zyme inducers may decrease plasma concentrations of nevirapine; nevirapine itself acts as a mild to moderate enzyme inducer and may thus reduce plasma concentrations of other drugs.

Rifampicin and St John's wort decrease the concentration of nevirapine; use with the antiretroviral is not recommended due to the possible loss of its activity and development of resistance. For further information on drug interactions of NNRTIs see Table 2, p.944.

Antivirals. For the effect of nevirapine on *HIV-protease inhibitors*, see p.883.

Methadone. Nevirapine may induce the metabolism of methadone (p.84) resulting in reduced plasma-methadone concentrations.

Antiviral Action

Nevirapine acts by non-competitive inhibition of HIV-1 reverse transcriptase; it binds to the enzyme, disrupting the conformation of its catalytic site and impairing its RNA- and DNA-dependent polymerase activity.

Resistance to nevirapine and emergence of cross-resistance to other non-nucleoside reverse transcriptase inhibitors has been seen.

Pharmacokinetics

Nevirapine is readily absorbed after oral doses and absorption is not affected by food or antacids. Bioavailability is greater than 90%. Nevirapine tablets and oral suspension are comparably bioavailable and interchangeable at doses up to 200 mg. Peak plasma concentrations occur 4 hours after a single dose. Nevirapine is about 60% bound to plasma proteins. Concentrations in the CSF are about 45% of those in plasma. Nevirapine crosses the placenta and is distributed into breast milk. It is extensively metabolised by hepatic microsomal enzymes, principally by the cytochrome P450 isoenzymes CYP3A4 and CYP2B6, to several hydroxylated metabolites. Autoinduction of these enzymes results in a 1.5- to 2-fold increase in apparent oral clearance after 2 to 4 weeks at usual dosage, and a decrease in terminal half-life from 45 hours to 25 to 30 hours over the same period. Nevirapine is mainly excreted in the urine as glucuronide conjugates of the hydroxylated metabolites.

In children, nevirapine elimination accelerates during the first years of life, reaching a maximum at around 2 years of age, followed by a gradual decline during the rest of childhood; values in children under 8 years are about twice those in adults.

◊ References.

1. Mirochnick M, *et al.* Nevirapine: pharmacokinetic considerations in children and pregnant women. *Clin Pharmacokinet* 2000; **39:** 281–93.
2. Almond LM, *et al.* Intracellular and plasma pharmacokinetics of nevirapine in human immunodeficiency virus-infected individuals. *Clin Pharmacol Ther* 2005; **78:** 132–42.
3. von Hentig N, *et al.* A comparison of the steady-state pharmacokinetics of nevirapine in men, nonpregnant women and women in late pregnancy. *Br J Clin Pharmacol* 2006; **62:** 552–9.

Uses and Administration

Nevirapine is a non-nucleoside reverse transcriptase inhibitor with activity against HIV-1. It is used in the treatment of HIV infection and AIDS (p.856). Viral resistance emerges rapidly when nevirapine is used alone, and it is therefore used with other antiretrovirals.

Nevirapine is given orally in an adult dose of 200 mg once daily for the first 14 days, then increased to 200 mg twice daily provided that no rash is present (see Precautions, above).

If treatment is interrupted for more than 7 days, it should be reintroduced using the lower dose for the first 14 days as for new treatment.

For details of doses in infants, children, and adolescents, see below.

Nevirapine is often used in regimens for the prophylaxis of vertical transmission (mother-to-child) of HIV infection. In women in whom HAART is not indicated, or where it is not available, a single oral dose of nevirapine 200 mg may be given at the onset of labour, together with a course of zidovudine and lamivudine, for perinatal cover (see HIV Infection Prophylaxis, p.858).

◊ References.

