Lamivudine *(BAN, USAN, rINN)*

3TC; (–)-2′-Deoxy-3′-thiacytidine; GR-109714X; Lamivudiini; Lamivudin; Lamivudina; Lamivudinum; Lamiwudyna; Lavmivudin. (–)-1-[(2R,5S)-2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine.

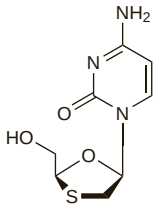
Ламивудин

$C_8H_{11}N_3O_3S$ = 229.3.

CAS — 131086-21-0; 134678-17-4.

ATC — J05AF05.

ATC Vet — QJ05AF05.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Lamivudine). A white or almost white powder. It exhibits polymorphism. Soluble in water, slightly soluble in alcohol; sparingly soluble in methyl alcohol. Protect from light.
USP 31 (Lamivudine). A white to off-white solid. Soluble in water. Protect from light.

Adverse Effects

Adverse effects commonly associated with lamivudine either as monotherapy or with other antiretrovirals for the treatment of HIV include abdominal pain, nausea, vomiting, diarrhoea, headache, fever, rash, alopecia, malaise, insomnia, cough, nasal symptoms, arthralgia, and musculoskeletal pain. There have also been reports of pancreatitis, anaemia, neutropenia, and thrombocytopenia. Increases in liver enzymes and serum amylase may occur. Lactic acidosis, usually associated with severe hepatomegaly and steatosis, has been reported during treatment with nucleoside reverse transcriptase inhibitors.

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 lamivudine, 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 lamivudine. Metabolic abnormalities such as hypertriglyceridaemia, hypercholesterolaemia, insulin resistance, hyperglycaemia, and hyperlactataemia have also been reported. NRTIs have also been associated with mitochondrial dysfunction manifesting as abnormal behaviour, anaemia, convulsions, hyperlipasaemia, hypertonia, and neutropenia. Elevated creatine phosphokinase, myalgia, myositis, and rarely rhabdomyolysis have been reported, particularly when nucleoside analogues have been given with HIV-protease inhibitors. Osteonecrosis has been reported, particularly in patients with advanced HIV disease or long-term exposure to combination antiretroviral therapy. For further information on adverse effects associated with NRTIs see Zidovudine, p.914.

Patients taking a lower dose of lamivudine for the treatment of chronic hepatitis B often have abdominal discomfort and pain, diarrhoea, fatigue, headache, nausea, malaise, respiratory-tract infections, and vomiting. The most frequently reported laboratory abnormalities are elevated creatine phosphokinase, increases in serum lipase, and raised liver enzymes, in particular alanine aminotransferase. There have been rare reports of lactic acidosis, pancreatitis, and muscle disorders such as cramps, myalgia, and rhabdomyolysis.

Effects on the blood. Although anaemia associated with lamivudine usually occurs when it is used with zidovudine, there has been a report[1] of severe anaemia in a 62-year-old HIV-infected man given lamivudine alone.

1. Weitzel T, *et al.* Severe anaemia as a newly recognized side-effect caused by lamivudine. *AIDS* 1999; **13:** 2309–11.

Effects on the hair. Hair loss was associated with lamivudine treatment in 5 patients.[1]

1. Fong IW. Hair loss associated with lamivudine. *Lancet* 1994; **344:** 1702.

Effects on the nervous system. Exacerbation of peripheral neuropathy has been reported in a patient after substitution of lamivudine for zalcitabine.[1]

1. Cupler EJ, Dalakas MC. Exacerbation of peripheral neuropathy by lamivudine. *Lancet* 1995; **345:** 460–1.

Hypersensitivity. Angioedema, urticaria, and anaphylactoid reaction occurred in a patient 30 minutes after receiving the first dose of lamivudine.[1]

1. Kainer MA, Mijch A. Anaphylactoid reaction, angioedema, and urticaria associated with lamivudine. *Lancet* 1996; **348:** 1519.

