2-Ethylhexyl salicylate; 2-Hydroxybenzoic acid 2-ethylhexyl ester.

ОКТИСАЛАТ

$C_{15}H_{22}O_3 = 250.3$.

CAS — 118-60-5.



NOTE. Escalol 587, Eusolex OS, and Neo-Heliopan OS are trade names that have been used for octisalate.

Pharmacopoeias. In *US*.

USP 31 (Octisalate). Store in airtight containers.

Profile

Octisalate is a substituted salicylate used topically as a sunscreen (p.1576). Salicylates effectively absorb light throughout the UVB range but absorb little or no UVA light (for definitions, see p.1580). Salicylate sunscreens may therefore be used to prevent sunburn, but are unlikely to prevent drug-related or other photosensitivity reactions associated with UVA light; combination with a benzophenone may give some added protection.

Salicylates may occasionally produce photosensitivity reactions or contact dermatitis.

Preparations

Proprietary Preparations numerous preparations are listed in Part 3.

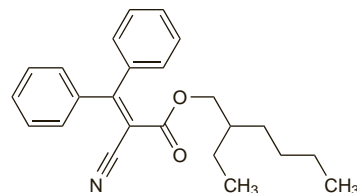
Octocrilene (rINN)

2-Ethylhexyl α -cyano- β -phenylcinnamate; Octocrilène; Octocrileno; Octocrilenum; Octocrylene (USAN). 2-Ethylhexyl 2-cyano-3,3-diphenylacrylate.

ОКТОКРИЛЕН

$C_{24}H_{27}NO_2 = 361.5$.

CAS — 6197-30-4.



NOTE. Escalol 597, Eusolex OCR, Neo-Heliopan 303, Parsol 340, and Uvinul N 539 T are trade names that have been used for octocrilene.

Pharmacopoeias. In *US*.

USP 31 (Octocrylene). Store in airtight containers.

Profile

Octocrilene, a substituted cinnamate, is a sunscreen (p.1576) with actions similar to those of octinoxate (above). It is effective against UVB light (for definitions, see p.1580).

Preparations

Proprietary Preparations numerous preparations are listed in Part 3.

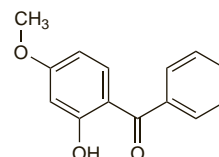
Oxybenzone (USAN, rINN)

Benzofenon-3; Benzophenone-3; Oxibenzona; Oxybenzonum. 2-Hydroxy-4-methoxybenzophenone.

ОКСИБЕНЗОН

$C_{14}H_{12}O_3 = 228.2$.

CAS — 131-57-7.



NOTE. Escalol 567, Eusolex 4360, Neo-Heliopan BB, Tinosorb B3, and Uvinul M 40 are trade names that have been used for oxybenzone.

Pharmacopoeias. In *US*.

USP 31 (Oxybenzone). A pale yellow powder. Practically insoluble in water; freely soluble in alcohol and in toluene. Store in airtight containers. Protect from light.

Profile

Oxybenzone is a substituted benzophenone used topically as a sunscreen (p.1576). Benzophenones effectively absorb light throughout the UVB range (wavelengths 290 to 320 nm) and also absorb some UVA light with wavelengths of 320 to about 360 nm and some UVC light with wavelengths of about 250 to 290 nm (for definitions, see p.1580). Benzophenones may therefore be used to prevent sunburn and may also provide some protection against drug-related or other photosensitivity reactions associated with UVA light; in practice they are usually combined with a sunscreen from another group.

Photocontact allergic dermatitis can be caused by topical application of benzophenone sunscreens. Oxybenzone is widely used and often found to be a photo-allergen in patients with these reactions. Contact allergy reactions occur less frequently.

Hypersensitivity. Chemical sunscreens are known to cause photosensitivity and contact allergy reactions. Oxybenzone is widely used and reported to be the sunscreen photo-allergen most commonly detected in photopatch testing.^{1,2} In a group of 5800 patients with suspected allergic contact dermatitis who were tested for contact allergens,³ a positive reaction to oxybenzone was recorded in 0.6%. There have also been rare reports of severe allergic reactions to oxybenzone including anaphylaxis; sensitivity was confirmed by patch testing.^{4,5} A history of atopy may predispose patients to such reactions.

