4. Knupp CA, *et al.* Disposition of didanosine in HIV-seropositive patients with normal renal function or chronic renal failure: influence of hemodialysis and continuous ambulatory peritoneal dialysis. *Clin Pharmacol Ther* 1996; **60:** 535–42.
5. Wintergerst U, *et al.* Lack of absorption of didanosine after rectal administration in human immunodeficiency virus-infected patients. *Antimicrob Agents Chemother* 1999; **43:** 699–701.
6. Abreu T, *et al.* Bioavailability of once- and twice-daily regimens of didanosine in human immunodeficiency virus-infected children. *Antimicrob Agents Chemother* 2000; **44:** 1375–6.

Pregnancy. Fetal blood concentrations of 14 and 19% of the maternal serum-didanosine concentrations have been reported.[1] There is evidence of extensive metabolism in the placenta.[2]

1. Pons JC, *et al.* Fetoplacental passage of 2′,3′-dideoxyinosine. *Lancet* 1991; **337:** 732.
2. Dancis J, *et al.* Transfer and metabolism of dideoxyinosine by the perfused human placenta. *J Acquir Immune Defic Syndr* 1993; **6:** 2–6.

Uses and Administration

Didanosine is a nucleoside reverse transcriptase inhibitor structurally related to inosine with antiviral activity against HIV-1. It is used in the treatment of HIV infection and AIDS (p.856). Viral resistance emerges rapidly when didanosine is used alone, and it is therefore used with other antiretrovirals.

Didanosine is given orally, usually as buffered chewable/dispersible tablets or enteric-coated capsules. Doses should be taken at least 30 minutes before, or 2 hours after, a meal. The total daily dose may be given as either a single dose or as two divided doses, the choice being dependent upon both the formulation and the strength used. For adults weighing more than 60 kg the recommended dose is 400 mg daily and for those under 60 kg, 250 mg daily is given.

For details of doses in children, see below.

Doses of didanosine may need to be amended when given with some other antiretrovirals. For further details see under Interactions, above.

Dosage reduction may be necessary in patients with renal (see below) or hepatic impairment, although no specific dose reductions are recommended in patients with hepatic impairment and close monitoring is required.

◊ Reviews.

1. Shelton MJ, *et al.* Didanosine. *Ann Pharmacother* 1992; **26:** 660–70.
2. Lipsky JJ. Zalcitabine and didanosine. *Lancet* 1993; **341:** 30–2.
3. Perry CM, Noble S. Didanosine: an updated review of its use in HIV infection. *Drugs* 1999; **58:** 1099–1135.
4. Moreno S, *et al.* Didanosine enteric-coated capsule: current role in patients with HIV-1 infection. *Drugs* 2007; **67:** 1441–62.

Administration in children. For the treatment of HIV infection in children, didanosine is given daily with other antiretroviral drugs in doses based on body-surface. Doses are taken on an empty stomach. In the USA an oral solution is available for paediatric use:

- in children aged between 2 weeks and 8 months the recommended dose is 100 mg/m^2 twice daily
- in children over 8 months of age the recommended dose is 120 mg/m^2 twice daily

In the UK chewable or dispersible tablets or enteric-coated capsules are available for use:

- the chewable or dispersible tablets may be given orally to children older than 3 months of age, as either a single dose or as two divided doses, in a dose of 240 mg/m^2 daily *or* 180 mg/m^2 daily if given with zidovudine
- enteric-coated capsules may be given orally to children older than 6 years of age in a dose of 240 mg/m^2 daily *or* 180 mg/m^2 daily if given with zidovudine

Administration in renal impairment. Dosage of didanosine should be reduced in patients with renal impairment. The following doses are recommended based on the patient's creatinine clearance (CC):

Adults greater than 60 kg:

- CC more than 60 mL/minute: usual adult doses
- CC 30 to 59 mL/minute: 200 mg daily as a single dose or in two equally divided doses
- CC 10 to 29 mL/minute: 150 mg once daily
- CC less than 10 mL/minute: 100 mg once daily

Adults less than 60 kg:

- CC more than 60 mL/minute: usual adult doses
- CC 30 to 59 mL/minute: 150 mg daily as a single dose or in two equally divided doses
- CC 10 to 29 mL/minute: 100 mg once daily
- CC less than 10 mL/minute: 75 mg once daily

Preparations

USP 31: Didanosine for Oral Solution; Didanosine Tablets for Oral Suspension.

