

PART III: CONSUMER INFORMATION

Pr **CRIXIVAN**[®]

indinavir sulfate capsules

This leaflet is part III of a three-part "Product Monograph" published when CRIXIVAN[®] was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about CRIXIVAN[®]. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Your physician has prescribed CRIXIVAN[®] for you because you have HIV infection. CRIXIVAN[®] can help reduce your chances of getting illnesses associated with HIV infection. CRIXIVAN[®] can also help lower the amount of HIV in your blood (called "viral load") and raise your CD4 (T) cell count. CRIXIVAN[®] may not have these effects in all patients.

HIV is a blood-borne disease spread by contact with blood or sexual contact with an infected individual.

What it does:

CRIXIVAN[®] is a member of a class of drugs called protease inhibitors. It is active against the Human Immunodeficiency Virus (HIV) helping to reduce the amount of virus within the body.

When it should not be used:

- a) Do not take CRIXIVAN[®] if you experience a severe allergic reaction to any component of the drug (see What the important nonmedicinal ingredients are).
- b) Do not take CRIXIVAN[®] with alfuzosin, atazanavir, alprazolam, amiodarone, cisapride (no longer marketed in Canada), ergot derivatives, lovastatin, oral (taken by mouth) midazolam, pimozone, rifampin, sildenafil when used to treat pulmonary arterial hypertension, simvastatin, St. John's wort (*Hypericum perforatum*), and triazolam.

What the medicinal ingredient is:

Indinavir sulfate

What the important nonmedicinal ingredients are:

Each capsule contains the following non-medicinal ingredients: anhydrous lactose (as a dry binder/filler), magnesium stearate (as a lubricant); gelatin, and titanium dioxide (empty capsule shell).

What dosage forms it comes in:

CRIXIVAN[®] is available as white semi-translucent capsules containing either 200 or 400 mg of indinavir as the active ingredient.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

A kidney condition (nephrolithiasis or urolithiasis, e.g. kidney stones) has occurred with Crixivan use. Contact your doctor immediately if symptoms such as flank (back) pain, bloody urine, or painful urination occur, often associated with fever, nausea or vomiting (see Side Effects and What to Do About Them).

BEFORE you use CRIXIVAN[®] talk to your doctor if:

- You have past or present medical problems, including liver or kidney problems, diabetes, hemophilia, high cholesterol and if you are taking cholesterol-lowering medicines called "statins".
- You are taking or plan to take any medication, such as non-prescription drugs or natural health products including herbs or dietary supplements. Some medicines should not be taken with CRIXIVAN[®] or may require a dosage adjustment (see Interactions with this medication).
- You are pregnant or planning to become pregnant. It is not known whether taking CRIXIVAN[®] may be harmful to an unborn baby. If you are pregnant, you should take CRIXIVAN[®] only if your doctor decides it is needed.
- You are breastfeeding or planning to do so. You should not breastfeed while taking CRIXIVAN[®]. Consult your doctor.
- You have problems with galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption, do not take CRIXIVAN[®] as this product contains lactose.

Other Warnings

- CRIXIVAN[®] is not a cure for HIV infection and you may continue to develop infections or other illnesses associated with HIV disease. Continue to see your doctor regularly and report any medical problems you have.
- CRIXIVAN[®] does not prevent a patient infected with HIV from passing the virus to other people. To protect others, you must continue to practice safe sex and take precautions to prevent others from coming into contact with your blood and other body fluids.

- The long term effects of CRIXIVAN[®] are unknown. Treatment with CRIXIVAN has not been shown to reduce the risk of transmission of HIV to others through sexual contact or blood contamination.

treatment with CRIXIVAN[®]. If you experience these you should avoid driving or operating machinery.

