

## Part 3: Treatments

### Chapter 20

#### Antivirals

**ACICLOVIR:** affects replication of DNA by targeting viral DNA polymerase; mode of elimination renal; i.v. (administer slowly), oral (poorly and erratically absorbed from gut but timing with respect to food doesn't matter) and topical (ophthalmic)

**Indications:** drug of choice for severe herpes simplex and varicella-zoster infections

**Side Effects:** i.v.: CNS toxicity including encephalopathy and seizures (coma, convulsions; should be administered slowly), crystalluria in renal insufficiency (adjust dose appropriately/increase dosage interval); oral: nausea in 2-8%, headache in 0.6-6%, vomiting, diarrhoea, hallucinations (high dose) common; constipation, abdominal pain, rash, confusion, dizziness, asthenia, agitation, vertigo, arthralgia, renal impairment uncommon; anorexia, fatigue, oedema, leucopenia, neutropenia rare; dose adjustment needed in renal failure and dialysis; safety in pregnancy not established; interacts with aminoglycosides, amphotericin, cyclosporin, diuretics (especially frusemide; may increase serum concentrations, particularly in patients > 60 y) and vancomycin (monitor renal function due to nephrotoxic potential); increases serum concentrations of probenecid and plasma theophylline levels

**VALACICLOVIR:** prodrug of aciclovir; improved bioavailability; not affected by food; requires fewer daily doses than aciclovir

**Indications:** herpes simplex and zoster (within 72 h of onset of rash)

**Side Effects:** as for **ACICLOVIR** but arthralgia, coma, convulsions not reported; safety in pregnancy not established; caution in breastfeeding (insufficient data); dose adjustment required in renal impairment

**PENCICLOVIR:** similar spectrum to aciclovir

**Indications:** limited use in treatment of orofacial herpes simplex

**FAMCICLOVIR:** well absorbed from gut (not affected by food); prodrug of penciclovir; requires fewer daily doses than aciclovir

**Indications:** severe initial genital herpes, herpes zoster, varicella within 24 h of onset of rash

**Side Effects:** as for **ACICLOVIR** but arthralgia, coma, convulsions not reported; dose interval adjustment required in renal failure and in dialysis

**Contraindications:** probably safe in pregnancy; avoid if breastfeeding (insufficient data; prefer aciclovir)

**VIDARABINE (ADENINE ARABINOSIDE, VIRA-A)**

**Indications:** herpes simplex encephalitis and meningitis, varicella-zoster complications (pneumonitis, encephalitis), mild conjunctivitis and retinochoroiditis due to herpes simplex

**Side Effects:** lacrimation, foreign body sensation, conjunctival injection, burning, irritation, superficial punctate keratitis, pain, photophobia, punctal occlusion, sensitivity

**IDOXURIDINE (2'-DEOXY-5-IODORUDINE, IDU)**

**Indications:** limited topical use in anterior uveitis, mild conjunctivitis and retinochoroiditis due to herpes simplex and in cutaneous herpes simplex; in WHO Model List of Essential Drugs

**Side Effects:** stinging, pruritus, oedema of eye or lids, rare photophobia; probably safe in pregnancy; caution in breastfeeding (insufficient data; prefer aciclovir)

**ATROPINE**

**Indications:** herpes simplex keratoconjunctivitis and iritis; in WHO Model List of Essential Drugs

**Side Effects:** rare conjunctival irritation

**BENZOCAINE**

**Indications:** pain relief in acute herpetic stomatitis

**Side Effects:** sensitivity may occur

**LIDOCAINE (LIGNOCAINE)**

**Indications:** pain relief in acute herpetic stomatitis

**CETYLPIRIDIUM CHLORIDE**

**Indications:** prevention of secondary infection in acute herpetic stomatitis

**CHLORHEXIDINE**

**Indications:** prevention of secondary infection in acute herpetic stomatitis

**GENTIAN VIOLET (METHYLOSANILINE CHLORIDE):** in WHO Model List of Essential Drugs

**Indications:** prevention of secondary infection in acute herpetic stomatitis

**POVIDONE IODINE:** in WHO Model List of Essential Drugs

**Indications:** prevention of secondary infection in acute herpetic stomatitis, genital herpes and zoster

**Side Effects:** very rare local irritation and sensitivity

**ACETAMINOPHEN (PARACETAMOL)**

**Indications:** primary cases of varicella in immunocompetent children < 12 y

**Side Effects:** potentially fatal liver damage with overdosage

**ASPIRIN (ACETYLSALICYLIC ACID)**

**Indications:** zoster neuralgia (topical), mucocutaneous lymph node syndrome

**Side Effects:** may cause Reye syndrome by interaction with influenza A, influenza B, varicella-zoster and other viruses

**CALAMINE LOTION**

**Indications:** varicella-zoster (topical)

**Side Effects:** rare sensitisation

**CARBAMAZEPINE**

**Indications:** zoster neuralgia

**Side Effects:** reductions in platelet and white cell counts, bone marrow depression, hepatic effects, skin reactions (including Stevens-Johnson syndrome, Lyell's syndrome), mild anticholinergic activity, dizziness, headache, ataxia, drowsiness, fatigue, diplopia, other neurological effects, isolated cases of psychiatric effects, gastrointestinal disturbances, rare cardiovascular effects, occasional antidiuretic hormone-like effect, disturbances of bone metabolism, rare multi-organ sensitivity, isolated cases of interstitial nephritis and renal failure, lens disturbances, musculoskeletal and respiratory effects; **Contraindications:** pregnancy

