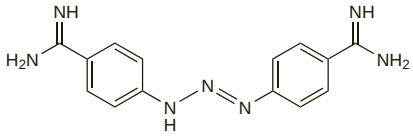
Diminazene Aceturate *(BANM, rINNM)*

Aceturato de diminazeno; Diminazène, Acéturate de; Diminazeni Aceturas. 1,3-Bis(4-amidinophenyl)triazene bis(*N*-acetylglycinate).

Диминазена Ацетурат

$C_{22}H_{29}N_9O_6$ = 515.5.

CAS — 536-71-0 (diminazene); 908-54-3 (diminazene aceturate).



(diminazene)

NOTE. Diminazene aceturate is often referred to by its veterinary proprietary name Berenil.

Profile

Diminazene aceturate, an aromatic diamidine derivative related to pentamidine, is an antiprotozoal that has been used in veterinary practice in the treatment of trypanosomiasis and babesiosis. It has also been tried in human infections.

Dinitolmide *(BAN, rINN)*

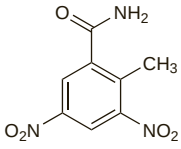
Dinitolmida; Dinitolmidum; Dinitrotoluamide; Methyldinitrobenzamide. 3,5-Dinitro-*o*-toluamide.

Динитолмид

$C_8H_7N_3O_5$ = 225.2.

CAS — 148-01-6.

ATC Vet — QP51AX12.



Pharmacopoeias. In *BP(Vet)*.

BP(Vet) 2008 (Dinitolmide). A cream to light tan powder. Practically insoluble in water; slightly soluble in alcohol, in chloroform, and in ether; soluble in acetone.

Profile

Dinitolmide is an antiprotozoal used in veterinary practice for the prevention of coccidiosis in poultry.

Eflornithine Hydrochloride

(BANM, USAN, rINNM)

DFMO; α-Difluoromethylornithine Hydrochloride; Éflornithine, Chlorhydrate d'; Eflornithini Hydrochloridum; Hidrocloruro de eflornitina; MDL-71782; MDL-71782A; RMI-71782. 2-(Difluoromethyl)-DL-ornithine monohydrochloride monohydrate.

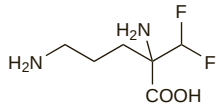
Эфлорнитина Гидрохлорид

$C_6H_{12}F_2N_2O_2$,HCl,H_2O = 236.6.

CAS — 67037-37-0 (eflornithine); 96020-91-6 (eflornithine hydrochloride).

ATC — D11AX16; P01CX03.

ATC Vet — QD11AX16.



(eflornithine)

Adverse Effects and Precautions

Myelosuppression may lead to anaemia, leucopenia, and thrombocytopenia. Some patients have had hearing loss and alopecia. Gastrointestinal disturbances, especially diarrhoea, may occur. Seizures have occurred in about 8% of patients given eflornithine but they may have been related to the disease rather than treatment.

Dosage should be reduced in patients with renal impairment.

Skin irritation, such as erythema or a stinging or burning sensation, has been reported after topical application of eflornithine.

Effects on the ears. A study in 58 patients[1] receiving eflornithine alone or with interferon alfa for the treatment of metastatic melanoma found that hearing loss was related to the cumulative dose of eflornithine and was worse in patients with pre-existing hearing deficit.

1. Croghan MK, *et al.* Dose-related α-difluoromethylornithine ototoxicity. *Am J Clin Oncol* 1991; **14:** 331–5.

Effects on the heart. Fatal cardiac arrest occurred in an AIDS patient with pneumocystis pneumonia during the intravenous infusion of eflornithine 100 mg/kg over 1 hour.[1] Sudden death after infusion of eflornithine had occurred in several other critically ill patients with AIDS.

1. Barbarash RA, *et al.* Alpha-difluoromethylornithine infusion and cardiac arrest. *Ann Intern Med* 1986; **105:** 141–2.

Pharmacokinetics

Eflornithine hydrochloride is absorbed from the gastrointestinal tract. After intravenous doses about 80% is excreted unchanged in the urine in 24 hours. The terminal elimination half-life is about 3 hours. It is distributed to the CSF.

Less than 1% of a dose is absorbed after topical application.

◊ References.