INTERACTIONS WITH THIS MEDICATION

Medications that may **not** be taken with CRIXIVAN[®] because it could result in serious or life-threatening events (such as problems with heart rhythm or excessive sleepiness) are amiodarone (e.g. Cordarone*), alprazolam (e.g. Xanax*), triazolam (e.g. Halcion*), cisapride, midazolam (e.g. Versed*), pimozide (e.g. Orap*), rifampin (e.g. Rifadin*, Rifater*, Rimactane*) and ergot medications (e.g. Cafergot*, Ergomar*, Wigraine*), lovastatin (e.g. Mevacor*), and simvastatin (e.g. Zocor*). Consult your physician before taking CRIXIVAN[®] with any other medication.

If you are taking protease inhibitors including CRIXIVAN[®], you should not be taking some of the cholesterol-lowering medicines called “statins” (e.g. lovastatin, simvastatin, rosuvastatin) as severe muscle pain and weakness have occurred or may occur when these drugs are taken together. Consult your physician if you have further questions.

Do not take CRIXIVAN[®] with St. John’s wort (*Hypericum perforatum*), an herbal supplement, or products containing St. John’s wort, as it may decrease the effect of CRIXIVAN[®] or other HIV-related drugs.

CRIXIVAN[®] may be taken with a number of medications that are commonly used by people with HIV infection. These include zidovudine (AZT*, e.g. Retrovir*), didanosine (ddl, e.g. Videx*), lamivudine (e.g. 3TC*), stavudine (d4T, e.g. Zerit*), fluconazole (e.g. Diflucan*), isoniazid, clarithromycin (e.g. Biaxin*), trimethoprim/sulfamethoxazole (e.g. Bactrim*, Roubac*, Septra*), and methadone.

Other medications may be taken with CRIXIVAN[®] but require dosage adjustment of that medication or of CRIXIVAN[®]. These include rifabutin (e.g. Mycobutin*), ketoconazole (e.g. Nizoral*), itraconazole (e.g. Sporanox*), delavirdine (e.g. Rescriptor*), efavirenz (e.g. Sustiva*) and midazolam administered by injection.

Tell your doctor if you are taking bosentan, colchicine, rosuvastatin, or salmeterol.

Tell your doctor if you are taking ritonavir.

Tell your doctor if you are taking calcium channel blockers (drugs to treat hypertension or chest pain).

Tell your doctor if you are taking venlafaxine (e.g. Effexor*).

Tell your doctor if you are taking trazodone (e.g. Desyrel*).

Tell your doctor if you are taking sildenafil (e.g. Viagra*), tadalafil (e.g., Cialis*) or vardenafil (e.g., Levitra*).

Can I drive or operate machinery while using CRIXIVAN[®]? Dizziness and blurred vision have been reported during

PROPER USE OF THIS MEDICATION

Usual dose:

CRIXIVAN[®] is in capsule form and must be taken orally. Take 800 mg (usually given as two 400 mg capsules) at regular 8-hour intervals. CRIXIVAN[®] must be taken at intervals of 8 hours for full effectiveness. It is very important to take CRIXIVAN[®] exactly as prescribed to help ensure full effectiveness of the product. Do not stop taking it without first telling your doctor.

CRIXIVAN[®] should be taken with water 1 hour before or 2 hours after a meal. If water is not preferred, CRIXIVAN[®] can be taken with skimmed or fat-free milk, juice, coffee, or tea; or a light meal such as dry toast and jam or fruit conserve, juice and coffee with skimmed or fat-free milk and sugar; or corn flakes, skimmed or fat-free milk and sugar. At any other time you can follow your regular diet.

Taking CRIXIVAN[®] with a meal that is high in calories, fat and protein reduces your body’s ability to absorb the drug and in turn reduces its effectiveness.

It is important for adults to drink at least 1.5 liters (approximately 48 ounces) of liquids during each day to ensure adequate hydration. This may help reduce the incidence of kidney stones (see SIDE EFFECTS AND WHAT TO DO ABOUT THEM).

If you take didanosine with CRIXIVAN[®], take them at least one hour apart on an empty stomach.

