

Crixivan (indinavir)



Crixivan 400-mg capsules are semitranslucent white capsules coded with "CRIXIVAN™ 400 mg" in green. Other dose formulations of Crixivan are available. Dosing may vary.



Also known as: Crixivan sulfate, IDV, MK639, L-735,524

Background and description. Crixivan is a protease inhibitor manufactured by Merck & Co., Inc. It was granted accelerated approval for use in combination with nucleoside reverse transcriptase inhibitors (NRTIs) by the US Food & Drug Administration (FDA) in March 1996.

Dose. The recommended dose of Crixivan is 800 mg (two 400 mg capsules) every 8 hours. Twice-a-day dosing is possible using Norvir to boost levels of Crixivan, but an optimal dosing regimen is still being studied, as are any potential dangers due to increased side effects from Crixivan.

Food restrictions. Crixivan must be taken without food, but with water, 1 hour before or 2 hours after a meal. It may also be taken with other liquids such as skim milk, juice, coffee, or tea or with a light meal. Patients taking Crixivan should drink approximately 48 ounces of liquids every 24 hours.

Storage. Crixivan should be stored in a tightly closed container at room temperature (59° to 86°F) and protected from moisture.

Patient assistance. Merck offers a patient assistance program for those who qualify. For more information call 800.850.3430.

Side effects and toxicity. The major side effect of Crixivan is the formation of kidney stones (nephrolithiasis), pain on urination (dysuria), and back and flank pain. Proper hydration may prevent the symptoms. Additionally, sustained creatinine elevations have been reported with long-term use of Crixivan. Metabolic (lipid and glucose) and morphologic (fat accumulation and fat atrophy) abnormalities have been associated with protease inhibitors in general. Both Crixivan and Reyataz are associated with increased levels of indirect ("unconjugated") bilirubin in the body (which can give a person a yellow-ish appearance). Therefore, taking these two protease inhibitors in the same regimen is not recommended. Other side effects that have been reported with Crixivan include hair

and toenail problems, allergic or skin reactions, changes in skin color, joint pain, etc. Pregnant women should not take Crixivan.

Drug interactions. Caution should be taken when Crixivan is given with calcium channel blockers, antiarrhythmics, anticonvulsants, or steroids. Crixivan should not be taken with the following: Propulsid (cisapride), Halcion (triazolam), Versed (midazolam), Cordarone (amiodarone), ergot derivatives (Wigraine, Cafergot, Migranal, Ergotrate, Methergine, DHE 45, etc.), and the lipid-lowering drugs Zocor (simvastatin) and Mevacor (lovastatin). Lipid-lowering drugs such as Lipitor (atorvastatin), Pravachol (pravastatin), or Lescol (fluvastatin) should be used with caution. Nizoral (ketoconazole) inhibits the metabolism of Crixivan and a dose reduction of Crixivan to 600 mg every 8 hours is recommended when combining the 2 drugs. Similarly the dose of Mycobutin (rifabutin) should be reduced by 50% when used with Crixivan. A lower dose of Desyrel (trazodone hydrochloride) should be considered when taken with Crixivan. Rifadin or Rimactane (rifampin) has been shown to decrease Crixivan levels in the body by 80%. Crixivan increases the levels of Viagra (sildenafil), Cialis (tadalafil), and Levitra (vardenafil)—and the risk of side effects of these agents—and dose reductions are recommended if taken with Crixivan. Also, St. John's Wort (*Hypericum perforatum*) is likely to decrease Crixivan levels in the body and therefore should be avoided when taking Crixivan.

Consideration should be given to increasing the Crixivan dose to 1000 mg every 8 hours when combined with Sustiva or Viramune. Rescriptor increases the levels of Crixivan; some studies have used reduced doses (400 or 600 mg) of Crixivan with 400 mg of Rescriptor 3 times a day to compensate for this increase. In addition, the buffering agent in original-formulation Videx interferes with the absorption of Crixivan and thus the drugs should be taken at least 1 hour apart. Finally, combining Crixivan with Viracept results in an increase in Crixivan levels. Studies have used 1250 mg of Viracept with 1200 mg of Crixivan twice a day with a low-fat snack.

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Additional info:

Resistance and cross-resistance. Mutations at positions 82 and 90 are most associated with treatment failure. Other mutations can occur at positions 20, 24, 48, 54, and 84. Resistance to Crixivan can lead to cross-resistance to other protease inhibitors.

Clinical data. The approval of Crixivan was based on 3 studies. The Merck 035 study showed durable long-term efficacy of the combination Crixivan/Retrovir/Epivir for the management of HIV. Up to 2 years after beginning triple-combination therapy, 78% of subjects had viral loads below 500 copies/mL, while 66% of subjects had viral loads below 50 copies/mL.

ACTG 320 compared Crixivan/Retrovir/Epivir versus Retrovir/Epivir. The study enrolled 1156 patients. It was terminated after an interim analysis, resulting in a median follow-up of 38 weeks. The percentages of patients with AIDS-defining illnesses or death were as follows: 35% progressed to an illness and 10% died in the Crixivan/Retrovir/Epivir arm; and 63% progressed to an illness and 19% died in the Retrovir/Epivir arm.

Study 028 was conducted in Brazil and enrolled 996 antiretroviral-naïve patients who were randomized to 1 of 3 arms: Crixivan/Retrovir, Crixivan alone, or Retrovir alone. Treatment regimens containing Retrovir were modified in a blinded manner with the optional addition of Epivir. The study was terminated after an interim analysis, resulting in a median follow-up of 56 weeks. The percentages of patients with AIDS-defining illnesses or death were as follows: 21% progressed to an illness and 8% died in the Crixivan/Retrovir arm; 27% progressed to an illness and 5% died in the Crixivan-alone

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To contact The Center for AIDS,
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