1. Berne B, Ros A-M. 7 years experience of photopatch testing with sunscreen allergens in Sweden. *Contact Dermatitis* 1998; **38**: 61–4.

2. Bryden AM, *et al.* Photopatch testing of 1155 patients: results of the U.K. multicentre photopatch study group. *Br J Dermatol* 2006; **155**: 737–47.

- Marks JG, *et al.* North American Contact Dermatitis Group patch-test results, 1998 to 2000. *Am J Contact Dermat* 2003; **14**: 59–62.
- Emonet S, *et al.* Anaphylaxis to oxybenzone, a frequent constituent of sunscreens. *J Allergy Clin Immunol* 2001; **107**: 556–7.
- Yesudian PD, King CM. Severe contact urticaria and anaphylaxis from benzophenone-3 (2-hydroxy 4-methoxy benzophenone). *Contact Dermatitis* 2002; **46**: 55–6.

Preparations

USP 31: Dioxbenzone and Oxybenzone Cream.

Proprietary Preparations numerous preparations are listed in Part 3.

Arg.: Biorevit Labial; Lelco; **Braz.:** Solaquin.

Padimate (BAN, rINN)

Amyl Dimethylaminobenzoate; Isoamyl Dimethylaminobenzoate; Padimate A (USAN); Padimato; Padimatium. A mixture of pentyl, isopentyl, and 2-methylbutyl 4-dimethylaminobenzoates.

ПАДИМАТ

$C_{14}H_{21}NO_2 = 235.3$.

CAS — 14779-78-3 (pentyl 4-dimethylaminobenzoate); 21245-01-2 (isopentyl 4-dimethylaminobenzoate).

Profile

Padimate, a substituted aminobenzoate, is a sunscreen (p.1576) with actions similar to those of aminobenzoic acid (p.1589). It is effective against UVB light (for definitions, see p.1580).

Preparations

Proprietary Preparations some preparations are listed in Part 3.

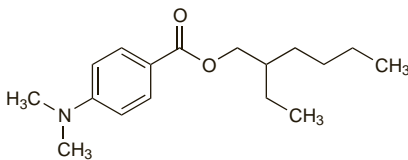
Padimate O (BANM, USAN)

Ethylhexyl Dimethyl PABA; Octyl Dimethyl PABA; Padimate O. 2-Ethylhexyl 4-(dimethylamino)benzoate.

ПАДИМАТ О

$C_{17}H_{27}NO_2 = 277.4$.

CAS — 21245-02-3.



NOTE. Escalol 507 and Eusolex 6007 are trade names that have been used for padimate O.

Pharmacopoeias. In US.

USP 31 (Padimate O). A light yellow, mobile liquid with a faint aromatic odour. Practically insoluble in water, in glycerol, and in propylene glycol; soluble in alcohol, in isopropyl alcohol, and in liquid paraffin. Store in airtight containers. Protect from light.

Profile

Padimate O, a substituted aminobenzoate, is a sunscreen (p.1576) with actions similar to those of aminobenzoic acid (p.1589). It is effective against UVB light (for definitions, see p.1580).

Preparations

USP 31: Padimate O Lotion.

Proprietary Preparations some preparations are listed in Part 3.

Pimecrolimus (BAN, USAN, rINN)

ASM-981; Pimécrolimus; Pimecrolímus; Pimecrolimusum; Pimecrolimus; Pimecrolimus; SDZ-ASM-981. (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)-3-((E)-2-[(1R,3R,4S)-4-Chloro-3-methoxycyclohexyl]-1-methylvinyl)-8-ethyl-5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-14,16-dimethoxy-4,10,12,18-tetramethyl-15,19-epoxy-3H-pyrido[2,1-c][1,4]oxazacyclotricosine-1,7,20,21(4H,23H)-tetrone.

Пимекролимус

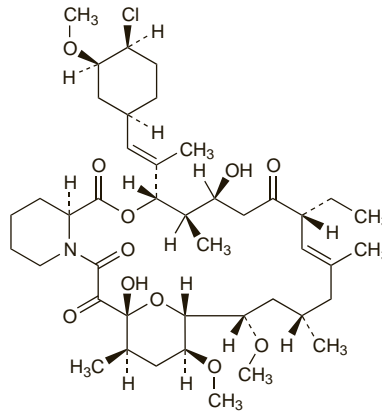
$C_{43}H_{68}ClNO_{11} = 810.5$.