1. Haegele KD, *et al.* Kinetics of α-difluoromethylornithine: an irreversible inhibitor of ornithine decarboxylase. *Clin Pharmacol Ther* 1981; **30:** 210–17.
2. Milord F, *et al.* Eflornithine concentrations in serum and cerebrospinal fluid of 63 patients treated for Trypanosoma brucei gambiense sleeping sickness. *Trans R Soc Trop Med Hyg* 1993; **87:** 473–7.
3. Malhotra B, *et al.* Percutaneous absorption and pharmacokinetics of eflornithine HCl 13.9% cream in women with unwanted facial hair. *J Clin Pharmacol* 2001; **41:** 972–8.

Uses and Administration

Eflornithine is an antiprotozoal that acts as an irreversible inhibitor of ornithine decarboxylase, the rate-limiting enzyme in polyamine biosynthesis; trypanosomes are more susceptible to the effects of eflornithine than are humans, probably because of their slower turnover of this enzyme.

Eflornithine is used in African trypanosomiasis due to *Trypanosoma brucei gambiense*. It is effective in the early and, more importantly, in the late stage of the disease (when there is CNS involvement).

In the treatment of African trypanosomiasis, eflornithine hydrochloride is given by intravenous infusion. The dose is 100 mg/kg every 6 hours for at least 14 days. Each dose should be given over a period of at least 45 minutes. Dosage should be reduced in patients with renal impairment.

Eflornithine hydrochloride is also applied topically twice daily for the reduction of unwanted facial hair in women. It is available as a cream containing 15% eflornithine hydrochloride monohydrate; in the UK this content is expressed as 11.5% eflornithine and in the USA as 13.9% anhydrous eflornithine hydrochloride.

Cryptosporidiosis. Eflornithine has been tried in the treatment of cryptosporidiosis (p.823) in AIDS patients.[1]

1. Rolston KVI, *et al.* Intestinal cryptosporidiosis treated with eflornithine: a prospective study among patients with AIDS. *J Acquir Immune Defic Syndr* 1989; **2:** 426–30.

Hirsutism. Topical eflornithine hydrochloride applied twice daily as a 13.9% cream is effective in reducing the growth of unwanted facial hair in females (see Hirsutism, p.2089), although it must be used indefinitely to prevent regrowth.[1] Its action is thought to be due to the irreversible inhibition of ornithine decarboxylase in hair follicles. It has also been used successfully in combination with laser hair removal.[2]

1. Barman Balfour JA, McClellan K. Topical eflornithine. *Am J Clin Dermatol* 2001; **2:** 197–201.
2. Hamzavi I, *et al.* A randomized bilateral vehicle-controlled study of eflornithine cream combined with laser treatment versus laser treatment alone for facial hirsutism in women. *J Am Acad Dermatol* 2007; **57:** 54–9.

Malignant neoplasms. Eflornithine has antimetabolic activity and is being studied as a potential chemopreventive agent in patients at high risk of a variety of malignant diseases, including cancer of the bladder, breast, cervix, colon, oesophagus, prostate, and skin.[1]

1. Meyskens FL, Gerner EW. Development of difluoromethylornithine (DFMO) as a chemoprevention agent. *Clin Cancer Res* 1999; **5:** 945–51.

African trypanosomiasis. Eflornithine is effective in the treatment of *Trypanosoma brucei gambiense* infections (p.827), and is particularly valuable in providing an alternative to melarsoprol in meningoencephalitic disease.[1-3] Eflornithine 100 mg/kg intravenously every 6 hours for 7 days, rather than the standard 14 days, produced long-term responses in 42 of 47 patients who had relapsed after other treatment regimens.[4] Similar positive results in relapsing cases were obtained with a short 7-day course in a multicentre randomised controlled study,[5] although this short course was inferior to the 14-day course for new cases, in whom it could not be recommended. A patient who had relapsed after treatment with melarsoprol and eflornithine given singly was cured when the drugs were given together.[6] Eflornithine is not effective when given alone in *T. b. rhodesiense* infections, and early reports of its use with suramin were not encouraging.[7] However, benefit has been reported from use with nifurtimox.[8]