Precautions

Lamivudine therapy should be stopped in patients who develop abdominal pain, nausea, or vomiting or with abnormal biochemical test results until pancreatitis has been excluded.

Treatment with lamivudine may be associated with lactic acidosis and should be stopped if there is a rapid increase in aminotransferase concentrations, progressive hepatomegaly, or metabolic or lactic acidosis of unknown aetiology. Lamivudine should be used with caution in patients with hepatomegaly or other risk factors for hepatic disease. Patients co-infected with HIV and chronic hepatitis B or C and treated with combination antiretroviral therapy are at increased risk for severe and potentially fatal hepatic adverse events. In patients with chronic hepatitis B, there is a risk of rebound hepatitis when lamivudine is stopped, and liver function should be monitored in such patients. The possibility of HIV infection should be excluded before beginning lamivudine therapy for hepatitis B, since the lower doses used to treat the latter may permit the development of lamivudine-resistant strains of HIV.

Dosage reduction may be necessary in patients with impaired renal function.

Interactions

The renal excretion of lamivudine may be inhibited by other drugs mainly eliminated by active renal secretion, for example trimethoprim. Usual prophylactic doses of trimethoprim are unlikely to necessitate reductions in lamivudine dosage unless the patient has renal impairment, but the co-administration of lamivudine with the high doses of trimethoprim (as co-trimoxazole) used in pneumocystis pneumonia and toxoplasmosis should be avoided. Although there is usually no clinically significant interaction with zidovudine, severe anaemia has occasionally been reported in patients given lamivudine with zidovudine (see Zidovudine, Interactions, p.915). Lamivudine may antagonise the antiviral action of zalcitabine and the two drugs should not be used together. Once daily triple nucleoside regimens of lamivudine and tenofovir with either abacavir or didanosine are associated with a high level of treatment failure and of emergence of resistance, and should be avoided.

Phenylpropanolamine. For a possible interaction between phenylpropanolamine and antiretrovirals, see Stavudine, p.907.

Antiviral Action

Lamivudine is converted intracellularly in stages to the triphosphate. This triphosphate halts the DNA synthesis of retroviruses, including HIV, through competitive inhibition of reverse transcriptase and incorporation into viral DNA. Lamivudine is also active against hepatitis B virus. Resistance to lamivudine has been reported in isolates of HIV and hepatitis B virus.

Pharmacokinetics

Lamivudine is rapidly absorbed after oral doses and peak plasma concentrations are achieved in about 1 hour. Absorption is delayed, but not reduced, by ingestion with food. Bioavailability is between 80 and 87%. Binding to plasma protein is reported to be up to 36%. Lamivudine crosses the blood-brain barrier with a ratio of CSF to serum concentrations of about 0.12. It crosses the placenta and is distributed into breast milk.

Lamivudine is metabolised intracellularly to the active antiviral triphosphate. Hepatic metabolism is low and it is cleared mainly unchanged by active renal excretion. An elimination half-life of 5 to 7 hours has been reported after a single dose.

◊ References.

1. Mueller BU, *et al.* Serum and cerebrospinal fluid pharmacokinetics of intravenous and oral lamivudine in human immunodeficiency virus-infected children. *Antimicrob Agents Chemother* 1998; **42:** 3187–92.
2. Johnson MA, *et al.* Clinical pharmacokinetics of lamivudine. *Clin Pharmacokinet* 1999; **36:** 41–66.
3. Bruno R, *et al.* Comparison of the plasma pharmacokinetics of lamivudine during twice and once daily administration in patients with HIV. *Clin Pharmacokinet* 2001; **40:** 695–700.
4. Asari A, *et al.* Pharmacokinetics of lamivudine in subjects receiving peritoneal dialysis in end-stage renal failure. *Br J Clin Pharmacol* 2007; **64:** 738–44.
5. Burger DM, *et al.* Age-dependent pharmacokinetics of lamivudine in HIV-infected children. *Clin Pharmacol Ther* 2007; **81:** 517–20.
6. Tremoulet AH, *et al.* Pediatric AIDS Clinical Trials Group. Population pharmacokinetics of lamivudine in human immunodeficiency virus-exposed and -infected infants. *Antimicrob Agents Chemother* 2007; **51:** 4297–4302.

