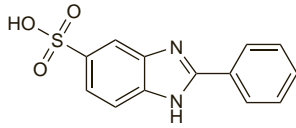


**Ensulizole** (USAN, rINN)

Ensulizol; Ensulizolum; Phenylbenzimidazole Sulphonic Acid. 2-Phenyl-1*H*-benzimidazole-5-sulphonic acid.

ЭНСУЛИЗОЛ

$C_{13}H_{10}N_2O_3S = 274.3$ .  
CAS — 27503-81-7.



NOTE. Eusolex 232 and Neo-Heliopan Hydro are trade names that have been used for ensulizole.

**Pharmacopoeias.** In US.

**USP 31** (Ensulizole). A white to ivory-coloured, odourless powder. Practically insoluble in water and in oily solvents; soluble in alcohol; its salts are freely soluble in water. Store in airtight containers at a temperature of 8° to 15°.

**Profile**

Ensulizole is used topically 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.

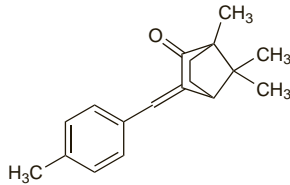
**Enzacamene** (USAN, rINN)

Enzacamène; Enzacameno; Enzacamenum; Methyl Benzylidene Camphor; 3-(4-Methylbenzylidene)borman-2-one; 3-(4-Methylbenzylidene)camphor; 1,7,7-Trimethyl-3-[(4-methylphenyl)methylene]bicyclo[2.2.1]heptan-2-one.

Энзакамен

$C_{18}H_{22}O = 254.4$ .

CAS — 36861-47-9 (D,L-form); 38102-62-4 (form unspecified).



NOTE. Eusolex 6300, Neo-Heliopan MBC, and Parsol 5000 are trade names that have been used for enzacamene.

**Pharmacopoeias.** In US.

**USP 31** (Enzacamene). A white, fine crystalline powder. M.p. between 66° and 68°. Practically insoluble in water; freely soluble in alcohol; very soluble in chloroform. Store in airtight containers.

**Profile**

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

**Preparations**

**Proprietary Preparations** numerous preparations are listed in Part 3.

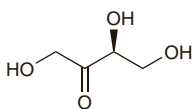
**Erythrulose**

DL-Glycero-tetrolulose. 1,3,4-Trihydroxy-2-butanone.

Эритрулаза

$C_4H_8O_4 = 120.1$ .

CAS — 40031-31-0 (DL-erythrulose); 496-55-9 (D-erythrulose); 533-50-6 (L-erythrulose).

**Profile**

Application to the skin of preparations containing L-erythrulose slowly produces a brown coloration similar to that caused by exposure to the sun, probably due to a reaction with the amino acids of the skin. It is often used with dihydroxyacetone (p.1594) in artificial tanning preparations. Recommended concentrations are up to 5% when used alone or up to 4% with dihydroxyacetone.

The symbol † denotes a preparation no longer actively marketed

**Preparations**

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

**Multi-ingredient:** **Braz:** Sunmax Autobronzeador; **UK:** Viticolor.

**Etretinate** (BAN, USAN, rINN)

Etretrinaatti; Etretrinat; Étrétinate; Etretrinato; Etretrinum; Ro-10-9359. Ethyl 3-methoxy-15-*apo-φ*-caroten-15-oate; Ethyl (*all-trans*)-9-(4-methoxy-2,3,6-trimethylphenyl)-3,7-dimethylnona-2,4,6,8-tetra-enoate.

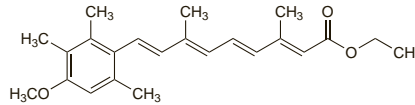
ЭТРЕТИНАТ

$C_{23}H_{30}O_3 = 354.5$ .

CAS — 54350-48-0.

ATC — D05BB01.

ATC Vet — QD05BB01.

**Adverse Effects and Precautions**

As for Isotretinoin, p.1599.