CAS — 137071-32-0.

ATC — D11AX15.

ATC Vet — QD11AX15.

The symbol † denotes a preparation no longer actively marketed



Adverse Effects and Precautions

As for topical tacrolimus (p.1843).

The most frequent adverse effects of topical pimecrolimus are a burning sensation, irritation, pruritus, erythema, and skin infections at the application site. Rarely anaphylactic reactions, sometimes severe, have been reported.

Cases of lymphadenopathy have been reported in patients using pimecrolimus cream. Treatment with pimecrolimus should be stopped in patients who develop lymphadenopathy in the absence of a clear aetiology or in the presence of acute infectious mononucleosis. All patients should be monitored to ensure that the condition resolves.

Carcinogenicity. Carcinogenicity studies in *animals* and reports of malignancies in patients treated with topical calcineurin inhibitors prompted the FDA to issue an alert about the possible risk and to make recommendations about the appropriate use of pimecrolimus and tacrolimus (see under Tacrolimus, p.1843).

Interactions

Alcohol intolerance, described as flushing, rash, burning, itching, or swelling, has occurred rarely after the consumption of alcohol by patients using topical pimecrolimus.

Pharmacokinetics

There is minimal systemic absorption and no accumulation from topical use of pimecrolimus. Studies in *animals* and *in vitro* have found no evidence of metabolism in the skin.

Pimecrolimus is absorbed from the gastrointestinal tract after oral doses, and is about 74 to 87% bound to plasma proteins. It is metabolised in the liver by the cytochrome P450 isoenzyme CYP3A subfamily. About 78% of a single dose is eliminated in the faeces as metabolites and less than 1% as unchanged pimecrolimus. Only about 2.5% of a dose is eliminated in the urine, as metabolites.

References

- Van Leent EJM, *et al.* Low systemic exposure after repeated topical application of pimecrolimus (Elidel, SD Z ASM 981) in patients with atopic dermatitis. *Dermatology* 2002; **204**: 63–8.
- Scott G, *et al.* Pharmacokinetics of pimecrolimus, a novel nonsteroid anti-inflammatory drug, after single and multiple oral administration. *Clin Pharmacokinet* 2003; **42**: 1305–14.
- Zollinger M, *et al.* Pimecrolimus: absorption, distribution, metabolism, and excretion in healthy volunteers after a single oral dose and supplementary investigations *in vitro*. *Drug Metab Dispos* 2006; **34**: 765–74.

Uses and Administration

Pimecrolimus is a macrolactam ascomycin derivative related to tacrolimus (p.1846) that acts as a calcineurin inhibitor and has similar anti-inflammatory and immunosuppressant actions. It is used for short-term and intermittent long-term treatment of mild to moderate atopic eczema (p.1579) in non-immunocompromised patients over the age of 2 years when conventional therapies are ineffective or unsuitable. Pimecrolimus is applied twice daily as a 1% cream until signs and

symptoms clear. Treatment should be stopped if there is no improvement after 6 weeks or if eczema is exacerbated.

Oral forms of pimecrolimus are also being investigated for the treatment of psoriasis and atopic eczema.

References

- Wellington K, Jarvis B. Topical pimecrolimus: a review of its clinical potential in the management of atopic dermatitis. *Drugs* 2002; **62**: 817–40.
- Anonymous. Topical pimecrolimus (Elidel) for treatment of atopic dermatitis. *Med Lett Drugs Ther* 2002; **44**: 48–50.
- Anonymous. Pimecrolimus cream for atopic dermatitis. *Drug Ther Bull* 2003; **41**: 33–6.
- Papp K, *et al.* Effect of pimecrolimus cream 1% on the long-term course of pediatric atopic dermatitis. *Int J Dermatol* 2004; **43**: 978–83.
- Meurer M, *et al.* Long-term efficacy and safety of pimecrolimus cream 1% in adults with moderate atopic dermatitis. *Dermatology* 2004; **208**: 365–72.
- Ascroft DM, *et al.* Efficacy and tolerability of topical pimecrolimus and tacrolimus in the treatment of atopic dermatitis: meta-analysis of randomised controlled trials. *BMJ* 2005; **330**: 516–22.
- Papp KA, *et al.* Long-term control of atopic dermatitis with pimecrolimus cream 1% in infants and young children: a two-year study. *J Am Acad Dermatol* 2005; **52**: 240–6.
- Wolff K, *et al.* Efficacy and tolerability of three different doses of oral pimecrolimus in the treatment of moderate to severe atopic dermatitis: a randomized controlled trial. *Br J Dermatol* 2005; **152**: 1296–1303.