Uses and Administration

Lamivudine is a nucleoside reverse transcriptase inhibitor structurally related to cytosine with antiviral activity against HIV-1 and hepatitis B virus. It is used in the treatment of HIV infection and AIDS, (p.856) and chronic hepatitis B infection (p.851). Viral resistance emerges rapidly when lamivudine is used alone in the treatment of HIV infection, and it is therefore used with other antiretrovirals.

For HIV infection, the dose of lamivudine for adults is 300 mg by mouth daily as a single dose or in two divided doses.

For chronic hepatitis B, the adult dose is 100 mg once daily by mouth. In patients with concomitant HIV and hepatitis B infection the dosage regimen appropriate for HIV should be used.

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

Reduction of dosage is recommended for patients with renal impairment (see below).

Fixed-dose combination products for the treatment of HIV infection and AIDS have been developed in order to improve patient adherence and avoid monotherapy, thereby decreasing the risk of acquired drug resistance. Products containing lamivudine in combination with zidovudine or abacavir and with abacavir plus zidovudine are available in some countries.

◊ Reviews.

1. Dando TM, Scott LJ. Abacavir plus lamivudine: a review of their combined use in the management of HIV infection. *Drugs* 2005; **65:** 285–302.

Administration in children. For the treatment of HIV infection in infants and children lamivudine is given orally either as tablets or a solution, together with other antiretroviral drugs. Doses are based on body-weight:

- in infants and children over 3 months of age and weighing less than 14 kg or in those unable to swallow tablets the oral solution may be given in a dose of 4 mg/kg twice daily to a maximum daily dose of 300 mg
- in children weighing 14 to 21 kg the tablet formulation may be given in a dose of 75 mg twice daily
- in children weighing 21 to 30 kg the tablet formulation may be given in a dose of 75 mg in the morning and 150 mg at night
- in children weighing over 30 kg the tablet formulation may be given in a dose of 150 mg twice daily

Dosage of lamivudine should be reduced in HIV-infected patients (at least 3 months of age and weighing less than 30 kg) with moderate to severe renal impairment (creatinine clearance (CC) below 50 mL/minute):

- CC 30 to 49 mL/minute: 4 mg/kg for the first dose then 4 mg/kg once daily
- CC 15 to 29 mL/minute: 4 mg/kg for the first dose then 2.6 mg/kg once daily

- CC 5 to 14 mL/minute: 4 mg/kg for the first dose then 1.3 mg/kg once daily
- CC less than 5 mL/minute: 1.3 mg/kg for the first dose then 0.7 mg/kg once daily

For the treatment of chronic hepatitis B infection in children and adolescents aged between 2 and 17 years, US licensed product information recommends an oral dose of lamivudine of 3 mg/kg once daily to a maximum daily dose of 100 mg. Dosage reduction would need to be considered in those with renal impairment. UK licensed product information does not recommend the use of lamivudine for the treatment of chronic hepatitis B in those under 17 years of age.

Administration in renal impairment. Dosage of lamivudine should be reduced in patients with moderate to severe renal impairment (creatinine clearance (CC) below 50 mL/minute).

adults: HIV infection:

- CC 30 to 49 mL/minute: 150 mg for the first dose then 150 mg once daily
- CC 15 to 29 mL/minute: 150 mg for the first dose then 100 mg once daily
- CC 5 to 14 mL/minute: 150 mg for the first dose then 50 mg once daily
- CC less than 5 mL/minute: 50 mg for the first dose then 25 mg once daily
- dialysis patients: no additional doses required after routine haemodialysis or peritoneal dialysis

adults: chronic hepatitis B infection:

- CC 30 to 49 mL/minute: 100 mg for the first dose then 50 mg once daily
- CC 15 to 29 mL/minute: 100 mg for the first dose then 25 mg once daily
- CC 5 to 14 mL/minute: 35 mg for the first dose then 15 mg once daily
- CC less than 5 mL/minute: 35 mg for the first dose then 10 mg once daily
- dialysis patients: no additional doses required after routine haemodialysis or peritoneal dialysis

children:

- see Administration in Children, above

Hepatitis. Lamivudine is one of the antivirals being used as an alternative to interferon alfa in the treatment of chronic hepatitis B (p.851).[1-3] In a preliminary study, lamivudine 100 or 300 mg daily reduced hepatitis B virus DNA to low or undetectable levels.[4] In a 1-year double-blind study involving about 350 patients with chronic hepatitis B, lamivudine 100 mg daily was associated with substantial histological improvement in many patients; a dose of 25 mg daily was less effective.[5] Relapses have been reported once treatment with lamivudine is stopped, and a case of reactivation of hepatitis B infection has been observed.[6] Lamivudine may also be effective in preventing re-infection with hepatitis B in patients during chemotherapy[7-9] and in those who have had liver transplants,[10,11] and beneficial responses have been seen in transplant patients with acute hepatitis B infection treated with lamivudine 100 mg daily for prolonged periods.[12]

1. Dienstag JL, *et al.* Lamivudine as initial treatment for chronic hepatitis B in the United States. *N Engl J Med* 1999; **341:** 1256–63.
2. Hagmeyer KO, Pan Y-Y. Role of lamivudine in the treatment of chronic hepatitis B virus infection. *Ann Pharmacother* 1999; **33:** 1104–12.
3. Jonas MM, *et al.* Clinical trial of lamivudine in children with chronic hepatitis B. *N Engl J Med* 2002; **346:** 1706–13. Correction. *ibid.*; **347:** 955.
4. Dienstag JL, *et al.* A preliminary trial of lamivudine for chronic hepatitis B infection. *N Engl J Med* 1995; **333:** 1657–61.
5. Lai C-L, *et al.* A one-year trial of lamivudine for chronic hepatitis B. *N Engl J Med* 1998; **339:** 61–8.
6. Honkoop P, *et al.* Hepatitis B reactivation after lamivudine. *Lancet* 1995; **346:** 1156–7.
7. Yeo W, *et al.* Lamivudine for the prevention of hepatitis B virus reactivation in hepatitis B s-antigen seropositive cancer patients undergoing cytotoxic chemotherapy. *J Clin Oncol* 2004; **22:** 927–34.
8. Idilman R. Lamivudine prophylaxis in HBV carriers with haemato-oncological malignancies who receive chemotherapy. *J Antimicrob Chemother* 2005; **55:** 828–31.
9. Loomba R, *et al.* Systematic review: the effect of preventive lamivudine on hepatitis B reactivation during chemotherapy. *Ann Intern Med* 2008; **148:** 519–28.
10. Grellier L, *et al.* Lamivudine prophylaxis against reinfection in liver transplantation for hepatitis B cirrhosis. *Lancet* 1996; **348:** 1212–15. Correction. *ibid.* 1997; **349:** 364.
11. Perrillo RP, *et al.* A multicenter United States-Canadian trial to assess lamivudine monotherapy before and after liver transplantation for chronic hepatitis B. *Hepatology* 2001; **33:** 424–32.
12. Andreone P, *et al.* Lamivudine treatment for acute hepatitis B after liver transplantation. *J Hepatol* 1998; **29:** 985–9.