Donation of blood should be avoided for at least 2 years after cessation of treatment. The period of time during which pregnancy must be avoided after stopping treatment has not been determined; detectable plasma-*etretinate* concentrations have been reported nearly 3 years after the last dose.

◇ In addition to the references cited below, further references to the adverse effects of *etretinate* can be found in Isotretinoin, p.1599, under Effects on the Blood, Cardiovascular System, Eyes, Liver, Musculoskeletal System, Serum Lipids, and the Skin, as well as under Vasculitic Syndromes.

**Carcinogenicity.** A report of 2 patients who developed lymphomas while receiving *etretinate*<sup>1</sup> prompted a report of 3 other malignancies in patients taking *etretinate*.<sup>2</sup>

1. Woll PJ, *et al.* Lymphoma in patients taking *etretinate*. *Lancet* 1987; **ii**: 563-4.

2. Harrison PV. Retinoids and malignancy. *Lancet* 1987; **ii**: 801.

**Effects on the kidneys.** Rare cases of impaired renal function associated with *etretinate* have been described.<sup>1,2</sup> In one report<sup>1</sup> it was also noted that in manufacturer-sponsored studies the mean serum-creatinine concentration had been raised in patients receiving *etretinate*.

1. Horber FF, *et al.* Impaired renal function and hypercalcaemia associated with *etretinate*. *Lancet* 1984; **ii**: 1093.

2. Cribier B, *et al.* Renal impairment probably induced by *etretinate*. *Dermatology* 1992; **185**: 266-8.

**Oedema.** A report of generalised oedema after treatment with *etretinate*.<sup>1</sup> Five other cases had been reported in the literature and rechallenge in 4 patients had provoked a recurrence. Generalised oedema as part of the capillary leak syndrome has been reported with *acitretin* (p.1586).

1. Allan S, Christmas T. Severe edema associated with *etretinate*. *J Am Acad Dermatol* 1988; **19**: 140.

**Pregnancy.** For further information on the teratogenicity of *etretinate*, see under *Acitretin*, p.1586.

**Interactions**

As for Isotretinoin, p.1602.

**Anticoagulants.** *Etretinate* has been reported to reduce the therapeutic efficacy of *warfarin* (see p.1430).

**Antiepileptics.** *Etretinate* was ineffective and none of its characteristic mucocutaneous adverse effects occurred in a patient with pityriasis rubra pilaris who was already taking *carbamazepine* and *valproate* for epilepsy. However, there was a clinical response after the carbamazepine had been withdrawn, suggesting that it may have reduced the bioavailability or increased the metabolism of *etretinate*.<sup>1</sup>

1. Mohammed KN. Unresponsiveness to *etretinate* during anticonvulsant therapy. *Dermatology* 1992; **185**: 79.

**Antineoplastics.** The risk of developing hepatotoxicity may be increased when *etretinate* is used with *methotrexate* (see Retinoids, p.748).

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

**Pharmacokinetics**

The mean bioavailability of *etretinate* is about 40% after oral doses but there is a large interindividual variation. Absorption can be increased if taken with milk or fatty food. *Etretinate* undergoes significant first-pass metabolism and plasma concentrations of the active carboxylic acid metabolite, *acitretin* (p.1586), may be detected before those of the parent drug; *acitretin* may itself be metabolised to *etretinate* (see p.1586). Both *etretinate* and *acitretin* are extensively bound to plasma protein. *Etretinate* appears to accumulate in adipose tissue after repeated dosing and has a prolonged elimination half-life of about 120 days; detectable serum concentrations have been observed up to 3 years after

stopping therapy. Up to 75% of a dose is excreted in the faeces mainly as unchanged drug. *Etretinate* is also excreted in the urine as metabolites. *Etretinate* crosses the placenta. Although it is not known whether *etretinate* is distributed into breast milk, this would be expected because of its lipophilicity; *acitretin*, a metabolite of *etretinate*, has been found in breast milk when it was given to a lactating woman (see p.1586).