Overdose:

If you take too much CRIXIVAN[®], contact your doctor, regional poison control centre or you hospital emergency department.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

Take CRIXIVAN[®] 3 times a day at regular 8-hour intervals. However, if you miss a dose by more than 2 hours, do not take it later in the day. Simply continue to follow your usual schedule. Do not take a double dose of CRIXIVAN[®].

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Any medicine may have unintended or undesirable effects, so-called side effects. CRIXIVAN[®] has been shown to be generally well tolerated. There have been reports of kidney stones and in some of these patients this led to more severe kidney problems including kidney failure. In most cases, kidney impairment and kidney failure were temporary and reversible. Call your physician if you develop sudden severe back pain, with or without blood in the urine caused by kidney stones.

* Cisapride is no longer marketed in Canada.

Some patients treated with CRIXIVAN® have had rapid breakdown of red blood cells (also called hemolytic anemia) which in some cases was severe or resulted in death.

Some patients treated with CRIXIVAN® have had liver problems including liver failure and death. Some patients had other illnesses or were taking other drugs. It is uncertain if CRIXIVAN® caused these liver problems.

Other side effects include weakness/fatigue; low red blood cell count; heart problems including heart attack; abdominal pain/swelling; inflammation of the pancreas; inflammation of the kidneys; infection of the kidneys; decreased kidney function; diarrhea; upset stomach; nausea; dizziness; headache; dry skin; change in skin color; hair loss; ingrown toenails with or without infection; crystals in the urine; numbness of the mouth; rash; severe skin reactions; allergic reactions; and taste perversion.

Changes in body fat have been seen in some patients taking antiretroviral therapy. These changes may include increased amount of fat in the upper back and neck (“buffalo hump”), breasts, and around the trunk. Loss of fat from the legs, arms, and face may also happen. The cause and long-term effects of these conditions are not known at this time.

In some patients with hemophilia, increased bleeding has been reported.

There have been reports of diabetes and increased blood sugar (also called hyperglycemia) in patients treated with protease inhibitors. In some of these patients, this led to ketoacidosis, a serious condition resulting from poorly controlled blood sugar. Before starting protease inhibitors, some patients already had diabetes, others did not. Some patients required adjustments to their diabetes medication. Other patients needed new diabetes medication.

Your physician has a more complete list of side effects.

Tell your physician promptly about these or any other unusual symptoms. If the condition persists or worsens, seek medical attention.

In addition, tell your physician if you experience any symptoms that suggest an allergic reaction after taking CRIXIVAN®.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Kidney problems including kidney stones, kidney failure and symptoms such as back pain, blood in the urine		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
	Hemolytic anemia, the rapid breakdown of blood cells and symptoms such as jaundice and dark urine		✓	
Uncommon	Severe allergic reaction/ difficulty of breathing			✓
	Increased bleeding in hemophiliacs		✓	
	New onset/ worsening of diabetes		✓	
Uncommon	Hepatitis		✓	

This is not a complete list of side effects. For any unexpected effects while taking CRIXIVAN®, contact your doctor or pharmacist.

Other considerations

Although CRIXIVAN® is not a cure for HIV infection, CRIXIVAN® can help increase the amount of time you will spend living without disease associated with HIV.

In some patients with advanced HIV infection (AIDS) and a history of opportunistic infection, signs and symptoms of inflammation from previous infections may occur when combination antiretroviral treatment is started.

See your physician for more details.

HOW TO STORE IT

Protect from moisture.

- Keep CRIXIVAN® capsules in the bottle they came in and at room temperature (15°C-30°C).
- Keep CRIXIVAN® capsules dry by leaving the small desiccant in the bottle. Keep the bottle closed.

Keep all medicines out of the reach of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect

or at Merck Canada Inc. by one of the following 2 ways:

- Call toll-free at 1-800-567-2594
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-800-369-3090, or
 - Mail to: Merck Canada Inc.
Pharmacovigilance
P.O. Box 1005
Pointe-Claire–Dorval, QC H9R 4P8

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program or Merck do not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

www.merck.ca

or by contacting the sponsor, Merck Canada Inc., at: 1-800-567-2594.

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