Lopinavir 200mg and Ritonavir 50mg Tablets USP

RIT-LOP 250

Composition:
Each film coated tablet contains:
Lopinavir USP 200mg
Ritonavir USP 50mg
Excipients ..... q.s.
Approved colour used.

Therapeutic Indication:
Lopinavir/ritonavir is indicated in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infected adults, adolescents and children above the age of 2 years.
The choice of lopinavir/ritonavir to treat protease inhibitor experienced HIV-1 infected patients should be based on individual viral resistance testing and treatment history of patients.

Contraindications:
Hypersensitivity to the active substances or to any of the excipients.
Severe hepatic insufficiency.
Lopinavir/Ritonavir tablets contain lopinavir and ritonavir, both of which are inhibitors of the P450 isoform CYP3A. Lopinavir/ritonavir should not be co-administered with medicinal products that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life threatening events.

Posology and Method of administration:
Lopinavir/ritonavir should be prescribed by physicians who are experienced in the treatment of HIV infection.
Lopinavir/ritonavir tablets must be swallowed whole and not chewed, broken or crushed.
Posology
Adults and adolescents
The standard recommended dosage of lopinavir/ritonavir tablets is 400/100 mg (two 200/50 mg) tablets twice daily taken with or without food. In adult patients, in cases where once daily dosing is considered necessary for the management of the patient, lopinavir/ritonavir tablets may be administered as 800/200 mg (four 200/50 mg tablets) once daily with or without food. The use of a once daily dosing should be limited to those adult patients having only very few protease inhibitor (PI) associated mutations (i.e. less than 3 PI mutations in line with clinical trial results,and should take into account the risk of a lesser sustainability of the virologic suppression and higher risk of diarrhoea compared to the recommended standard twice daily dosing.
Paediatric population (2 years of age and above)
The adult dose of lopinavir/ritonavir tablets (400/100 mg twice daily) may be used in children 40 kg or greater or with a Body Surface Area (BSA)* greater than 1.4 m2. For children weighing less than 40 kg or with a BSA between 0.5 and 1.4 m2 and able to swallow tablets, please refer to the dosing guideline tables below. Based on the current data available, lopinavir/ritonavir should not be administered once daily in paediatric patients.
Before prescribing lopinavir/ritonavir 100/25 mg tablets, infants and young children should be assessed for the ability to swallow intact tablets. For infants and young children unable to swallow tablets, more suitable formulations containing lopinavir/ritonavir should be checked for their availability.
If more convenient for patients, the lopinavir/ritonavir 200/50 mg tablets may also be considered alone or in combination with the lopinavir/ritonavir 100/25 mg tablet to achieve the recommended dose.
* Body surface area can be calculated with the following equation:
BSA (m^2) = $\sqrt{}$ (Height (cm) X Weight (kg) / 3600)
Children less than 2 years of age
The safety and efficacy of lopinavir/ritonavir in children aged less than 2 years have not yet been established.
Hepatic impairment
In HIV-infected patients with mild to moderate hepatic impairment, an increase of approximately 30% in lopinavir exposure has been observed but is not expected to be of clinical relevance.No data are available in patients with severe hepatic impairment. Lopinavir/ritonavir must not be given to these patients.
Renal impairment
Since the renal clearance of lopinavir and ritonavir is negligible, increased plasma concentrations are not expected in patients with renal impairment. Because lopinavir and ritonavir are highly protein bound, it is unlikely that they will be significantly removed by haemodialysis or peritoneal dialysis.
Pregnancy and postpartum
• No dose adjustment is required for lopinavir/ritonavir during pregnancy and postpartum.
• Once daily administration of lopinavir/ritonavir is not recommended for pregnant women due to the lack of pharmacokinetic and clinical data.
Method of administration
Lopinavir/ritonavir tablets are administered orally and must be swallowed whole and not chewed, broken or crushed. Lopinavir/ritonavir tablets can be taken with or without food.