1. Chappuis F, *et al.* Eflornithine is safer than melarsoprol for the treatment of second-stage *Trypanosoma brucei gambiense* human African trypanosomiasis. *Clin Infect Dis* 2005; **41:** 748–51.
2. Balasegaram M, *et al.* Melarsoprol versus eflornithine for treating late-stage Gambian trypanosomiasis in the Republic of the Congo. *Bull WHO* 2006; **84:** 783–91.
3. Priotto G, *et al.* Safety and effectiveness of first line eflornithine for *Trypanosoma brucei gambiense* sleeping sickness in Sudan: cohort study. *BMJ* 2008; **336:** 705–8.
4. Khonde N, *et al.* A seven days course of eflornithine for relapsing Trypanosoma brucei gambiense sleeping sickness. *Trans R Soc Trop Med Hyg* 1997; **91:** 212–13.
5. Pepin J, *et al.* Short-course eflornithine in Gambian trypanosomiasis: a multicentre randomized controlled trial. *Bull WHO* 2000; **78:** 1284–95.
6. Simarro PP, Asumu PN. Gambian trypanosomiasis and synergism between melarsoprol and eflornithine: first case report. *Trans R Soc Trop Med Hyg* 1996; **90:** 315.
7. Clerinx J, *et al.* Treatment of late stage rhodesiense trypanosomiasis using suramin and eflornithine: report of six cases. *Trans R Soc Trop Med Hyg* 1998; **92:** 449–50.
8. Priotto G, *et al.* Nifurtimox-eflornithine combination therapy for second-stage *Trypanosoma brucei gambiense* sleeping sickness: a randomized clinical trial in Congo. *Clin Infect Dis* 2007; **45:** 1435–42.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Vaniqa; ***Cz.:*** Vaniqa; ***Fr.:*** Vaniqa; ***Ger.:*** Vaniqa; ***Irl.:*** Vaniqa; ***Ital.:*** Vaniqa; ***Neth.:*** Vaniqa; ***Port.:*** Vaniqa; ***Spain:*** Vaniqa; ***UK:*** Vaniqa; ***USA:*** Ornidyl; Vaniqa.

Emetine Hydrochloride *(BANM)*

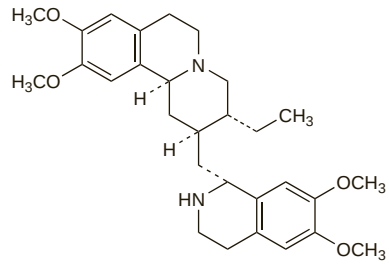
Cloridrato de Emetina; Emet. Hydrochlor.; Emetiinihydrokloridi; Emetina, hidrocloruro de; Emetin-dihydrochlorid; Émétine, chlorhydrate d'; Emetine Dihydrochloride; Emetin-hidroklorid; Emetinhydroklorid; Emetini Chloridum; Emetini Dihydrochloridum; Emetini hydrochloridum; Emetino hidrochloridas; Emetyny dichlorowodorek; Ipecine Hydrochloride; Methylcephaëline Hydrochloride. 6′,7′,10,11-Tetramethoxyemetan dihydrochloride heptahydrate; (2*S*,3*R*,11b*S*)-3-Ethyl-1,3,4,6,7,11b-hexahydro-9,10-dimethoxy-2-[(1*R*)-1,2,3,4-tetrahydro-6,7-dimethoxy-1-isoquinolylmethyl]-2*H*-benzo[*a*]quinolizine dihydrochloride heptahydrate.

Эметина Гидрохлорид

$C_{29}H_{40}N_2O_4$,2HCl,$7H_2O$ = 679.7.

CAS — 483-18-1 (emetine); 316-42-7 (anhydrous emetine hydrochloride); 7083-71-8 (emetine hydrochloride, hydrate); 79300-08-6 (emetine hydrochloride, heptahydrate).

ATC — P01AX02.



(emetine)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Viet.*

Eur. also has a monograph for Emetine Hydrochloride Pentahydrate; *Int.* permits the heptahydrate or pentahydrate in the same monograph. *US* has a monograph for the anhydrous salt.

Ph. Eur. 6.2 (Emetine Hydrochloride Heptahydrate; Emetine Hydrochloride BP 2008). A white or slightly yellow crystalline powder. Freely soluble in water and in alcohol. A 2% solution in water has a pH of 4.0 to 6.0. Protect from light.

Ph. Eur. 6.2 (Emetine Hydrochloride Pentahydrate). A white or slightly yellow crystalline powder. Freely soluble in water and in alcohol. A 2% solution in water has a pH of 4.0 to 6.0. Protect from light.