should not be given etravirine in a regimen containing only NRTIs.

Interactions
Etravirine is metabolised mainly by the cytochrome P450 isoenzymes CYP3A4, CYP2C9, and CYP2C19. It is an inducer of CYP3A4 and an inhibitor of CYP2C9 and CYP2C19. Consequently it may compete with other drugs metabolised by these systems, potentially resulting in mutually altered plasma concentrations and possibly toxicity. Enzyme inducers may decrease plasma concentrations of etravirine.

Etravirine should not be given with other NNRTIs. It should also not be used in regimens with HIV-protease inhibitors given without ritonavir-boosting but use with ritonavir-boosted tipranavir, fosamprenavir, or atazanavir should be avoided. For further information on drug interactions of NNRTIs see Table 2, p.944.

Antiviral Action
Etravirine acts by inhibition of HIV-1 reverse transcriptase and blocks viral RNA- and DNA-dependent DNA polymerase activities. It is a flexible molecule designed to fit in the active pocket of viral reverse transcriptase in different ways, even when the shape of that pocket changes because of viral mutations. This is considered to reduce the risk of the development of resistance; phase II studies in treatment-experienced patients have shown activity against HIV resistant to other NNRTIs (delavirdine, efavirenz, and nevirapine).

Pharmacokinetics
Etravirine is readily absorbed after oral doses and peak plasma concentrations occur after about 2.5 to 4 hours; absorption is increased by food. It is about 99.9% bound to plasma proteins. Etravirine is extensively metabolised by hepatic microsomal enzymes, principally by the cytochrome P450 isoenzymes CYP3A4, CYP2C9, and CYP2C19 families, to substantially less active metabolites. The mean plasma half-life after usual dosage is about 41 hours and ranges from 21 to 61 hours. About 93.7% of a dose appears in the faeces (81.2 to 86.4% as unchanged drug), and 1.2% in the urine (unchanged drug was not detected in the urine).

Uses and Administration
Etravirine is a non-nucleoside reverse transcriptase inhibitor with activity against HIV-1. It is given with other antiretrovirals for the treatment of HIV infection and AIDS (p.856) in treatment-experienced patients, who have evidence of viral replication and HIV-1 strains resistant to a NNRTI and other antiretrovirals. Etravirine is given orally in a usual dose of 200 mg twice daily after food.

◊ References.

1. Madruga JV, *et al.* Efficacy and safety of TMC125 (etravirine) in treatment-experienced HIV-1-infected patients in DUET-1: 24-week results from a randomised, double-blind, placebo-controlled trial. *Lancet* 2007; **370:** 29–38.
2. Lazzarin A, *et al.* Efficacy and safety of TMC125 (etravirine) in treatment-experienced HIV-1-infected patients in DUET-2: 24-week results from a randomised, double-blind, placebo-controlled trial. *Lancet* 2007; **370:** 39–48.

Preparations
Proprietary Preparations (details are given in Part 3)
USA: Intelence.

Famciclovir *(BAN, USAN, rINN)*

AV-42810; BRL-42810; Famciclovirum; Famciklovir; Famsikloviiri; Famsiklovir. 2[2-(2-Amino-9*H*-purin-9-yl)ethyl]trimethylene diacetate.

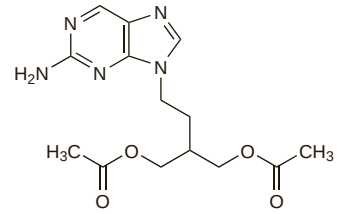
Фамцикловир

$C_{14}H_{19}N_5O_4$ = 321.3.

CAS — 104227-87-4.

ATC — J05AB09; S01AD07.

ATC Vet — QJ05AB09; QS01AD07.



Pharmacopoeias. In *Chin.*

Adverse Effects and Precautions
The most common adverse effects of famciclovir are headache and nausea. Other adverse effects rarely reported include jaundice, vomiting, dizziness, skin rash, pruritus, urticaria, somnolence, confusion, and hallucinations. In addition, abdominal pain and fever have been reported in immunocompromised patients given famciclovir.

