Zilip; ***Neth.:*** Famvir; Vectavir; ***Norw.:*** Vectavir; ***NZ:*** Vectavir†; ***Port.:*** Denovir; Fenivir; ***Rus.:*** Fenistil Pencivir (Фенистил Пенцивир); ***Spain:*** Vectavir; ***Swed.:*** Vectavir; ***Switz.:*** Famvir; ***Turk.:*** Vectavir; ***UK:*** Fenistil; Vectavir; ***USA:*** Denavir.

Peptide T

D-Ala-peptide-T-amide; Péptido T.

Пептид Т

Profile

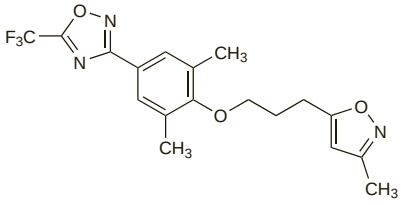
Peptide T is an octapeptide segment of the envelope glycoprotein of HIV. It has been investigated for the treatment of HIV infection and HIV-associated neurological disorders. Peptide T has also been tried in the treatment of psoriasis.

Pleconaril *(USAN, rINN)*

Pléconaril; Pleconarilo; Pleconarilum; VP-63843; Win-63843. 3-{4-[3-(3-Methyl-5-isoxazolyl)propoxy]-3,5-xylyl}-5-(trifluoromethyl)-1,2,4-oxadizole.

Плеконарил

$C_{18}H_{18}F_3N_3O_3$ = 381.3.
CAS — 153168-05-9.
ATC — J05AX06.
ATC Vet — QJ05AX06.



Profile

Pleconaril is an antiviral with activity against a range of picornaviruses. It has been investigated for the oral treatment of viral meningitis and encephalitis, upper respiratory-tract viral infections, and other enteroviral infections. However, there have been concerns over efficacy, viral resistance, and interactions with oral contraceptives. Development of an intranasal formulation for the common cold has also been investigated.

◊ References.

1. Nowak-Wegrzyn A, *et al.* Successful treatment of enterovirus infection with the use of pleconaril in 2 infants with severe combined immunodeficiency. *Clin Infect Dis* 2001; **32:** E13–E14.
2. Rotbart HA, Webster AD. Treatment of potentially life-threatening enterovirus infections with pleconaril. *Clin Infect Dis* 2001; **32:** 228–35.
3. Aradottir E, *et al.* Severe neonatal enteroviral hepatitis treated with pleconaril. *Pediatr Infect Dis J* 2001; **20:** 457–9.
4. Starlin R, *et al.* Acute flaccid paralysis syndrome associated with echovirus 19, managed with pleconaril and intravenous immunoglobulin. *Clin Infect Dis* 2001; **33:** 730–2.
5. Hayden FG, *et al.* Oral pleconaril treatment of picornavirus-associated viral respiratory illness in adults: efficacy and tolerability in phase II clinical trials. *Antivir Ther* 2002; **7:** 53–65.
6. Abzug MJ, *et al.* Double blind placebo-controlled trial of pleconaril in infants with enterovirus meningitis. *Pediatr Infect Dis J* 2003; **22:** 335–41.
7. Hayden FG, *et al.* Efficacy and safety of oral pleconaril for treatment of colds due to picornaviruses in adults: results of 2 double-blind, randomized, placebo-controlled trials. *Clin Infect Dis* 2003; **36:** 1523–32.

Poly I.poly C12U

Poli(I)^{2}poli(C_{12}U); Poly(I):poly(C_{12},U).

Поли I.Поли C12U

Profile

Poly I.poly C12U is a synthetic mismatched polymer of double-stranded RNA with antiviral and immunomodulatory activity (see also Poly I. Poly C, p.2370). It is under investigation in the treatment of HIV infection, and also in renal cell carcinoma, chronic fatigue syndrome, invasive melanoma, and hepatitis B and C.

Preparations

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

Propagermanium *(rINN)*

Propagermanio. A polymer obtained from 3-(trihydroxygermyl)propionic acid.