1. Floridia M, *et al.* A randomized, double-blind trial on the use of a triple combination including nevirapine, a nonnucleoside reverse transcriptase HIV inhibitor, in antiretroviral-naive patients with advanced disease. *J Acquir Immune Defic Syndr Hum Retrovirol* 1999; **20:** 11–19.
2. Guay LA, *et al.* Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. *Lancet* 1999; **354:** 795–802.
3. Bardsley-Elliot A, Perry CM. Nevirapine: a review of its use in the prevention and treatment of paediatric HIV infection. *Paediatr Drugs* 2000; **2:** 373–407.
4. Dorenbaum A, *et al.* Two-dose intrapartum/newborn nevirapine and standard antiretroviral therapy to reduce perinatal HIV transmission: a randomized trial. *JAMA* 2002; **288:** 189–98.
5. Moodley D, *et al.* A multicenter randomized controlled trial of nevirapine versus a combination of zidovudine and lamivudine to reduce intrapartum and early postpartum mother-to-child transmission of human immunodeficiency virus type 1. *J Infect Dis* 2003; **187:** 725–35.
6. Taha TE, *et al.* Short postexposure prophylaxis in newborn babies to reduce mother-to-child transmission of HIV-1: NVAZ randomised clinical trial. *Lancet* 2003; **362:** 1171–7.
7. Lallemant M, *et al.* Single-dose perinatal nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. *N Engl J Med* 2004; **351:** 217–28.
8. Shapiro RL, *et al.* Maternal single-dose nevirapine versus placebo as part of an antiretroviral strategy to prevent mother-to-child HIV transmission in Botswana. *AIDS* 2006; **20:** 1281–8.
9. Lockman S, *et al.* Response to antiretroviral therapy after a single, peripartum dose of nevirapine. *N Engl J Med* 2007; **356:** 135–47.
10. Parienti JJ, *et al.* SIROCCO study team. Efavirenz to nevirapine switch in HIV-1-infected patients with dyslipidemia: a randomized, controlled study. *Clin Infect Dis* 2007; **45:** 263–6.
11. Dart Trial Team. Twenty-four-week safety and tolerability of nevirapine vs. abacavir in combination with zidovudine/lamivudine as first-line antiretroviral therapy: a randomized double-blind trial (NORA). *Trop Med Int Health* 2008; **13:** 6–16.

Administration in children. For the treatment of HIV infection in infants, children, and adolescents nevirapine is given orally with other antiretroviral drugs. The following doses by bodyweight have been suggested according to age:

- from 15 days to 8 years: 4 mg/kg once daily for 14 days and then, if no rash is present, 7 mg/kg twice daily
- 8 to 16 years: 4 mg/kg once daily for 14 days then 4 mg/kg twice daily thereafter

Alternatively, the dose may be calculated according to body-surface; an oral dose of 150 mg/m^2 once daily for two weeks is given followed by 150 mg/m^2 twice daily thereafter. A total dose of 400 mg daily should not be exceeded.

For information on the use of nevirapine in regimens for the prophylaxis of vertical transmission (mother-to-child) of HIV infection see HIV Infection Prophylaxis, p.858.

Administration in renal impairment. Dose adjustments are not required for patients with a creatinine clearance more than 20 mL/min. Patients on dialysis should receive an additional 200 mg of nevirapine after each dialysis session.

Preparations

USP 31: Nevirapine Oral Suspension; Nevirapine Tablets.

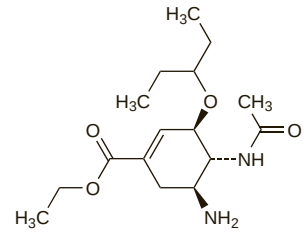
Proprietary Preparations (details are given in Part 3)

Arg.: Filide; Nerapin; Neviralea†; Protease; Ritvir; Virainhi; Viramune; ***Austral.:*** Viramune; ***Austria:*** Viramune; ***Belg.:*** Viramune; ***Braz.:*** Viramune; ***Canad.:*** Viramune; ***Chile:*** Viramune; ***Cz.:*** Viramune; ***Denm.:*** Viramune; ***Fin.:*** Viramune; ***Fr.:*** Viramune; ***Ger.:*** Viramune; ***Gr.:*** Viramune; ***Hong Kong:*** Viramune; ***Hung.:*** Viramune; ***India:*** Neve; Nevimune; ***Indon.:*** Viramune; ***Irl.:*** Viramune; ***Israel:*** Viramune; ***Ital.:*** Viramune; ***Jpn:*** Viramune; ***Malaysia:*** Nevipan; Viramune; ***Mex.:*** Viramune; ***Neth.:*** Viramune; ***Norw.:*** Viramune; ***NZ:*** Viramune; ***Pol.:*** Viramune; ***Port.:*** Viramune; ***Rus.:*** Viramune (Вирамун); ***S.Afr.:*** Viramune; ***Singapore:*** Viramune; ***Spain:*** Viramune; ***Swed.:*** Viramune; ***Switz.:*** Viramune; ***Thai.:*** Viramune; ***Turk.:*** Viramune; ***UK:*** Viramune; ***USA:*** Viramune; ***Venez.:*** Nevimune; Viramune.