HIV infection and AIDS. Lamivudine is a potent inhibitor of HIV-1 and HIV-2 *in vitro*, including variants resistant to zidovudine.[1] Resistance emerges rapidly when lamivudine is given alone to patients with HIV infections,[2] although sustained responses have been reported despite the emergence of resistance.[3] Combination therapy with lamivudine delays, and may even reverse, the emergence of zidovudine resistance and produces a sustained synergistic antiretroviral effect,[4] but HIV strains resistant to both lamivudine and zidovudine may arise.[5] As discussed on p.856, combination therapy, typically with two nucleoside reverse transcriptase inhibitors and either a non-nucleoside reverse transcriptase inhibitor or an HIV-protease inhibitor, is standard therapy for HIV infection. Treatment with lamivudine plus zidovudine has produced better responses than either drug alone in antiretroviral-naive patients,[6,7] and has produced additional responses in antiretroviral-experienced patients,[8,9] with little additional toxicity. The addition of lamivudine to existing antiretroviral therapy was reported to slow the progression of the disease and improve survival,[10] and treatment with lamivudine, indinavir, and nevirapine produced beneficial responses in patients who had previously failed on combined nucleoside analogue therapy.[11] Clinically useful CNS concentrations of lamivudine were achieved in patients with HIV infection given combination therapy with lamivudine and zidovudine or stavudine.[12]

Lamivudine is also used in prophylactic regimens after occupational exposure to HIV infection (see p.858) and has been tried for reducing vertical transmission from mother to neonate.[13,14]

1. Anonymous. Lamivudine: impressive benefits in combination with zidovudine. *WHO Drug Inf* 1996; **10:** 5–7.
2. Wainberg MA, *et al.* Development of HIV-1 resistance to (–)2′-deoxy-3′-thiacytidine in patients with AIDS or advanced AIDS-related complex. *AIDS* 1995; **9:** 351–7.
3. Ingrand D, *et al.* Phase I/II study of 3TC (lamivudine) in HIV-positive, asymptomatic or mild AIDS-related complex patients: sustained reduction in viral markers. *AIDS* 1995; **9:** 1323–9.
4. Larder BA, *et al.* Potential mechanism for sustained antiretroviral efficacy of AZT-3TC combination therapy. *Science* 1995; **269:** 696–9.
5. Miller V, *et al.* Dual resistance to zidovudine and lamivudine in patients treated with zidovudine-lamivudine combination therapy: association with therapeutic failure. *J Infect Dis* 1998; **177:** 1521–32.
6. Eron JJ, *et al.* Treatment with lamivudine, zidovudine, or both in HIV-positive patients with 200 to 500 CD4+ cells per cubic millimeter. *N Engl J Med* 1995; **333:** 1662–9.
7. Katlama C, *et al.* Safety and efficacy of lamivudine-zidovudine combination therapy in antiretroviral-naive patients: a randomized controlled comparison with zidovudine monotherapy. *JAMA* 1996; **276:** 118–25.
8. Staszewski S, *et al.* Safety and efficacy of lamivudine-zidovudine combination therapy in zidovudine-experienced patients: a randomized controlled comparison with zidovudine monotherapy. *JAMA* 1996; **276:** 111–17.
9. Bartlett JA, *et al.* Lamivudine plus zidovudine compared with zalcitabine plus zidovudine in patients with HIV infection: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1996; **125:** 161–72.
10. CAESAR Coordinating Committee. Randomised trial of addition of lamivudine or lamivudine plus loviride to zidovudine-containing regimens for patients with HIV-1 infection: the CAESAR trial. *Lancet* 1997; **349:** 1413–21.
11. Harris M, *et al.* A pilot study of nevirapine, indinavir, and lamivudine among patients with advanced human immunodeficiency virus disease who have had failure of combination nucleoside therapy. *J Infect Dis* 1998; **177:** 1514–20.
12. Foudraine NA, *et al.* Cerebrospinal-fluid HIV-1 RNA and drug concentrations after treatment with lamivudine plus zidovudine or stavudine. *Lancet* 1998; **351:** 1547–51.
13. Mandelbrot L, *et al.* Lamivudine-zidovudine combination for prevention of maternal-infant transmission of HIV-1. *JAMA* 2001; **285:** 2083–93.
14. The Petra Study Team. Efficacy of three short-course regimens of zidovudine and lamivudine in preventing early and late transmission of HIV-1 from mother to child in Tanzania, South Africa, and Uganda (Petra study): a randomised, double-blind, placebo-controlled trial. *Lancet* 2002; **359:** 1178–86.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: 3TC; Amilitrap; Birvac†; Ganvirel; Heptodine; Hivirux†; Imunoxa; Kess; Lamibergen; Lamilea; Oralmuv; Ultraviral; Vuclodir; Zeffix†; ***Austral.:*** 3TC; Zeffix; ***Austria:*** Epivir; Zeffix; ***Belg.:*** Epivir; Zeffix; ***Braz.:*** Epivir; Lami; Vudirax; Zeffix†; ***Canad.:*** 3TC; Heptovir; ***Chile:*** 3TC/Epivir; ***Cz.:*** Epivir; Zeffix; ***Denm.:*** Epivir; Zeffix; ***Fin.:*** Epivir; Zeffix; ***Fr.:*** Epivir; Zeffix; ***Ger.:*** Epivir; Kivexa; Zeffix; ***Gr.:*** Epivir; Zeffix; ***Hong Kong:*** 3TC; Zeffix; ***Hung.:*** Epivir; Zeffix; ***India:*** Ladiwin; Lamda; Lamidac; Lamirex†; Lamivir; ***Indon.:*** 3TC; 3TC-HBV; ***Irl.:*** Epivir; Zeffix; ***Israel:*** Epivir; Zeffix; ***Ital.:*** Epivir; Zeffix; ***Jpn:*** Epivir†; ***Malaysia:*** 3TC; Zeffix; ***Mex.:*** 3TC; ***Neth.:*** Epivir; Zeffix; ***Norw.:*** Epivir; Zeffix; ***NZ:*** 3TC; Zeffix; ***Philipp.:*** Zeffix; ***Pol.:*** Epivir; Zeffix; ***Port.:*** Epivir; Zeffix; ***Rus.:*** Epivir (Эпивир); Zeffix (Зеффикс); ***S.Afr.:*** 3TC; ***Singapore:*** Epivir; Zeffix; ***Spain:*** Epivir; Zeffix; ***Swed.:*** Epivir; Zeffix; ***Switz.:*** 3TC; Zeffix; ***Thai.:*** Epivir; Zeffix; ***Turk.:*** Epivir; Zeffix; ***UK:*** Epivir; Zeffix; ***USA:*** Epivir; ***Venez.:*** Epivir; Heptodine†; Lamivir.