**SALINE PACKS**

**Indications:** zoster

**INTERFERON ALPHA:** affects translation by targeting mRNA; s.c. administration; expensive

**Indications:** hepatitis B, hepatitis C, very frequent recurrences of genital herpes (topical), AIDS (effective in Kaposi's sarcoma; phase I trials in combination with zidovudine show antiviral effect), prophylaxis for upper respiratory infection

**Side Effects:** thyroid dysfunction, neutropenia, thrombocytopenia, fever, chills, transient bone marrow suppression (increased with zidovudine), myalgia, arthralgia, fatigue, headache, anorexia, weight loss, nausea, vomiting, diarrhoea, dizziness, rash, dry skin, pruritus, partial alopecia, depression in up to 10%, anxiety, decreased mental status (somnolence, forgetfulness, confusion) in up to 30%, change in taste, may cause hepatic decompensation in patients with cirrhosis; decreases theophylline clearance

**Contraindications:** avoid in moderate to severe renal failure (glomerular filtration rate < 50 mL/min) and in dialysis; severe depression; safety in pregnancy not established

**PEGINTERFERON ALPHA-2A**

**Indications:** chronic hepatitis C in adults with compensated liver disease

**THYMOSIN ALPHA-1:** synthetic polypeptide in Phase III trials for treatment of hepatitis C and in Phase II trials for hepatitis B

**NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS:** antiretroviral drugs

**Indications:** HIV infection

**Side Effects:** hyperlactatemia, lactic acidosis, hepatic steatosis, lipodystrophy

**ZIDOVUDINE (AZIDOTHYMDINE, AZT, ZDV):** nucleoside analogue reverse transcriptase inhibitor; inhibits reverse transcription through chain termination; i.v. and oral (not affected by food) administration; penetrates CSF; in WHO Model List of Essential Drugs

**Indications:** treatment and prophylaxis of HIV infection

**Side Effects:** headache (soon after starting), macrocytic anaemia (uncommon with lower doses), associated malaise, fatigue, dyspepsia, nausea (common), vomiting, bloating, neutropenia (uncommon with lower doses), confusion, nail pigmentation, myalgia, late myositis and congestive cardiomyopathy; 82% develop severe to life-threatening toxic effects (mainly increased haematological toxicity) when treated with zidovudine and ganciclovir concomitantly (may necessitate zidovudine dose reduction or cessation); amphotericin B, flucytosine, interferon, dapsone, i.v. pentamidine, vincristine, vinblastine, adriamycin and doxorubicin also increase haematological toxicity; probenecid, methadone, cimetidine, clofibrate, NSAIDs may increase serum levels and produce toxicity; increased risk of neutropenia and hepatotoxicity with paracetamol; phenytoin decreases levels; ribavirin antagonises antiviral activity; methadone increases area under concentration-time curve by ~40%; may cause opiate withdrawal symptoms in patients on methadone; clarithromycin and rifampicin decrease plasma levels (space 2 h apart); rare reports of profound anaemia with lamivudine; lorazepam and oxazepam increase bioavailability; increased risk of neutropenia with vancomycin; dose adjustment required in renal failure and in dialysis

**Contraindications:** severe pancytopenia; safety in pregnancy not established; avoid if breastfeeding (insufficient data)

**DIDANOSINE (2', 3'-DIDEOXYINOSINE, ddI):** nucleoside analogue reverse transcriptase inhibitor; oral (take ½ - 1 h before food)

**Indications:** treatment of HIV; AIDS prophylaxis in significant documented exposure to blood or body fluid containing human immunodeficiency virus from donor on zidovudine > 6 mo

**Side Effects:** rash/pruritus in 28%, neutropenia in 27%, xerostoma in 25-37%, CNS depression in 23%, increase in haemoglobin ~2 g/dL in 20%, elevation in levels of liver enzymes in 18%, muscle cramps in 17%, diarrhoea in 16-60%, stomatitis in 16%, abdominal pain in 13-25%, joint pain in 11%, hypocalcaemia in 10%, hyperamylasaemia in 9-17%, peripheral neuropathy in 8-34% (increased risk with isoniazid, ethambutol, ethionamide, dapsone, phenytoin, metronidazole), nausea/vomiting in 7-25%, headache in 4-35%, constipation in 3-13%, skin rash in 3-12%, asthma in 2-25%, pancreatitis in 2-14% (increased risk with alcohol, i.v. pentamidine), insomnia in 1-25%, optic neuritis, fulminant hepatitis, retinal depigmentation, nausea; in children, elevated uric acid, elevated triglycerides; buffered formulations decrease bioavailability of azithromycin, quinolones, itraconazole capsules, ketoconazole, tetracyclines, dapsone (space doses by 2-3 h); decreased absorption of both didanosine buffered preparations and delaviridine (space 1 h apart); buffered formulations reduce indinavir absorption (space 1 h apart); possible didanosine toxicity with ganciclovir (decreased renal excretion); tenofovir increases plasma levels if taken within 2 h (possible toxicity); methadone decreases area under concentration-time curve by 60%; probably safe in pregnancy; dose interval adjustment required in renal failure and in dialysis