Multi-ingredient: ***India:*** Duovir N; Triomune; ***S.Afr.:*** Triomune; ***Venez.:*** Triomune.

Oseltamivir Phosphate

(BANM, USAN, rINNM)



(oseltamivir)

Fosfato de oseltamivir; GS-4104/002; Oséltamivir, Phosphate d'; Oseltamiviri Phosphas; Ro-64-0796/002. Ethyl (3*R*,4*R*,5*S*)-4-acetamido-5-amino-3-(1-ethylpropoxy)-1-cyclohexene-1-carboxylate phosphate (1:1).

Осельтамивира Фосфат

$C_{16}H_{28}N_2O_4,H_3PO_4$ = 410.4.

CAS — 196618-13-0 (oseltamivir); 204255-11-8 (oseltamivir phosphate).

ATC — J05AH02.

ATC Vet — QJ05AH02.

Adverse Effects

The most commonly reported adverse effects associated with oseltamivir treatment or prophylaxis in adults are nausea and vomiting, abdominal pain, bronchitis, insomnia, and vertigo. Diarrhoea, dizziness, headache, cough, and fatigue may occur, but many adverse effects may be difficult to distinguish from the symptoms of influenza. Other adverse effects occurring less commonly have included unstable angina, anaemia, pseudomembranous colitis, pneumonia, pyrexia, and peritonsillar abscess. There have been occasional reports of anaphylaxis and skin rashes, including toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. Elevated liver enzymes and hepatitis have been reported rarely. Prophylaxis in adults has also been associated with aches and pains, dyspepsia, rhinorrhoea, and upper respiratory-tract infections.

The most commonly reported adverse effects in children receiving treatment or prophylaxis with oseltamivir are vomiting and other gastrointestinal problems. Other commonly occurring adverse events include asthma, bronchitis, conjunctivitis, dermatitis, epistaxis, ear disorders and otitis media, lymphadenopathy, pneumonia, and sinusitis.

There have been postmarketing reports (mainly in Japanese children and adolescents) of neuropsychiatric adverse effects (see below).

Neuropsychiatric effects. A FDA review of the Adverse Event Reporting System (AERS) database from March 2004 to April 2005 reported 75 cases of serious adverse effects linked to the use of oseltamivir in children; 69 from Japan, 5 from USA, and 1 from Canada. Thirty-two cases of neuropsychiatric adverse effects including cases of delirium, abnormal behaviour, hallucinations, convulsions, and encephalitis, were reported, with 31 of these cases being reported from Japan. Twelve deaths were reported; 4 from sudden death, 4 due to cardiopulmonary arrest, and others due to disturbance of consciousness (without falling), pneumonia, asphyxiation, and acute pancreatitis with cardiopulmonary arrest. All deaths were reported from Japan.[1] The Japanese Ministry of Health Labour and Welfare reported that from 2001 to May 2007 they received 1377 adverse effects reports associated with the use of oseltamivir, including 567 reports of serious neuropsychiatric adverse effects and 211 cases of abnormal behaviour. Death was reported in 71 cases.[2] After the suicides of 2 adolescents, the Japanese authorities advised against the use of oseltamivir in adolescents aged 10 to 19 years.[3] However, given that influenza itself may have neuropsychiatric sequelae, any causal relationship with the drug remains unproven.[1,3]

1. FDA, Center for Drug Evaluation and Research. Pediatric safety update for Tamiflu: Pediatric Advisory Committee meeting (issued 18 November 2005). Available at: http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4180b_06_06_summary.pdf (accessed 13/06/08).
2. Hama R. Oseltamivir's adverse reactions: Fifty sudden deaths may be related to central suppression. *BMJ* 2007; **335:** 59.
3. Maxwell SRJ. Tamiflu and neuropsychiatric disturbance in adolescents. *BMJ* 2007; **334:** 1232–3.

Precautions

Oseltamivir is not recommended in patients with severe renal impairment and it should be given with caution and dosage should be reduced in patients with moderate renal impairment.

Patients should be monitored for abnormal behaviour throughout the treatment period.

Breast feeding. Oseltamivir and its active metabolite are distributed into breast milk in *rodents*. Licensed product informa-

tion recommends that it should only be given to breast-feeding mothers if the potential benefit justifies the potential risk.

Pregnancy. Studies in *rodents* given high doses of oseltamivir have not found it to be fetotoxic or embryotoxic. There is little data available on the use of oseltamivir in pregnant women and licensed product information recommends that it should only be given to pregnant women if the potential benefit justifies the potential risk.