Proprietary Preparations (details are given in Part 3)

Arg.: Aso DDI†; Bandotan†; Dibistic†; Megavir†; Ronvir†; Videx; ***Austral.:*** Videx; ***Austria:*** Videx; ***Belg.:*** Videx; ***Braz.:*** Didanox†; Videx; ***Canad.:*** Videx; ***Chile:*** Videx; ***Cz.:*** Videx; ***Denm.:*** Videx; ***Fin.:*** Videx; ***Fr.:*** Videx; ***Ger.:*** Videx; ***Gr.:*** Videx; ***Hong Kong:*** Videx; ***Hung.:*** Videx; ***India:*** Dinex; ***Indon.:*** Videx; ***Irl.:*** Videx; ***Israel:*** Videx†; ***Ital.:*** Videx; ***Malaysia:*** Videx; ***Mex.:*** Apodasi†; Didasten; Videx; ***Neth.:*** Videx; ***Norw.:*** Videx; ***NZ:*** Videx; ***Pol.:*** Videx; ***Port.:*** Videx; ***Rus.:*** Videx (Видекс); ***S.Afr.:*** Videx; ***Singapore:*** Videx; ***Spain:*** Videx; ***Swed.:*** Videx; ***Switz.:*** Videx; ***Thai.:*** Videx; ***Turk.:*** Videx; ***UK:*** Videx; ***USA:*** Videx; ***Venez.:*** Videx.

Multi-ingredient: ***India:*** Odivir Kit.

Docosanol *(USAN)*

Behenyl Alcohol; *n*-Docosanol; Docosyl Alcohol; lK-2. 1-Docosanol.

Докозанол

$C_{22}H_{46}O$ = 326.6.

CAS — 661-19-8.

ATC — D06BB11.

ATC Vet — QD06BB11.

Profile

Docosanol is an antiviral used topically five times daily as a 10% cream in the treatment of recurrent herpes labialis (p.854). Docosanol acts by inhibiting fusion between the cell plasma membrane and the herpes simplex virus, thereby preventing viral entry into cells and subsequent viral replication. It has been investigated for genital herpes.

◊ References.

1. Habbema L, *et al.* n-Docosanol 10% cream in the treatment of recurrent herpes labialis: a randomised, double-blind, placebo-controlled study. *Acta Derm Venereol* 1996; **76:** 479–81.
2. Sacks SL, *et al.* Clinical efficacy of topical docosanol 10% cream for herpes simplex labialis: a multicenter, randomized, placebo-controlled trial. *J Am Acad Dermatol* 2001; **45:** 222–30.
3. Leung DT, Sacks SL. Docosanol: a topical antiviral for herpes labialis. *Expert Opin Pharmacother* 2004; **5:** 2567–71.

Preparations

Proprietary Preparations (details are given in Part 3)

Canad.: Abreva; ***Cz.:*** Erazaban; ***Gr.:*** Healip; ***Swed.:*** Healip; ***USA:*** Abreva.

Edoxudine *(USAN, rINN)*

Edoxudina; Édoxudine; Edoxudinum; EDU; Ethyl Deoxyuridine; EUDR; ORF-15817; RWJ-15817. 2′-Deoxy-5-ethyluridine.

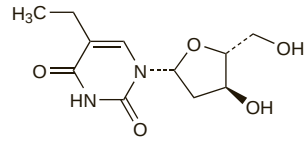
Эдоксудин

$C_{11}H_{16}N_2O_5$ = 256.3.