Dosage should be reduced in patients with renal impairment. Acute renal failure has occurred in patients with renal impairment taking inappropriately high doses of famciclovir.

◊ References.

1. Saltzman R, *et al.* Safety of famciclovir in patients with herpes zoster and genital herpes. *Antimicrob Agents Chemother* 1994; **38:** 2454–7.

Interactions
As for Penciclovir, p.901.

Antiviral Action
As for Penciclovir, p.901.

Pharmacokinetics
Famciclovir is rapidly absorbed after oral doses. Absorption is delayed but not reduced by food. Famciclovir is rapidly converted to penciclovir (see p.901), peak plasma concentrations occurring within about 1 hour of a dose, and virtually no famciclovir is detectable in the plasma or urine. Bioavailability of penciclovir is reported to be 77%. Famciclovir is mainly excreted in the urine (partly by renal tubular secretion) as penciclovir and its 6-deoxy precursor; elimination is reduced in patients with renal impairment.

◊ References.

1. Pue MA, Benet LZ. Pharmacokinetics of famciclovir in man. *Antiviral Chem Chemother* 1993; **4** (suppl 1): 47–55.
2. Boike SC, *et al.* Pharmacokinetics of famciclovir in subjects with varying degrees of renal impairment. *Clin Pharmacol Ther* 1994; **55:** 418–26.
3. Boike SC, *et al.* Pharmacokinetics of famciclovir in subjects with chronic hepatic disease. *J Clin Pharmacol* 1994; **34:** 1199–1207.
4. Gill KS, Wood MJ. The clinical pharmacokinetics of famciclovir. *Clin Pharmacokinet* 1996; **31:** 1–8.

Uses and Administration
Famciclovir is a prodrug of the antiviral penciclovir (p.901). It is given orally in the treatment of herpes zoster (see Varicella-zoster Infections, p.855) and genital and mucocutaneous herpes (see Herpes Simplex Infections, p.854).

For **herpes zoster**, famciclovir is given in a dose of 250 mg three times daily, or 750 mg once daily, for 7 days (in the USA the recommended dose is 500 mg three times daily for 7 days); immunocompromised patients are given 500 mg three times daily for 10 days.

For **herpes simplex infections**, famciclovir is given in a dose of 250 mg three times daily for 5 days for first episodes of genital herpes; immunocompromised patients are given 500 mg twice daily for 7 days. For acute treatment of recurrent episodes of genital herpes, 125 mg is given twice daily for 5 days (in the USA, the recommended dose is 1 g twice daily for 1 day). Treatment should start in the prodromal period as soon as the first signs or symptoms appear. Immunocompromised patients are given 500 mg twice daily for 7 days.

For suppression of recurrent episodes of genital herpes, 250 mg is given twice daily; HIV patients may be given 500 mg twice daily. Such suppressive treatment is interrupted every 6 to 12 months to observe possible changes in the natural history of the disease.

For acute treatment of recurrent mucocutaneous herpes in HIV-infected patients, 500 mg is given twice daily for 7 days.

In the USA, famciclovir may also be given for the treatment of recurrent herpes labialis as a single 1.5 g dose, preferably begun in the prodromal period.

Doses of famciclovir should be reduced in patients with renal impairment (see below).

◊ Reviews.

1. Perry CM, Wagstaff AJ. Famciclovir: a review of its pharmacological properties and therapeutic efficacy in herpesvirus infections. *Drugs* 1995; **50:** 396–415.
2. Faro S. A review of famciclovir in the management of genital herpes. *Infect Dis Obstet Gynecol* 1998; **6:** 38–43.
3. Vinh DC, Aoki FY. Famciclovir for the treatment of recurrent genital herpes: a clinical and pharmacological perspective. *Expert Opin Pharmacother* 2006; **7:** 2271–86.
4. Simpson D, Lyseng-Williamson KA. Famciclovir: a review of its use in herpes zoster and genital and orolabial herpes. *Drugs* 2006; **66:** 2397–2416.