Interactions

Oseltamivir may potentially inhibit replication of the influenza virus in live influenza virus vaccines. Therefore, US licensed product information states that live influenza virus vaccines should not be given until 48 hours after stopping oseltamivir and that oseltamivir should not be given for 2 weeks after live influenza virus vaccines have been given. Inactivated (split virion or surface antigen) vaccines are not expected to be affected by oseltamivir.

Antiviral Action

Oseltamivir has antiviral activity similar to that of zanamivir (p.913). Its active metabolite, oseltamivir carboxylate, selectively blocks the viral surface enzyme neuraminidase, thereby preventing the release of virus particles from infected cells. Oseltamivir is active against influenza A and B viral neuraminidase.

Resistance. Oseltamivir-resistant type A virus, including H5N1 subtypes, have been reported in patients being treated for influenza.[1-3] A study[1] in Japan found that 9 of 50 (18%) children with influenza A (H3N2) virus infection who had been treated with oseltamivir had a virus with a drug-resistance mutation in the neuraminidase gene (predominantly R292K). Another study[4] in Japan reported resistant influenza A (H1N1) viruses with the H274Y mutation in 7 of 43 (16%) oseltamivir-treated children. In both these studies the children were given an oral dose of 2 mg/kg twice daily. However, a larger study[5] in the US reported no resistance in children who received age- and weight-tailored (and therefore sometimes substantially higher) doses than those used in the Japanese studies. No viruses resistant to zanamivir have been isolated from immunocompetent people,[6] although there is a case of resistance in an immunocompromised child.[7]

1. Kiso M, *et al.* Resistant influenza A viruses in children treated with oseltamivir: descriptive study. *Lancet* 2004; **364:** 759–65.
2. de Jong MD, *et al.* Oseltamivir resistance during treatment of influenza A (H5N1) infection. *N Engl J Med* 2005; **353:** 2667–72.
3. Le QM, *et al.* Avian flu: isolation of drug-resistant H5N1 virus. *Nature* 2005; **437:** 1108. Correction. *ibid.*; **438:** 754.
4. Ward P, *et al.* Oseltamivir (Tamiflu) and its potential for use in the event of an influenza pandemic. *J Antimicrob Chemother* 2005; **55** (suppl 1): i5–i21.
5. Hayden FG, *et al.* Management of influenza in households: a prospective, randomized comparison of oseltamivir treatment with or without postexposure prophylaxis. *J Infect Dis* 2004; **189:** 440–9.
6. Moscona A. Oseltamivir-resistant influenza? *Lancet* 2004; **364:** 733–4.
7. Gubareva LV, *et al.* Evidence for zanamivir resistance in an immunocompromised child infected with influenza B virus. *J Infect Dis* 1998; **178:** 1257–62.

Pharmacokinetics

Oseltamivir is readily absorbed from the gastrointestinal tract after oral doses and is extensively metabolised in the liver to the active entity, oseltamivir carboxylate. At least 75% of an oral dose reaches the systemic circulation as the carboxylate. Binding to plasma proteins is about 3% for the carboxylate and 42% for the parent drug. Oseltamivir has a plasma half-life of 1 to 3 hours and the carboxylate a plasma half-life of 6 to 10 hours. The carboxylate is not metabolised further and is eliminated in the urine.

◊ Reviews.

1. Abe M, *et al.* Pharmacokinetics of oseltamivir in young and very elderly subjects. *Ann Pharmacother* 2006; **40:** 1724–30.

Uses and Administration

Oseltamivir is a prodrug of oseltamivir carboxylate, an inhibitor of the enzyme neuraminidase (sialidase), which has a role in the infectivity and replication of influenza A and B viruses. It is used in adults and children over 1 year of age for the treatment and postexposure prophylaxis of influenza A and B (below).

Oseltamivir is given orally as the phosphate, but doses are expressed in terms of the base. Oseltamivir phosphate 98.5 mg is equivalent to about 75 mg of oseltamivir. For the *treatment* of adults a dose of 75 mg is given twice daily for 5 days, beginning as soon as possible (within 48 hours) after the onset of symptoms. For *postexposure prophylaxis* the usual dose is 75 mg given once daily for at least 10 days and for up to 6 weeks during an epidemic; therapy should begin within 48 hours of exposure.

For details of doses in children, see below.

Dosage should be reduced in patients with moderate renal impairment (see below).