**Contraindications:** history of pancreatitis, severe peripheral neuropathy; avoid if breastfeeding (insufficient data)

**EMTRICITABINE:** nucleoside analogue reverse transcriptase inhibitor

**Indications:** HIV infection

**Side Effects:** skin discolouration of palms and soles, acute exacerbation of hepatitis B in co-infected patients on discontinuation; probably safe in pregnancy

**Contraindications:** avoid in breastfeeding (insufficient data)

**ZALCITABINE (DIDEOXYCYTIDINE, ddC):** nucleoside analogue reverse transcriptase inhibitor; oral (take ½ to 1 h before food)

**Indications:** may increase CD4 counts in patients with human immunodeficiency virus infection

**Side Effects:** peripheral neuropathy (increased risk with alcohol, i.v. pentamidine and nephrotoxic drugs including amphotericin, aminoglycosides and foscarnet), stomatitis, mouth ulcers, rash, pancreatitis (rare)

**Contraindications:** pregnancy; severe peripheral neuropathy; avoid if breastfeeding (insufficient data)

**STAVUDINE (D4T):** nucleoside analogue reverse transcriptase inhibitor; oral (timing to food does not matter)

**Indications:** HIV/AIDS

**Side Effects:** peripheral neuropathy (increased risk with alcohol, i.v. pentamidine), pancreatitis; methadone decreases area under concentration-time curve by 18%; ribavirin may reduce effects

**Contraindications:** severe peripheral neuropathy; safety in pregnancy not established; avoid if breastfeeding (insufficient data)

**LAMIVUDINE (3TC):** nucleoside analogue reverse transcriptase inhibitor; oral (timing to food does not matter)

**Indications:** HIV/AIDS (may be active against strains resistant to zidovudine), chronic hepatitis B

**Side Effects:** abnormal liver function, anaemia and neutropenia (advanced disease), pancreatitis (primarily in children), may cause severe and fatal exacerbation of hepatitis B infection if resistance develops or in co-infected HIV/hepatitis B patients on discontinuation; rare reports of profound anaemia with zidovudine; safety in pregnancy not established; reduce dose in impaired renal function

**Contraindications:** avoid if breastfeeding (insufficient data)

**ABACAVIR:** carbocyclic nucleoside analogue reverse transcriptase inhibitor; oral (timing to food does not matter)

**Indications:** HIV/AIDS

**Side Effects:** potentially fatal HLA-linked hypersensitivity reactions (fever, headache, myalgia, gastrointestinal symptoms, respiratory symptoms, with or without rash); safety in pregnancy not established

**Contraindications:** avoid if breastfeeding

**TENOFOVIR DISOPROXIL FUMARATE:** nucleotide analogue reverse transcriptase inhibitor; oral; take with or after food (increases bioavailability); once daily dosing

**Indications:** HIV/AIDS

**Side Effects:** nephrotoxicity, nausea, vomiting, flatulence, diarrhoea, asthenia, headache, hypophosphataemia, renal impairment (rare), acute exacerbation of hepatitis B in co-infected on discontinuation; increased plasma levels of didanosine if taken within 2 h (possible toxicity); safety in pregnancy not established

**Contraindications:** avoid in breastfeeding (insufficient data)

#### **NON-NUCLEOSIDE ANALOGUE REVERSE TRANSCRIPTASE INHIBITORS**

**Indications:** HIV/AIDS (in combination with nucleoside analogue reverse transcriptase inhibitors)

**Side Effects:** skin rash, abnormal liver function, fever

**NEVIRAPINE:** non-nucleoside analogue reverse transcriptase inhibitor; oral (timing to food does not matter)

**Indications:** HIV/AIDS

**Side Effects:** hepatotoxicity (especially women with CD4 count > 250/ $\mu$ L and men with CD4 count > 400/ $\mu$ L), skin reactions (including Stevens-Johnson syndrome), fever; decreases saquinavir levels by 27%, indinavir by 28%, also amprenavir and lopinavir (increased metabolism); decreases caspofungin plasma levels; ketoconazole increases levels while ketoconazole levels are lowered; rifampicin and St John's wort decrease levels; may induce metabolism of voriconazole while voriconazole may inhibit metabolism of nevirapine; precipitates symptoms of narcotic withdrawal in methadone recipients, requiring ? 45% increase in dose; safety in pregnancy not established

**Contraindications:** treatment with ketoconazole, rifampicin, St John's wort; avoid if breastfeeding (insufficient data); not recommended for post-exposure prophylaxis

**LOVIRIDE:** non-nucleoside analogue reverse transcriptase inhibitor

**Indications:** HIV/AIDS

**DELAVIRDINE:** non-nucleoside analogue reverse transcriptase inhibitor; high pill burden; relation to food does not matter