Administration in renal impairment. Doses of famciclovir need to be reduced in patients with renal impairment. UK licensed product information recommends the following oral doses based on creatinine clearance (CC):

Immunocompetent patients:

Herpes zoster or an initial episode of genital herpes
- CC 30 to 59 mL/minute per 1.73 m^2: 250 mg twice daily
- CC 10 to 29 mL/minute per 1.73 m^2: 250 mg once daily

Acute recurrent genital herpes, treatment
- CC 30 to 59 mL/minute per 1.73 m^2: no dosage adjustment necessary
- CC 10 to 29 mL/minute per 1.73 m^2: 125 mg once daily

Recurrent genital herpes, suppression
- CC 30 mL/minute per 1.73 m^2 and over: 250 mg twice daily
- CC 10 to 29 mL/minute per 1.73 m^2: 125 mg twice daily

Immunocompromised patients:

Herpes zoster
- CC 40 mL/minute per 1.73 m^2 and over: 500 mg three times daily
- CC 30 to 39 mL/minute per 1.73 m^2: 250 mg three times daily
- CC 10 to 29 mL/minute per 1.73 m^2: 125 mg three times daily

Herpes simplex infections
- CC 40 mL/minute per 1.73 m^2 and over: 500 mg twice daily
- CC 30 to 39 mL/minute per 1.73 m^2: 250 mg twice daily
- CC 10 to 29 mL/minute per 1.73 m^2: 125 mg twice daily

Patients on haemodialysis should be given doses of famciclovir immediately after dialysis.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Pentavir; Zosvir†; ***Austral.:*** Famvir; ***Austria:*** Famvir; ***Belg.:*** Famvir; ***Braz.:*** Famvir; Fanclomax; Penvir; ***Canad.:*** Famvir; ***Cz.:*** Famvir; ***Denm.:*** Famvir; ***Fin.:*** Famvir; ***Fr.:*** Oravir; ***Ger.:*** Famvir; ***Gr.:*** Famvir; ***Hong Kong:*** Famvir; ***Hung.:*** Famvir; ***India:*** Famtrex; ***Irl.:*** Famvir; ***Israel:*** Famvir†; ***Ital.:*** Famvir; Ziravir; ***Neth.:*** Famvir; ***NZ:*** Famvir†; ***Port.:*** Famvir; Zyvir; ***Rus.:*** Famvir (Фамвир); ***S.Afr.:*** Famvir; ***Singapore:*** Famvir; ***Spain:*** Ancivin; Famvir; ***Swed.:*** Famvir; ***Switz.:*** Famvir; ***Thai.:*** Famvir; ***Turk.:*** Famvir; ***UK:*** Famvir; ***USA:*** Famvir.

Fomivirsen Sodium *(BANM, USAN, rINNM)*

Fomivirseeninatrium; Fomivirsén sódico; Fomivirsen Sodique; Fomivirsennatrium; Fomivirsenum Natricum; Isis-2922; Natrii Fomivirsenum.

Натрий Фомивирсен

$C_{204}H_{243}N_{63}Na_{20}O_{114}P_{20}S_{20}$ = 7122.0.

CAS — 144245-52-3 (fomivirsen); 160369-77-7 (fomivirsen sodium).

ATC — S01AD08.

ATC Vet — QS01AD08.

Adverse Effects and Precautions
Adverse effects after intra-ocular injection of fomivirsen are confined to the treated eye. They include intra-ocular inflammation, transient increases in intra-ocular pressure, retinal detachment and oedema, and visual abnormalities. Other adverse effects associated with the intravitreal injection procedure include vitreal haemorrhage, endophthalmitis, uveitis, and cataract formation.

Patients should be monitored during treatment for changes in intra-ocular pressure and visual field and for extra-ocular CMV disease or disease in the contralateral eye.