Oseltamivir has been tried both for prophylaxis and treatment of H5N1 disease (avian influenza) and many countries are stockpiling the drug in order to contain any potential pandemic until an effective vaccine can be developed.

Administration in children. Oseltamivir is given orally in the treatment and prophylaxis of influenza A and B in children aged 1 year and over. Doses determined by body-weight may be given twice daily for treatment, or once daily for prophylaxis, of influenza A and B as follows:

- children over 40 kg: 75 mg
- more than 23 kg to 40 kg: 60 mg
- more than 15 kg to 23 kg: 45 mg
- 15 kg or less: 30 mg

Therapy should begin within 48 hours of exposure.

Administration in renal impairment. Dosage of oseltamivir should be reduced in patients with moderate renal impairment, according to creatinine clearance (CC):

- CC 10 to 30 mL/minute: *treatment of influenza*: 75 mg once daily or 30 mg twice daily; *prevention*: 75 mg on alternate days or 30 mg daily
- CC less than 10 mL/minute: not recommended
- dialysis patients: not recommended

Influenza. Reviews[1-8] of oseltamivir and other neuraminidase inhibitors in the treatment and prophylaxis of influenza (p.859). There is some evidence[9] that zanamivir is more effective than oseltamivir for influenza B.

1. Gubareva LV, *et al.* Influenza virus neuraminidase inhibitors. *Lancet* 2000; **355:** 827–35.
2. McClellan K, Perry CM. Oseltamivir: a review of its use in influenza. *Drugs* 2001; **61:** 263–83.
3. Jefferson TO, *et al.* Neuraminidase inhibitors for preventing and treating influenza in healthy adults. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2006 (accessed 13/06/08).
4. Matheson NJ, *et al.* Neuraminidase inhibitors for preventing and treating influenza in children. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2007 (accessed 13/06/08).
5. Cooper NJ, *et al.* Effectiveness of neuraminidase inhibitors in treatment and prevention of influenza A and B: systematic review and meta-analyses of randomised controlled trials. *BMJ* 2003; **326:** 1235–9.
6. Dutkowski R, *et al.* Safety and pharmacology of oseltamivir in clinical use. *Drug Safety* 2003; **26:** 787–801.
7. Ward P, *et al.* Oseltamivir (Tamiflu) and its potential for use in the event of an influenza pandemic. *J Antimicrob Chemother* 2005; **55** (suppl 1): i5–i21.
8. Democratis J, *et al.* Use of neuraminidase inhibitors to combat pandemic influenza. *J Antimicrob Chemother* 2006; **58:** 911–15.
9. Kawai N, *et al.* A comparison of the effectiveness of zanamivir and oseltamivir for the treatment of influenza A and B. *J Infect* 2008; **56:** 51–7.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Agucort; Tamiflu; ***Austral.:*** Tamiflu; ***Austria:*** Tamiflu; ***Belg.:*** Tamiflu; ***Braz.:*** Tamiflu; ***Canad.:*** Tamiflu; ***Chile:*** Rimivat; Tamiflu; Virobin; ***Cz.:*** Tamiflu; ***Denm.:*** Tamiflu; ***Fin.:*** Tamiflu; ***Fr.:*** Tamiflu; ***Ger.:*** Tamiflu; ***Gr.:*** Tamiflu; ***Hong Kong:*** Tamiflu; ***Hung.:*** Tamiflu; ***Irl.:*** Tamiflu; ***Israel:*** Tamiflu; ***Ital.:*** Tamiflu; ***Jpn:*** Tamiflu; ***Malaysia:*** Fluhalt; Tamiflu; ***Neth.:*** Tamiflu; ***Norw.:*** Tamiflu; ***NZ:*** Tamiflu; ***Philipp.:*** Tamiflu; ***Pol.:*** Tamiflu; ***Port.:*** Tamiflu; ***S.Afr.:*** Tamiflu; ***Singapore:*** Tamiflu; ***Swed.:*** Tamiflu; ***Switz.:*** Tamiflu; ***Thai.:*** Tamiflu; ***Turk.:*** Tamiflu; ***UK:*** Tamiflu; ***USA:*** Tamiflu.

Penciclovir *(BAN, USAN, rINN)*

BRL-39123; BRL-39123-D (penciclovir sodium); Penciclovirum; Penciklovir; Pensikloviiri; Pensiklovir. 9-[4-Hydroxy-3-(hydroxymethyl)butyl]guanine.