Interaction with other medcinal poroducts and other forms of interaction:
Lopinavir/Ritonavir tablets contain lopinavir and ritonavir, both of which are inhibitors of the P450 isoform CYP3A in vitro. Co-administration of lopinavir/ritonavir and medicinal products primarily metabolised by CYP3A may result in increased plasma concentrations of the other medicinal product, which could increase or prolong its therapeutic and adverse reactions. Lopinavir/ritonavir does not inhibit CYP2D6, CYP2C9, CYP2C19, CYP2E1, CYP2B6 or CYP1A2 at clinically relevant concentrations .
Lopinavir/ritonavir has been shown in vivo to induce its own metabolism and to increase the biotransformation of some medicinal products metabolised by cytochrome P450 enzymes (including CYP2C9 and CYP2C19) and by glucuronidation. This may result in lowered plasma concentrations and potential decrease of efficacy of co-administered medicinal products.
All interaction studies, when otherwise not stated, were performed using lopinavir/ritonavir capsules, which gives an approximately 20% lower exposure of lopinavir than the 200/50 mg tablets.

Fertility, Pregnancy and Lactation:
Pregnancy
As a general rule, when deciding to use antiretroviral agents for the treatment of HIV infection in pregnant women and consequently for reducing the risk of HIV vertical transmission to the newborn, the animal data as well as the clinical experience in pregnant women should be taken into account in order to characterise the safety for the foetus.
Lopinavir/ritonavir has been evaluated in over 3000 women during pregnancy, including over 1000 during the first trimester.
In post-marketing surveillance through the Antiretroviral Pregnancy Registry, established since January 1989, an increased risk of birth defects exposures with lopinavir/ritonavir has not been reported among over 1000 women exposed during the first trimester. The prevalence of birth defects after any trimester exposure to lopinavir is comparable to the prevalence observed in the general population. No pattern of birth defects suggestive of a common etiology was seen. Studies in animals have shown reproductive toxicity (see section 5.3). Based on the data mentioned, the malformative risk is unlikely in humans. Lopinavir can be used during pregnancy if clinically needed.
Breast-feeding
Studies in rats revealed that lopinavir is excreted in the milk. It is not known whether this medicinal product is excreted in human milk. As a general rule, it is recommended that women living with HIV do not breast-feed their babies in order to avoid transmission of HIV.
Fertility
Animal studies have shown no effects on fertility. No human data on the effect of lopinavir/ritonavir on fertility are available.

Undesirable Effects:
The safety of lopinavir/ritonavir has been investigated in over 2600 patients in Phase II-IV clinical trials, of which over 700 have received a dose of 800/200 mg (6 capsules or 4 tablets) once daily. Along with nucleoside reverse transcriptase inhibitors (NRTIs), in some studies, lopinavir/ritonavir was used in combination with efavirenz or nevirapine.
The most common adverse reactions related to lopinavir/ritonavir therapy during clinical trials were diarrhoea, nausea, vomiting, hypertriglyceridaemia and hypercholesterolemia. The risk of diarrhoea may be greater with once daily dosing of lopinavir/ritonavir. Diarrhoea, nausea and vomiting may occur at the beginning of the treatment while hypertriglyceridaemia and hypercholesterolemia may occur later. Treatment emergent adverse events led to premature study discontinuation for 7% of subjects from Phase II-IV studies.
It is important to note that cases of pancreatitis have been reported in patients receiving lopinavir/ritonavir, including those who developed hypertriglyceridaemia. Furthermore, rare increases in PR interval have been reported during lopinavir/ritonavir therapy

Overdose:
To date, there is limited human experience of acute overdose with lopinavir/ritonavir.
The adverse clinical signs observed in dogs included salivation, emesis and diarrhoea/abnormal stool. The signs of toxicity observed in mice, rats or dogs included decreased activity, ataxia, emaciation, dehydration and tremors.
There is no specific antidote for overdose with lopinavir/ritonavir. Treatment of overdose with lopinavir/ritonavir is to consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. If indicated, elimination of unabsorbed active substance is to be achieved by emesis or gastric lavage. Administration of activated charcoal may also be used to aid in removal of unabsorbed active substance. Since lopinavir/ritonavir is highly protein bound, dialysis is unlikely to be beneficial in significant removal of the active substance.

Storage:
Store protected from moisture at a temperature not exceeding 25°C.

Keep medicines out of reach of children.

Presentation: A pack of 20 Tablets

Manufactured by:

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