Administration in infants. A 6-week, double-blind, randomised study of 186 infants between the age of 3 and 23 months, followed by a 20-week open-label phase, showed that 1% pimecrolimus cream, applied twice daily was both safe and effective in mild to moderate atopic eczema.¹ A review² of data from 10 studies that included 1133 infants between 3 and 23 months of age who were treated for up to 2 years found that the level of systemic exposure to pimecrolimus was very low and comparable to that observed in older children and adults. Treatment was reported to be effective and there was no evidence of immunosuppression or an increase in the rate of infections. Licensed product information, however, does not recommend its use in patients under 2 years of age as the effect of pimecrolimus cream on the developing immune system in infants is unknown (for concerns about possible carcinogenicity see above).

- Ho VC, *et al.* Safety and efficacy of nonsteroid pimecrolimus cream 1% in the treatment of atopic dermatitis in infants. *J Pediatr* 2003; **142**: 155–62.
- Paul C, *et al.* Safety and tolerability of 1% pimecrolimus cream among infants: experience with 1133 patients treated for up to 2 years. Abstract: *Pediatrics* 2006; **117**: 202–3. Full version: <http://pediatrics.aappublications.org/cgi/reprint/117/1/e118> (accessed 27/09/07)

Lichen. There are a few case reports^{1,2} of benefit from pimecrolimus 1% cream in the management of oral lichen planus (p.1580). In most cases it was applied twice daily, and in some cases adhesive gel or paste was also used. Improvement in oral lesions occurred within 2 to 4 weeks in 3 cases.¹ In a placebo-controlled study³ of 20 patients with oral erosive lichen planus, pimecrolimus 1% cream was applied twice daily for 4 weeks. Although pain scores were reduced with pimecrolimus, the reduction in erythema was not maintained. There was also a trend towards an improvement in ulceration but changes in scores were not statistically significant. Topical pimecrolimus has also been tried in the management of genital lichen planus. In a series⁴ of 11 women, 9 experienced benefit after 4 to 6 weeks of treatment; with follow-up of up to 10 months, 6 of them had experienced a complete response and 3 a partial response.

The resolution of signs and symptoms of lichen sclerosis (p.1580) has been reported in 7 female patients (aged 4 to 48 years) with the use of topical pimecrolimus 1% cream twice daily for 3 to 4 months.^{5,6} A poor response was reported in a 62-year-old woman who used the cream less frequently because of burning and stinging.⁵

- Esquivel-Pedraza L, *et al.* Treatment of oral lichen planus with topical pimecrolimus 1% cream. *Br J Dermatol* 2004; **150**: 771–3.
- Dissemond J, *et al.* Pimecrolimus in an adhesive ointment as a new treatment option for oral lichen planus. *Br J Dermatol* 2004; **150**: 782–4.
- Swift JC, *et al.* The effectiveness of 1% pimecrolimus cream in the treatment of oral erosive lichen planus. *J Periodontol* 2005; **76**: 627–35.
- Lonsdale-Eccles AA, Velangi S. Topical pimecrolimus in the treatment of genital lichen planus: a prospective case series. *Br J Dermatol* 2005; **153**: 390–4.
- Goldstein AT, *et al.* Pimecrolimus for the treatment of vulvar lichen sclerosis: a report of 4 cases. *J Reprod Med* 2004; **49**: 778–80.
- Boms S, *et al.* Pimecrolimus 1% cream for anogenital lichen sclerosis in childhood. *BMC Dermatol* 2004; **4**: 14. Available at: <http://www.biomedcentral.com/1471-5945/4/14> (accessed 27/09/07)

Psoriasis. Topical pimecrolimus may have some benefit¹ in the treatment of psoriasis (p.1583). Although studies have generally found it to be less effective than topical corticosteroids or topical calcipotriol,^{2,4} one study² in patients with chronic plaque psoriasis did report that pimecrolimus 1% ointment applied under occlusion had a similar efficacy to clobetasol propionate 0.05% ointment.