**Indications:** HIV/AIDS

**Side Effects:** rash (including Stevens-Johnson syndrome), abnormal liver function, fever; increases saquinavir levels by 3-6 fold; decreases metabolism of alprazolam, midazolam and triazolam (may cause prolonged sedation or respiratory depression), cisapride (may lead to QT interval prolongation), clarithromycin, amprenavir, saquinavir and indinavir (may increase toxicity); interacts with didanosine buffered preparations to decrease absorption of both drugs (space 1 h apart); increases risk of ergotism with ergot derivatives; H<sub>2</sub>-receptor antagonists and proton pump inhibitors may reduce absorption by increasing gastric pH; interacts with nelfinavir to increase nelfinavir levels (may cause neutropenia) and decrease delavirdine levels; rifampicin and rifabutin markedly decrease delavirdine effect (increased metabolism) and increase rifampicin toxicity (decreased metabolism); St John's wort decreases levels; interacts with voriconazole to increase plasma levels of both drugs; safety in pregnancy not established

**Contraindications:** < 12 y old; treatment with cisapride, (dihydro)ergotamine, H<sub>2</sub>-receptor antagonists, midazolam, proton pump inhibitors, rifabutin, rifampicin, simvastatin, St John's wort, triazolam; avoid in breastfeeding (insufficient data)

**EFAVIRENZ:** non-nucleoside reverse transcriptase inhibitor; once daily oral (timing to food does not matter)

**Indications:** component of initial triple therapy regimen for HIV/AIDS

**Side Effects:** neuropsychological effects (drowsiness, dizziness, disturbed sleep, vivid dreams, impaired concentration, light headedness, abnormal thinking) common but usually settle over few weeks; skin rash, abnormal liver function; decreases plasma levels of amprenavir, caspofungin, indinavir, lopinavir, saquinavir; increases cisapride plasma levels, increasing risk of QT prolongation; increases risk of ergotism with ergot derivatives; decrease metabolism of midazolam and triazolam (may cause prolonged sedation or respiratory depression), increases plasma levels of nelfinavir and ritonavir (efavirenz levels may increase with ritonavir); rifampicin and St John's wort decrease plasma levels; may inhibit or induce voriconazole metabolism, while voriconazole may inhibit metabolism; theoretical interaction with oral contraceptives

**Contraindications:** pregnancy; avoid in breastfeeding (insufficient data); treatment with cisapride, (dihydro)ergotamine, midazolam, pimozide, St John's wort, triazolam, voriconazole

### **PROTEASE INHIBITORS**

**Indications:** HIV/AIDS (in combination with 2 nucleoside analogue reverse transcriptase inhibitors)

**Side Effects:** 40% nausea/vomiting, 40% diarrhoea, 34% weakness, 30% abdominal pain, 24% headaches, 18% lipodystrophy, hyperlipidemia (most common with ritonavir, least common with atazanavir), hyperglycaemia, abnormal liver function; metabolised by cytochrome P450 system, so many potential drug interactions; reduces metabolism of midazolam, triazolam and, to a lesser extent, alprazolam (may cause prolonged sedation or respiratory depression), cisapride, pimozide, amiodarone and lignocaine (increased risk of cardiac arrhythmias), dextropropoxyphene, fentanyl and tramadol (increased risk of adverse opioid effects), synercid (possible toxicity); increased risk of ergotism with ergot derivatives; increases metabolism of pethidine and produces higher norpethidine levels (increased risk of seizures); carbamazepine, phenytoin, phenobarbitone increase metabolism; marked decrease in plasma levels with rifampicin may cause loss of virological response and resistance (avoid combination); increased plasma levels of simvastatin may cause myopathy and rhabdomyolysis; increased plasma levels of sildenafil increases risk of hypotension and priapism; St John's wort decreases plasma levels; interacts with voriconazole to inhibit metabolism of both drugs

**ATAZANAVIR:** protease inhibitor; always combine with ritonavir if administered with tenofovir or efavirenz

**Indications:** treatment of HIV infection

**Side Effects:** hyperbilirubinaemia/jaundice, rash, prolongation of PR interval; probably safe in pregnancy

**Contraindications:** not approved for use in children; treatment with cisapride, (dihydro)ergotamine, flecainide, midazolam, pimozide, proton pump inhibitors, quinidine, rifampicin, simvastatin, St John's wort, triazolam; avoid in breastfeeding (insufficient data)

**FOSAMPRENAVIR:** protease inhibitor

**Indications:** treatment of HIV infection

**Side Effects:** nausea, vomiting, diarrhoea, rash, perioral paraesthesia

**Contraindications:** not approved for use in children; safety in pregnancy not established; avoid in breastfeeding (insufficient data); treatment with cisapride, diazepam, (dihydro)ergotamine, flecainide, midazolam, pimozide, rifampicin, simvastatin, St John's wort, triazolam

**SAQUINAVIR:** protease inhibitor; take with or after food (increased absorption with high fat meals)

**Indications:** treatment of HIV; occupational exposure to HIV

**Side Effects:** as for **PROTEASE INHIBITORS**, diarrhoea, nausea, abdominal discomfort; discontinuation rate 47%; rifampicin, rifabutin, phenytoin, carbamazepine decrease bioavailability; ketoconazole increases bioavailability; potential for significant interaction (although less so than with other protease inhibitors) with drugs that induce or inhibit hepatic enzyme CYP3A4 (terfenadine, astemizole, cisapride, alprazolam, triazolam, midazolam, erythromycin, diltiazem, nifedipine, verapamil, fluoxetine, fluvoxamine), due to competitive metabolism, especially with antihistamines, leading to possibility of cardiac arrhythmias; interacts with amprenavir to decrease plasma levels of both drugs;

dexamethasone decreases bioavailability; clindamycin, delavirdine, grapefruit juice, azithromycin, increase plasma levels, with possible toxicity; efavirenz, nevirapine decrease plasma levels; probably safe in pregnancy