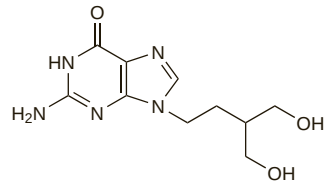
Пенцикловир

$C_{10}H_{15}N_5O_3$ = 253.3.

CAS — 39809-25-1 (penciclovir); 97845-62-0 (penciclovir sodium).

ATC — D06BB06; J05AB13.

ATC Vet — QD06BB06; QJ05AB13.



Adverse Effects and Precautions

Penciclovir applied topically may cause transient stinging, burning, and numbness.

For adverse effects of penciclovir after systemic use of famciclovir, see p.876.

Interactions

Plasma concentrations of penciclovir may be increased in patients receiving *probenecid* with the prodrug famciclovir.

Antiviral Action

Penciclovir has antiviral activity similar to that of aciclovir (p.863). It is active *in vitro* and *in vivo* against herpes simplex virus types 1 and 2 and against varicella-zoster virus. This activity is due to intracellular conversion by virus-induced thymidine kinase into penciclovir triphosphate, which inhibits replication of viral DNA and persists in infected cells for more than 12 hours. It also has activity against Epstein-Barr virus and hepatitis B virus.

◊ References.

1. Vere-Hodge RA. Famciclovir and penciclovir: the mode of action of famciclovir including its conversion to penciclovir. *Antiviral Chem Chemother* 1993; **4:** 67–84.
2. Boyd MR, *et al.* Penciclovir: a review of its spectrum of activity, selectivity, and cross-resistance pattern. *Antiviral Chem Chemother* 1993; **4** (suppl 1): 3–11.
3. Bacon TH, Boyd MR. Activity of penciclovir against Epstein-Barr virus. *Antimicrob Agents Chemother* 1995; **39:** 1599–1602.

Pharmacokinetics

Penciclovir is poorly absorbed from the gastrointestinal tract. For systemic use it is usually given orally as the prodrug famciclovir, which is rapidly converted to penciclovir. Peak plasma concentrations proportional to the dose (over the range 125 to 750 mg) are achieved after 45 minutes to 1 hour. The plasma elimination half-life is about 2 hours. The intracellular half-life of the active triphosphate metabolite is longer. Penciclovir is less than 20% bound to plasma proteins. Penciclovir is mainly excreted unchanged in the urine.

Uses and Administration

Penciclovir is a nucleoside analogue structurally related to guanine, which is active against herpesviruses. It is applied topically as a 1% cream every 2 hours during waking hours for 4 days in the treatment of herpes labialis (see Herpes Simplex Infections, p.854).

For systemic use, penciclovir is given orally as the prodrug famciclovir (see p.876). Intravenous dosage of penciclovir has been investigated.

◊ References.

1. Spruance SL, *et al.* Penciclovir cream for the treatment of herpes simplex labialis: a randomized, multicenter, double-blind, placebo-controlled trial. *JAMA* 1997; **277:** 1374–9.
2. Lazarus HM, *et al.* Intravenous penciclovir for treatment of herpes simplex infections in immunocompromised patients: results of a multicenter, acyclovir-controlled trial. *Antimicrob Agents Chemother* 1999; **43:** 1192–7.
3. Boon R, *et al.* Penciclovir cream for the treatment of sunlight-induced herpes simplex labialis: a randomized, double-blind, placebo-controlled trial. *Clin Ther* 2000; **22:** 76–90.
4. Raborn GW, *et al.* Effective treatment of herpes simplex labialis with penciclovir cream: combined results of two trials. *J Am Dent Assoc* 2002; **133:** 303–9.
5. Lin L, *et al.* Topical application of penciclovir cream for the treatment of herpes simplex facialis/labialis: a randomized, double-blind, multicentre, aciclovir-controlled trial. *J Dermatol Treat* 2002; **13:** 67–72.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Pentavir; ***Austral.:*** Vectavir; ***Austria:*** Famvir; Vectavir; ***Belg.:*** Vectavir; ***Braz.:*** Penvir Labia; Vectavir; ***Cz.:*** Vectavir; ***Denm.:*** Vectavir; ***Fin.:*** Vectavir; ***Ger.:*** Fenistil Pencivir; Vectavir†; ***Gr.:*** Fenivir; Vectavir; ***Hong Kong:*** Vectavir†; ***Hung.:*** Fenivir; Vectavir†; ***Israel:*** Vectavir†; ***Ital.:*** Vectavir;