CAS — 15176-29-1.

ATC — D06BB09.

ATC Vet — QD06BB09.



Profile

Edoxudine is an antiviral that has been used topically in the treatment of mucocutaneous herpes simplex infections (p.854); it has also been used as an ophthalmic preparation.

Preparations

Proprietary Preparations (details are given in Part 3)

Switz.: Edurid†.

Efavirenz *(BAN, rINN)*

5B706; DMP-266; Efavirentsi; Éfavirenz; Efavirenzum; L-743; L-743726. (*S*)-6-Chloro-4-(cyclopropylethynyl)-1,4-dihydro-4-(trifluoromethyl)-2*H*-3,1-benzoxazin-2-one.

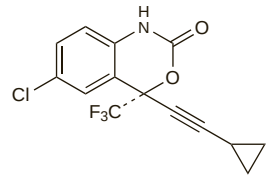
Эфавиренз

$C_{14}H_9ClF_3NO_2$ = 315.7.

CAS — 154598-52-4.

ATC — J05AG03.

ATC Vet — QJ05AG03.



Adverse Effects

The most common adverse effects associated with antiretroviral regimens containing efavirenz are skin rashes and psychiatric or CNS disturbances. Mild to moderate rashes (usually maculopapular eruptions) generally appear within the first 2 weeks of starting therapy and may resolve within a month of continued treatment; of severe forms including erythema multiforme and Stevens-Johnson syndrome have been reported occasionally. CNS symptoms include agitation, amnesia, confusion, dizziness, euphoria, headache, insomnia or somnolence, impaired concentration, abnormal thinking or dreaming, convulsions, depersonalisation, and hallucinations. Nervous system symptoms usually begin during the first one or two days of therapy and generally resolve after the first 2 to 4 weeks; they may occur more frequently when efavirenz is taken with meals, possibly due to increased efavirenz plasma concentrations. Serious psychiatric adverse effects include severe depression, suicidal ideation and attempts, aggressive behaviour, and psychotic reactions including paranoia and mania. Other adverse effects include nausea and vomiting, diarrhoea, fatigue, and pancreatitis. Raised liver enzyme values and raised serum-cholesterol and -triglyceride concentrations have been reported. Hepatic failure and photoallergic dermatitis have occurred.

Immune reconstitution syndrome (an inflammatory immune response resulting in clinical deterioration) has been reported during the initial phase of treatment with combination antiretroviral therapy, including efavirenz, in HIV-infected patients with severe immune deficiency. Accumulation or redistribution of body fat (lipodystrophy) including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and cushingoid appearance have been seen in patients receiving antiretroviral therapy, including efavirenz. Metabolic abnormalities such as hypertriglyceridaemia, hypercholesterolaemia, insulin resistance, hyperglycaemia, and hyperlactataemia have also been reported.

◊ References.

1. Clifford DB, *et al.* Impact of efavirenz on neuropsychological performance and symptoms in HIV-infected individuals. *Ann Intern Med* 2005; **143:** 714–21.

Effects on the mouth. Burning mouth syndrome was diagnosed in a patient 2 weeks after adding efavirenz to her longstanding combination antiretroviral treatment regimen.[1] Efavirenz was stopped and the syndrome resolved within 1 week.

1. Borrás-Blasco J, *et al.* Burning mouth syndrome due to efavirenz therapy. *Ann Pharmacother* 2006; **40:** 1471–2.

Precautions

Efavirenz is contra-indicated in patients with severe hepatic impairment (Child-Pugh class C), and should be used with caution, and liver enzymes values monitored, in patients with mild to moderate liver disease. Patients co-infected with chronic hepatitis B or C and treated with combination antiretroviral therapy are at increased risk for severe and potentially fatal hepatic adverse events. Caution should be exercised in patients