**Contraindications:** treatment with amiodarone, cisapride, (dihydro)ergotamine, flecainide, midazolam, pimozone, quinidine, rifabutin, rifampicin, simvastatin, St John's wort, triazolam; avoid if breastfeeding (insufficient data); not approved for use in children

**INDINAVIR:** protease inhibitor; take ½ - 1 h before food; almost always combined with low dose ritonavir

**Indications:** treatment of HIV; occupational exposure to HIV

**Side Effects:** as for **PROTEASE INHIBITORS**, renal calculus with inadequate fluid intake, hyperbilirubinemia, nausea, interstitial nephritis; discontinuation rate 33%; rifabutin and rifampicin decrease bioavailability; increases rifabutin levels (substitute azithromycin); ketoconazole increases bioavailability; didanosine buffered preparations, grapefruit juice reduce absorption (space 1 h apart); prolongs sedation due to midazolam (substitute propofol); produces arrhythmia with cisapride (substitute metoclopramide) or terfenadine (substitute loratadine); potential for significant interaction with other drugs that induce or inhibit hepatic enzyme CYP3A4 (astemizole, alprazolam, triazolam, diltiazem, erythromycin, nifedipine, verapamil, fluoxetine, fluvoxamine); interaction with clarithromycin may increase mortality; delavirdine decreases metabolism and may increase toxicity; efavirenz, nevirapine decrease plasma levels; interacts with nelfinavir to increase plasma levels of both drugs; safety in pregnancy not established

**Contraindications:** renal calculi; treatment with amiodarone, cisapride, (dihydro)ergotamine, flecainide, midazolam, pimozone, rifampicin, simvastatin, St John's wort, triazolam; avoid if breastfeeding (insufficient data); not approved for use in children

**RTONAVIR:** protease inhibitor; oral (take with or after food (absorption enhanced)); inhibits cytochrome P450 enzyme system, boosting levels of co-administered protease inhibitor

**Indications:** treatment of HIV; occupational exposure to HIV

**Side Effects:** as for **PROTEASE INHIBITORS**, perioral paraesthesia; discontinuation rate 61%; increases saquinavir levels by 30 fold and also other protease inhibitors (may be desired effect); increases rifabutin levels (substitute azithromycin); prolongs sedation due to midazolam (substitute propofol); produces arrhythmia with cisapride (substitute metoclopramide) or terfenadine (substitute loratadine); potential for significant interaction with other drugs that induce or inhibit hepatic enzyme CYP3A4 (astemizole, alprazolam, triazolam, erythromycin, diltiazem, nifedipine, verapamil, fluoxetine, fluvoxamine); interaction with clarithromycin may increase mortality; increased risk of QT prolongation with amiodarone, quinidine; interacts with efavirenz to increase plasma levels of both drugs; increased risk of cardiac arrhythmias with flecainide; safety in pregnancy not established; theoretical interaction with oral contraceptives

**Contraindications:** treatment with amiodarone, cisapride, (dihydro)ergotamine, flecainide, fluticasone, midazolam, pethidine, pimozone, quinidine, simvastatin, St John's wort, triazolam; avoid if breastfeeding (insufficient data)

**NELFINAVIR:** protease inhibitor; take with or after food to increase absorption and decrease gastrointestinal side effects

**Indications:** HIV/AIDS

**Side Effects:** as for **PROTEASE INHIBITORS**; increases rifabutin levels (substitute azithromycin); prolongs sedation due to midazolam (substitute propofol); produces arrhythmia with cisapride (substitute metoclopramide) or terfenadine (substitute loratadine); potential for significant interaction with other drugs that induce or inhibit hepatic enzyme CYP3A4 (astemizole, alprazolam, triazolam, erythromycin, diltiazem, nifedipine, verapamil, fluoxetine, fluvoxamine); interaction with clarithromycin may increase mortality; increased risk of QT prolongation with amiodarone, quinidine; efavirenz increases plasma levels; increases plasma levels of calcium channel blockers; interacts with delavirdine to increase nelfinavir levels (possible neutropenia) and decrease delavirdine levels; interaction with indinavir may increase toxicity of both drugs (decreased metabolism); may reduce caspofungin plasma levels; probably safe in pregnancy; theoretical interaction with oral contraceptives

**Contraindications:** treatment with amiodarone, cisapride, (dihydro)ergotamine, midazolam, pimozone, quinidine, rifampicin, simvastatin, St John's wort, triazolam; avoid if breastfeeding (insufficient data)

**AMPRENAVIR:** protease inhibitor; oral (timing to food does not matter)

**Indications:** HIV/AIDS

**Side Effects:** as for **PROTEASE INHIBITORS**, rash, perioral paraesthesia; increased diazepam levels may cause prolonged sedation or respiratory depression; efavirenz, nevirapine, dexamethasone decrease plasma levels; delavirdine

increases plasma levels; interaction with saquinavir decreases plasma levels of both drugs; increases plasma levels of amlodipine, dapson, felodipine, quinidine, tacrolimus, tricyclic antidepressants, verapamil; theoretical interaction with oral contraceptives