## ◇ References.

1. Lucek RW, Colburn WA. Clinical pharmacokinetics of the retinoids. *Clin Pharmacokinet* 1985; **10**: 38-62.
2. DiGiovanna JJ, *et al.* *Etretinate*: persistent serum levels after long-term therapy. *Arch Dermatol* 1989; **125**: 246-51.
3. Larsen FG. Pharmacokinetics of *etretinate* and *acitretin* with special reference to treatment of psoriasis. *Acta Derm Venereol (Stockh)* 1994; **190** (suppl): 1-33.
4. Wiegand UW, Chou RC. Pharmacokinetics of *acitretin* and *etretinate*. *J Am Acad Dermatol* 1988; **39** (suppl): S25-S33.

**Uses and Administration**

*Etretinate* is a retinoid and is a derivative of *tretinoin* (p.1618). It has been given orally for the treatment of severe, extensive psoriasis that has not responded to other treatment, especially generalised and palmo-plantar pustular psoriasis. It has also been used in severe congenital ichthyosis, severe Darier's disease (keratosis follicularis) as well as other disorders of keratinisation, and oral lichen planus. *Acitretin* (p.1586) is now preferred to *etretinate*.

Therapy is generally started at doses of 0.75 to 1 mg/kg daily in divided oral doses. A maximum dose of 1.5 mg/kg daily should not be exceeded (some licensed product information has suggested a maximum of 75 mg daily). Erythrodermic psoriasis may respond to lower initial doses of 250 micrograms/kg daily, increased at weekly intervals by 250 micrograms/kg daily until optimal response occurs. After the initial response, generally after 8 to 16 weeks of therapy, maintenance doses of 500 to 750 micrograms/kg daily have been given. Therapy should be stopped once lesions have sufficiently resolved.

## ◇ References.

1. Magis NLJ, *et al.* The treatment of psoriasis with *etretinate* and *acitretin*: a follow up of actual use. *Eur J Dermatol* 2000; **10**: 517-21.
2. 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.

**Preparations**

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

**Jpn:** Tigason.

**Fumaric Acid**

Acidum Fumaricum; Allomalenic Acid; Boletic Acid; E297; Fumárico, ácido; Kwas fumarowy; *trans*-Butenedioic acid.

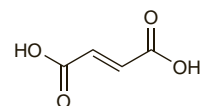
Фумаровая Кислота

$C_4H_2(CO_2H)_2 = 116.1$ .

CAS — 110-17-8 (*fumaric acid*); 624-49-7 (*dimethyl fumarate*).

ATC — D05AX01.

ATC Vet — QD05AX01.



**Pharmacopoeias.** In Pol. Also in USNF.

**USNF 26** (Fumaric Acid). White, odourless granules or crystalline powder. Slightly soluble in water and in ether; soluble in alcohol; very slightly soluble in chloroform.

**Profile**

Fumaric acid and some of its derivatives have been used in the treatment of psoriasis and other skin disorders.

Fumaric acid is also used as an acidifier and flavouring agent in foods.

**Skin disorders.** Fumaric acid, its sodium salts, and derivatives such as dimethyl fumarate, monoethyl fumarate (ethyl hydrogen fumarate), and octyl hydrogen fumarate have been used, both topically and systemically, in the treatment of psoriasis (p.1583) and other skin disorders. Dimethyl fumarate appears to be the most active compound given orally but combination with various salts of monoethyl fumarate has been claimed to improve efficacy.<sup>1-6</sup> However, there have been reports of acute renal failure associated with treatment and the German Federal Office of Health has expressed the opinion that the available evidence did not establish the value of fumaric acid derivatives in psoriasis or other skin disorders.<sup>7</sup> A subsequent retrospective analysis of 41 patients who received fumaric acid esters orally, for between 1 and 14 years, suggested that these drugs might be effective,<sup>8</sup> and a later review suggested that they may be of value in refractory psoriasis.<sup>9</sup> Reported adverse effects in the earlier analysis<sup>8</sup> were generally mild, with only 1 case of elevated serum creatinine; however, lymphocytopenia was noted in 76% of patients and treatment consequently stopped in 4 patients. Other adverse effects with oral therapy have included disturbances of liver func-