Пропагерманий

$(C_3H_5GeO_{3.5})_n$.
CAS — 12758-40-6.

Profile

Propagermanium is an immunomodulator that has been used in chronic hepatitis B infections. Acute exacerbation of hepatitis, including some fatalities, has been reported in patients receiving propagermanium.

◊ References.

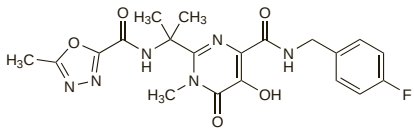
1. Hirayama C, *et al.* Propagermanium: a nonspecific immune modulator for chronic hepatitis B. *J Gastroenterol* 2003; **38:** 525–32.

Raltegravir *(USAN, rINN)*

Raltégravir; Raltegravirum. *N*-{2-[4-(4-Fluorobenzylcarbamoyl)-5-hydroxy-1-methyl-6-oxo-1,6-dihydropyrimidin-2-yl]propan-2-yl}-5-methyl-1,3,4-oxadiazole-2-carboxamide.

Ральтегравир

$C_{20}H_{21}FN_6O_5$ = 444.4.
CAS — 518048-05-0.
ATC — J05AX08.
ATC Vet — QJ05AX08.



Raltegravir Potassium *(USAN, rINNM)*

Kalii Raltegravirum; MK-0518; Raltegravir potásico; Raltégravir Potassique. Potassium 4-[(4-fluorobenzyl)carbamoyl]-1-methyl-2-(1-methyl-1-{[(5-methyl-1,3,4-oxadiazol-2-yl)carbonyl]amino}ethyl)-6-oxo-1,6-dihydropyrimidin-5-olate.

Калия Ральтегравир

$C_{20}H_{20}FKN_6O_5$ = 482.5.
CAS — 871038-72-1.

Adverse Effects and Precautions

On the basis of limited data, raltegravir appears to be well tolerated; non-specific adverse effects associated with raltegravir-based regimens include headache, abdominal pain, vomiting, asthenia, fatigue, and dizziness. Abnormal creatine phosphokinase values may occur and myopathy and rhabdomyolysis have been reported although a causal relationship has not been established; nonetheless, caution is advised in patients at increased risk of these conditions.

Interactions

Raltegravir is not a substrate for cytochrome P450 isoenzymes, and does not appear to interact with drugs metabolised by this mechanism. However, rifampicin induces the glucuronidase responsible for raltegravir metabolism (UGT1A1) and reduces plasma concentrations of raltegravir.

Antivirals. Plasma concentrations of raltegravir were modestly increased by *atazanavir* and ritonavir-boosted atazanavir in healthy subjects; this increase is not considered to be clinically significant.[1]

1. Iwamoto M, *et al.* Atazanavir modestly increases plasma levels of raltegravir in healthy subjects. *Clin Infect Dis* 2008; **47:** 137–40.

Pharmacokinetics

Raltegravir is absorbed on oral dosage, with peak concentrations achieved about 3 hours after a dose. There is considerable inter-individual variation in the pharmacokinetics. It is metabolised via glucuronidation, catalysed by the enzyme uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1), and excreted in both urine and faeces as unchanged drug and metabolites.

Uses and Administration

Raltegravir is an inhibitor of HIV integrase, an enzyme essential for insertion of viral DNA into the host genome, and thus for replication. It is added to treatment with other antiretrovirals for salvage therapy in patients with HIV infection and AIDS (p.856) who have evidence of viral replication and HIV-1 strains resistant to multiple antiretrovirals.

It is given orally as the potassium salt but doses are calculated in terms of the base; 434 mg of raltegravir potassium is equivalent to about 400 mg of raltegravir. The usual dose is the equivalent of 400 mg of raltegravir twice daily, with or without food.

◊ References.