**Contraindications:** treatment with cisapride, diazepam, dihydroergotamine, ergotamine, midazolam, pimozone, rifampicin, simvastatin, St John's wort, triazolam

**LOPINAVIR:** protease inhibitor; oral (take with or after food); supplied as combination with ritonavir

**Indications:** HIV/AIDS

**Side Effects:** as for **PROTEASE INHIBITORS**, nausea, vomiting, diarrhoea; efavirenz, nevirapine decrease plasma levels; increased risk of cardiac arrhythmias with flecainide; safety in pregnancy not established

**Contraindications:** treatment with amiodarone, cisapride, (dihydro)ergotamine, flecainide, fluticasone, midazolam, pimozone, rifampicin, simvastatin, St John's wort, triazolam, voriconazole; avoid in breastfeeding (insufficient data)

**ENFUVRITIDE (T20):** HIV entry inhibitor

**Indications:** HIV infection

**Side Effects:** injection site reactions, hypersensitivity, increased incidence of bacterial pneumonia

**Contraindications:** avoid in pregnancy and breastfeeding (insufficient data)

#### **GRANULOCYTE COLONY STIMULATING FACTOR**

**Indications:** appears effective in preventing infectious morbidity and mortality in advanced HIV infection; reduces amputation rate in diabetics with limb-threatening foot infections

**Side Effects:** medullary bone pain; infrequent arthralgias and myalgias; erythema, swelling, pruritus at site of infection

**GANCICLOVIR (DIHYDROMYPROPOXYMETHYLAMINE, DHPG):** inhibits replication of viral DNA; i.v., intraocular implants or injections

**Indications:** prophylaxis and treatment of life- and sight-threatening cytomegalovirus infections in immunocompromised patients, acute meningoencephalitis in AIDS

**Side Effects:** dose-dependent suppressive effects on rapidly growing cells (bone marrow (neutropenia in 15-42% (manage with granulocyte colony stimulating factor), granulocytopenia, thrombocytopenia in 5-20% (switch to foscarnet if < 25 000)), spermatogonia (rare), germinal layers of skin and gastrointestinal mucosa; increased toxicity in combination with zidovudine and other nucleoside analogues and other bone marrow suppressive agents (adriamycin, amphotericin, dapson, flucytosine, pentamidine, cotrimoxazole, vinblastine, vincristine) may necessitate dose reduction or cessation of these agents); CNS effects (disorientation, psychosis) in 18%, nausea in 6%, fever in 6%, rash in 6%, anaemia in 5-10%; anorexia, flatulence, seizures, elevated liver enzymes, pain and phlebitis at injection site, sweating, pruritus, increased serum creatinine and urea concentration common; hepatitis, azoospermia; increased risk of didanosine toxicity (decreased renal excretion); increased risk of generalised seizures with imipenem; dosage interval adjustment necessary in renal failure and in dialysis; probenecid may increase serum concentrations and reduce elimination; safety in breastfeeding not established

**Contraindications:** pregnancy

**VALGANCICLOVIR:** prodrug of ganciclovir; oral (take with or after food; well absorbed)

**Indications:** induction and maintenance treatment of cytomegalovirus retinitis (as effective as i.v. ganciclovir), cytomegalovirus prophylaxis in selected solid organ transplant recipients

**Side Effects:** granulocytopenia in 27%, anaemia in 26%, thrombocytopenia, diarrhoea, nausea, vomiting; others as for **GANCICLOVIR**; overdose can cause fatal bone marrow suppression; dose adjustment required in renal impairment

**Contraindications:** hypersensitivity, pregnancy, breastfeeding (insufficient data)

**CIDOFOVIR:** i.v.

**Indications:** cytomegalovirus infections

**Side Effects:** nephrotoxicity (give probenecid before and after infusion)

**Contraindications:** pregnancy, moderate to severe renal impairment, co-administration of other nephrotoxic agents

**FOSCARNET (TRISODIUM PHOSPHONFORMATE):** inhibits reverse transcriptase; i.v. administration; penetrates CSF; synergy with zidovudine

**Indications:** cytomegalovirus retinitis, aciclovir resistant herpes simplex pneumonitis, enterocolitis or oesophagitis when ganciclovir cannot be used or resistance is suspected

**Side Effects:** headache, thrombophlebitis, nephrotoxicity (acute renal failure; increased risk with aminoglycosides, amphotericin B, aciclovir, i.v. pentamidine, cidofovir, cyclosporin, other nephrotoxic drugs), involuntary muscle contractions, agitation, confusion, hypophosphatemia (in 20-30%) and hyperphosphatemia (in 10-20%), hypocalcaemia (increased risk with i.v. pentamidine, other calcium lowering agents) and hypercalcemia, hypokalemia, hypomagnesaemia, fatigue, nausea (in 25-40%), vomiting, fever, neurologic toxicity, ulceration of genitals, oropharynx, oesophagus, elevated enzymes, elevated creatinine (in 20-30%), tetany, perioral numbness, finger paresthesias, weakness, anaemia, dysuria, dizziness, anxiety, cough, dyspnoea, fatigue, nausea, vomiting, pruritus, rash common; cholestatic liver changes, hepatosplenomegaly, nephrogenic diabetes insipidus, pulmonary haemorrhage, pneumonitis, granulocytopenia, leucopenia uncommon; anaphylaxis, seizures rare; dose adjustment required in mild renal failure  
**Contraindications:** safety in pregnancy and breastfeeding not established