Multi-ingredient: Arg.: 3TC Complex; 3TC/AZT; Ganvirel Duo; Hivirux Complex†; Imunoxa Complex; Kess Complex; Kivexa; Muvidina; Tricivir; Trivudin; Ultraviral Duo; Zetavudin; ***Austral.:*** Combivir; Kivexa; Trizivir; ***Austria:*** Combivir; Trizivir; ***Belg.:*** Combivir; Kivexa; Trizivir; ***Braz.:*** Biovir; Duovir†; Vir-Complex†; Zidolam; ***Canad.:*** Combivir; Kivexa; Trizivir; ***Chile:*** Combivir; Kivexa; Tricivir; ***Cz.:*** Combivir; Kivexa; Trizivir; ***Denm.:*** Combivir; Kivexa; Trizivir; ***Fin.:*** Combivir; Kivexa; Trizivir; ***Fr.:*** Combivir; Kivexa; Trizivir; ***Ger.:*** Combivir; Trizivir; ***Gr.:*** Combivir; Kivexa; Trizivir; ***Hong Kong:*** Combivir; Trizivir; ***Hung.:*** Combivir; Kivexa; Trizivir; ***India:*** Combirex†; Duovir; Duovir N; Lamda-Z; Lamivir S; Lamuzid; Odivir Kit; Triomune; ***Irl.:*** Combivir; Kivexa; Trizivir; ***Israel:*** Combivir; Trizivir; ***Ital.:*** Combivir; Kivexa; Trizivir; ***Malaysia:*** Combivir; ***Mex.:*** Combivir; Kivexa; Trizivir; ***Neth.:*** Combivir; Kivexa; Trizivir; ***Norw.:*** Combivir; Kivexa; Trizivir; ***NZ:*** Combivir; Kivexa; Trizivir; ***Philipp.:*** Combivir; ***Pol.:*** Combivir; Kivexa; Trizivir; ***Port.:*** Combivir; Kivexa; Trizivir; ***Rus.:*** Combivir (Комбивир); Trizivir (Тризивир); ***S.Afr.:*** Combivir; Duovir; Lamzid; Retrovir/3TC Post-HIV Exposure†; Triomune; Trizivar; ***Singapore:*** Combivir; Trizivir†; ***Spain:*** Combivir; Kivexa; Trizivir; ***Swed.:*** Combivir; Kivexa; Trizivir; ***Switz.:*** Combivir; Trizivir; ***Thai.:*** Combid; ***Turk.:*** Combivir; ***UK:*** Combivir; Kivexa; Trizivir; ***USA:*** Combivir; Epzicom; Trizivir; ***Venez.:*** Combivir; Duovir; Triomune; Trizivir.