1. Markowitz M, *et al.* Antiretroviral activity, pharmacokinetics, and tolerability of MK-0518, a novel inhibitor of HIV-1 integrase, dosed as monotherapy for 10 days in treatment-naive HIV-1-infected individuals. *J Acquir Immune Defic Syndr* 2006; **43:** 509–15. Correction. *ibid.* 2007; **44:** 492.
2. Grinsztejn B, *et al.* Protocol 005 Team. Safety and efficacy of the HIV-1 integrase inhibitor raltegravir (MK-0518) in treatment-experienced patients with multidrug-resistant virus: a phase II randomised controlled trial. *Lancet* 2007; **369:** 1261–9.
3. Markowitz M, *et al.* Protocol 004 Part II Study Team. Rapid and durable antiretroviral effect of the HIV-1 Integrase inhibitor raltegravir as part of combination therapy in treatment-naive patients with HIV-1 infection: results of a 48-week controlled study. *J Acquir Immune Defic Syndr* 2007; **46:** 125–33.
4. Iwamoto M, *et al.* Safety, tolerability, and pharmacokinetics of raltegravir after single and multiple doses in healthy subjects. *Clin Pharmacol Ther* 2008; **83:** 293–9.
5. Croxtall JD, *et al.* Raltegravir. *Drugs* 2008; **68:** 131–8.

Preparations

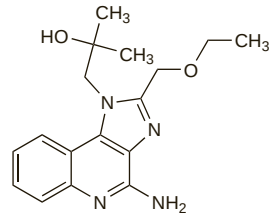
Proprietary Preparations (details are given in Part 3)
Cz.: Isentress; ***Fr.:*** Isentress; ***UK:*** Isentress; ***USA:*** Isentress.

Resiquimod *(rINN)*

R-848; Résiquimod; Resiquimodum; S-28463; VML-600. 4-Amino-2-(ethoxymethyl)-α,α-dimethyl-1*H*-imidazo[4,5-*c*]quinoline-1-ethanol.

Резихимод

$C_{17}H_{22}N_4O_2$ = 314.4.
CAS — 144875-48-9.



Profile

Resiquimod is an immune response modifier that has been investigated for the topical treatment of genital herpes.

◊ References.

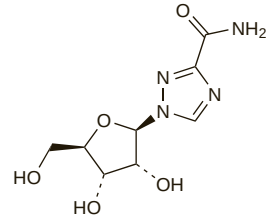
1. Spruance SL, *et al.* Application of a topical immune response modifier, resiquimod gel, to modify the recurrence rate of recurrent genital herpes: a pilot study. *J Infect Dis* 2001; **184:** 196–200.
2. Mark KE, *et al.* Topical resiquimod 0.01% gel decreases herpes simplex virus type 2 genital shedding: a randomized, controlled trial. *J Infect Dis* 2007; **195:** 1324–31.

Ribavirin *(BAN, USAN, rINN)*

ICN-1229; Ribaviriini; Ribavirina; Ribavirinas; Ribavirine; Ribavirinum; RTCA; Tribavirin. 1-β-D-Ribofuranosyl-1*H*-1,2,4-triazole-3-carboxamide.

Рибавирин

$C_8H_{12}N_4O_5$ = 244.2.
CAS — 36791-04-5.
ATC — J05AB04.
ATC Vet — QJ05AB04.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.
Ph. Eur. 6.2 (Ribavirin). A white or almost white crystalline powder. It exhibits polymorphism. Freely soluble in water; slightly soluble in alcohol; slightly soluble or very slightly soluble in dichloromethane. A 2% solution in water has a pH of 4.0 to 6.5. Protect from light.
USP 31 (Ribavirin). A white crystalline powder. Freely soluble in water; slightly soluble in dehydrated alcohol. Store in airtight containers.

Adverse Effects

When given *by inhalation*, ribavirin has sometimes led to worsening of lung function, bacterial pneumonia, and pneumothorax, to cardiovascular effects (including a fall in blood pressure and cardiac arrest), and, rarely, to anaemia, haemolysis, and reticulocytosis. Conjunctivitis and skin rash have also occurred. Precipitation of inhaled ribavirin and consequent accumulation of fluid has occurred in the tubing of ventilating equipment.

The most common adverse effects reported by patients taking *oral* ribavirin, with either interferon alfa or peginterferon alfa, are psychiatric reactions (such as