#### **ADEFOVIR**

**Indications:** cytomegalovirus infections, viral hepatitis

**Side Effects:** nephrotoxicity

**CIDOFOVIR:** i.v.

**Indications:** cytomegalovirus infections; smallpox, cowpox and vaccinia (investigational)

**Side Effects:** nephrotoxicity (give with probenecid before and after infusion, but reduce zidovudine dose by 50% on days when cidofovir/probenecid administered (inhibits renal clearance of zidovudine); increased risk with aminoglycosides, amphotericin, foscarnet, i.v. pentamidine, vancomycin, NSAIDs), neutropenia, diarrhoea, anorexia, nausea, vomiting, headache common; asthenia uncommon; retinal detachment, tachycardia rare

**Contraindications:** pregnancy, breastfeeding (insufficient data), moderate to severe renal impairment, co-administration of other nephrotoxic agents

#### **ENTECAVIR**

**Indications:** viral hepatitis

**AMANTADINE:** probably blocks uncoating of virus; mode of elimination renal; oral (take with or after food)

**Indications:** used to limited extent for influenza A prophylaxis or early treatment; prophylactically gives 30-70% reduction in infection and illness and decreased duration and quantity of virus shedding; less effective in treatment but probably somewhat beneficial; major antigen shift, persons allergic to eggs, unimmunised high risk patient, hospitalised patients and personnel, institutionalised individuals, particularly elderly; started when influenza outbreak has begun in the community; give with vaccine if available; chronic hepatitis c

**Side Effects:** incidence 10-25% (discontinuation rate 6-14%); nausea, abdominal pain, restlessness, rare psychiatric disturbances, blurred vision, convulsions with large doses, nervousness, headache, difficulty in concentration, dizziness or light-headedness, slurred speech, ataxia, depression, lethargy, insomnia, anxiety, livedo reticularis, ankle oedema, urinary retention, skin rash, vomiting, leucopenia, congestive heart failure; safety in pregnancy not established; drugs with a stimulant effect on the central nervous system (dexamphetamine, caffeine, benzhexol, benztropine, orphenadrine) may have their effect enhanced; dosage interval adjustment needed in renal failure and in dialysis

**Contraindications:** babies < 1 y, patients with active convulsive disorders, breastfeeding

**Precautions:** psychiatric illness, epilepsy, elderly with cerebral atherosclerosis, recurrent asthma, cardiovascular disease

**RIMANTADINE:** affects assembly of the virion by targeting membrane proteins (ion channel)

**Indications:** treatment and prophylaxis of influenza A

**Side Effects:** as for amantadine but uncommon

**ZANAMIVIR:** neuraminidase inhibitor; inhalation

**Indications:** uncomplicated acute influenza in > 7 y.o. symptomatic > 2 d; prevention of spread within households

**Side Effects:** may exacerbate bronchospasm in severe asthmatics (rare); probably safe in pregnancy

**Contraindications:** avoid in breastfeeding (insufficient data)

**OSELTAMVIR PHOSPHATE:** neuraminidase inhibitor; oral (timing to food does not matter)

**Indications:** influenza A and B prophylaxis (? 13 y) and treatment (? 1 y)

**Side Effects:** nausea, vomiting common; recent reports of possibly related bizarre behaviour in some individuals; probably safe in pregnancy

**Contraindications:** breastfeeding (insufficient data)

**RIBAVIRIN:** affects processing of RNA transcripts; i.v., oral (timing to food does not matter but consistency required) and aerosol administration; penetrates CSF; broad antiviral spectrum including respiratory syncytial virus, influenza A and B, parainfluenza, adenovirus

**Indications:** use currently limited to respiratory syncytial virus infection in infants at high risk for severe or complicated or in whom prolonged illness might worsen underlying chronic disease (aerosol), Lassa fever treatment and prophylaxis, severe measles in immunocompromised, relapsing hepatitis C and acute adenoviral pneumonia; has also been used in haemorrhagic fever with renal syndrome, nephropathica epidemica, rift valley fever prophylaxis, *Phlebotomus* fever prophylaxis, myocarditis and pericarditis due to influenza viruses, and (as aerosol) in influenza A and B, parainfluenza, URTI, croup, acute viral bronchiolitis and bronchopneumonia, pneumonitis

**Side Effects:** haemolytic anaemia, reticulocytosis common; may reduce effects of stavudine; dose adjustment required in renal failure and dialysis

**Contraindications:** pregnancy (avoid until 6 mo after completion of therapy); avoid in breastfeeding (insufficient data)

**PLECONARIL:** blocks enteroviral attachment to cellular receptors by occupying key capsid pocket on virus

**Indications:** severe enteroviral infection in patients with hypogammaglobulinemia

**Side Effects:** nausea in 6%, vomiting in 3%, headache in 3%, stomachache in 3%, fatigue in 3%, anorexia in 3%, urinary incontinence in 3%, worsening ataxia in 3%

**PALIVIZUMAB:** IgG monoclonal antibody

**Indications:** immunoprophylaxis against respiratory syncytial virus in some premature infants

#### **HYDRATION**

**Indications:** acute bronchiolitis, bronchitis, catarrh, common or feverish cold, croup, epidemic influenza, 'influenza-like illness', laryngotracheitis, tracheobronchitis, URTI