Lopinavir *(BAN, USAN, rINN)*

A-157378.0; ABT-378; Lopinaviiri; Lopinavirum. (αS)-Tetrahydro-*N*-((αS)-α-{(2*S*,3*S*)-2-hydroxy-4-phenyl-3-[2-(2,6-xylyloxy)acetamido]butyl}phenethyl)-α-isopropyl-2-oxo-1(2*H*)-pyrimidineacetamide.

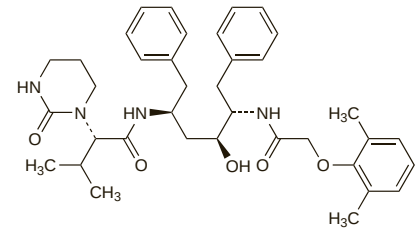
Лопинавир

$C_{37}H_{48}N_4O_5$ = 628.8.

CAS — 192725-17-0.

ATC — J05AE06.

ATC Vet — QJ05AE06.



Adverse Effects

The most common adverse effect associated with antiretroviral regimens containing lopinavir (formulated with ritonavir) is diarrhoea of mild to moderate severity. Pancreatitis has been seen in patients receiving lopinavir, including those who developed marked triglyceride elevations; in some cases fatalities have occurred. Other commonly reported adverse effects include asthenia, headache, insomnia, pain, paraesthesia, gastrointestinal disturbances, acne, and rash. Abnormal laboratory test results associated with lopinavir-containing regimens include increases in serum cholesterol and triglycerides and raised liver enzymes.

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 lopinavir, 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 lopinavir. Metabolic abnormalities such as hypertriglyceridaemia, hypercholesterolaemia, insulin resistance, hyperglycaemia, and hyperlactataemia have also been reported. Elevated creatine phosphokinase, myalgia, myositis, and rarely rhabdomyolysis have been reported with HIV-protease inhibitors, particularly when given with nucleoside analogues. Osteonecrosis has been reported, particularly in patients with advanced HIV disease or long-term exposure to combination antiretroviral therapy.

For further information on adverse effects associated with HIV-protease inhibitors see under Indinavir Sulfate, p.882.

Precautions

Patients with advanced HIV disease may be at increased risk of elevated triglycerides and pancreatitis, and patients with a history of pancreatitis may be at increased risk for recurrence during treatment with ritonavir-boosted lopinavir. Such therapy should be stopped if symptoms of pancreatitis occur.

The oral solution (*Kaletra, Abbott*) has a high content of alcohol and propylene glycol, present as excipients, and appropriate precautions should be taken; it is contra-indicated in infants and young children, in pregnancy, and in hepatic or renal impairment. For further information on propylene glycol toxicity, see Adverse Effects and Precautions, p.2374.