#### **STEAM**

**Indications:** acute bronchiolitis and bronchopneumonia, bronchitis, catarrh, common or feverish cold, croup, epidemic influenza, 'influenza-like illness', laryngotracheitis, tracheobronchitis, URTI; recent studies show little benefit

#### **ZINC GLUCONATE (LOZENGES)**

**Indications:** upper respiratory tract infection

#### **DISOXARIL**

**Indications:** persistent enteroviral meningitis in agammaglobulinemic individuals

#### **METHISAZONE**

**Indications:** smallpox

#### **STEROIDS**

**Indications:** varicella-zoster iridocyclitis (drops)

#### **CORTICOSTEROIDS**

**Indications:** viral arthritis

**Side Effects:** usually not significant at dosages and duration of therapy used for this indication

#### **BETAMETHASONE**

**Indications:** acute haemorrhagic conjunctivitis

**Side Effects:** hypersensitivity

#### **DEXAMETHASONE**

**Indications:** acute pharyngitis, severe croup requiring hospitalisation, herpes simplex meningitis

**Side Effects:** usually not significant at dosages and duration of therapy used for these indications

#### **PREDNISOLONE**

**Indications:** zoster in elderly

**Side Effects:** usually not significant at dosages and duration of therapy used for this indication; pancreatitis on higher doses or longer exposures

#### **PREDNISONE**

**Indications:** non-infectious oesophageal ulcers in AIDS, viral meningoencephalitis

**Side Effects:** usually not significant at dosages and duration of therapy used for this indication

#### **NON-STEROIDAL ANTI-INFLAMMATORY DRUGS**

**Indications:** viral arthritis

**Side Effects:** gastrointestinal effects, tinnitus, oedema, fluid retention, rash, pruritis, dizziness, headache, nervousness, decreased appetite, uncommon congestive heart failure, depression, insomnia, severe skin reactions, rare haematological reactions, hepatotoxicity, gastrointestinal ulceration and haemorrhaging, amblyopia

#### **CRYOTHERAPY**

**Indications:** anorectal, external genital, meatal, oral, perianal and vaginal/cervical warts

#### **ELECTROSURGERY**

**Indications:** anorectal, external genital, meatal, oral, perianal and vaginal/cervical warts

**5-FLUOROURACIL:** in WHO Model List of Essential Drugs

**Indications:** urethral warts

**Side Effects:** causes neutropenia by myelosuppression

**PODOPHYLLIN (PODOPHYLLUM):** in WHO Model List of Essential Drugs

**Indications:** warts other than oral, cervical, rectal, anorectal, urethral or venereal warts in pregnancy

**Side Effects:** occasional severe discomfort

**Contraindications:** pregnancy, breastfeeding

#### **PODOFILOX (PODOPHYLLOTOXIN)**

**Indications:** anogenital warts (5% gel; 37% clearance)

**Side Effects:** burning, inflammation, itching, erosion in 29-91%

**Contraindications:** pregnancy, breastfeeding

**IMQUIMOD:** cytokine inducer

**Indications:** anogenital warts (topical; 50% resolution), erythroplasia of Queyrat

**Side Effects:** erythema (6% severe, 34% moderate), erosion or oedema in < 1%; safety in pregnancy, breastfeeding and transplant patients not established

#### **BICHLOROACETIC ACID**

**Indications:** warts

**Side Effects:** safe in pregnancy and lactation

**Contraindications:** large areas, friable warts

#### **TRICHLOROACETIC ACID**

**Indications:** warts

**Side Effects:** safe in pregnancy and lactation

**Contraindications:** large areas, friable warts

#### **SURGERY**

**Indications:** anorectal, external genital, meatal, oral, perianal and vaginal/cervical warts

#### **THIOTEPA**

**Indications:** urethral warts

**Side Effects:** bone marrow depression, allergic reactions

#### **DIETARY RESTRICTION**

**Indications:** epidemic viral diarrhoea, viral gastroenteritis

#### **REHYDRATION**

**Indications:** epidemic viral diarrhoea, viral gastroenteritis, acute diarrhoea and vomiting, traveller's diarrhoea, postnatal gastroenteritis

#### **IMMUNOSTIMULATION**

**Indications:** prophylaxis and treatment of cytomegaloviral diffuse interstitial pneumonia and cytomegalic inclusion disease, viral meningoencephalitis, prophylaxis of varicella-zoster, hepatitis A, hepatitis B, mucocutaneous lymph node syndrome

#### **LEVAMISOLE**

**Indications:** used as an immunostimulant (in doses 40-60 times higher than as an antihelminthic) in abnormal monocyte chemotaxis during influenza infection, abnormal neutrophil chemotaxis in herpes simplex virus infection, deactivation by chemoattractants, hyper-IgE-recurrent-infection syndrome, hypogammaglobulinemia (IgA deficiency)

**POSTCONVALESCENT PLASMA**

**Indications:** Argentinian haemorrhagic fever

**PROSTAGLANDIN E<sub>1</sub>**

**Indications:** mucocutaneous lymph node syndrome

**VOLUME REPLACEMENT**

**Indications:** dengue