

CRIXIVAN[®] *indinavir sulphate*

(200 mg & 400 mg capsules)



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• NEW ZEALAND •

What is in this leaflet

This leaflet answers some common questions about CRIXIVAN. It does not contain all the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you taking CRIXIVAN against the benefits they expect it will have for you.

If you have any concerns about taking this medicine, ask your doctor, pharmacist or treatments officer at your local NZ AIDS Foundation.

Keep this leaflet with the medicine. You may need to read it again.

What CRIXIVAN is used for

CRIXIVAN, a protease inhibitor, is used to help treat HIV (Human Immunodeficiency Virus) infection. It should be used in combination with other appropriate medicines used to treat the HIV virus, including zidovudine (AZT, Retrovir), didanosine (ddl, Videx) or lamivudine (3TC).

CRIXIVAN belongs to a group of medicines called HIV protease inhibitors. It works in a different way to the other medicines used to treat HIV. CRIXIVAN works by interrupting the formation of new HIV particles in already infected cells. When HIV is attacked by CRIXIVAN, the virus is not able to reproduce normally. This helps reduce the amount of virus in the body and helps protect new cells from infection.

CRIXIVAN helps reduce the amount of virus in the body and thus increases the CD4

count, it also improves survival and slows the progression of the disease.

You may continue to develop infections or other illnesses associated with HIV disease while you are taking CRIXIVAN.

Before you take CRIXIVAN

When you must not take it

Do not take CRIXIVAN if:

- you have an allergy to CRIXIVAN or any of the ingredients listed at the end of this leaflet
- the packaging is torn or shows signs of tampering
- the expiry date on the pack has passed. If you take this medicine after the expiry date has passed, it may not work.

If you are not sure whether you should start taking CRIXIVAN, talk to your doctor.

Do not give CRIXIVAN to children
Safety and effectiveness in children have not been established.

Before you start to take it

Tell your doctor if you:

- have any allergies to any other medicines or any other substances, such as foods, preservatives or dyes
- have any medical conditions, especially:
 - liver disease due to cirrhosis
 - diabetes mellitus
 - haemophilia
- are pregnant or intend to become pregnant.

It is not known whether CRIXIVAN is harmful to an unborn baby when taken by a pregnant woman. If there is a need to take CRIXIVAN when you are pregnant

your doctor will discuss the risks and benefits to you and the unborn baby.

- are breast-feeding or plan to breast-feed. It is not known whether CRIXIVAN passes into breast milk. Because certain medicines pass into breast milk, if you are taking CRIXIVAN your doctor will tell you to stop breast feeding.
- are taking atazanavir
- are taking cholesterol-lowering medicines, called "statins".

If you have not told your doctor about any of the above, tell them before you take any CRIXIVAN.

Taking other medicines

Tell your doctor if you are taking any other medicines, including medicines that you buy without a prescription from your pharmacy, supermarket or health food shop, such as herbal products, or dietary supplements.

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

Tell your doctor if you are taking venlafaxine.

Tell your doctor if you are taking trazodone.

Tell your doctor if you are taking sildenafil, tadalafil, or vardenafil.

Tell your doctor if you are taking ritonavir.

Some medicines should not be taken with CRIXIVAN as they may cause a life-threatening interaction. These include:

- amiodarone (Cordarone*), used to treat an irregular heartbeat
- terfenadine (Teldane*) and astemizole (Hismanal*), antihistamines used for hay fever and other allergic conditions
- cisapride (Prepulsid*), used to treat stomach reflux
- alprazolam (Xanax*), triazolam (Halcion*, Hypam*, Trycam*), used to treat anxiety, depression or for sleeplessness

- oral (taken by mouth) midazolam (Hypnovel*), used as a sedative before surgical procedures
- some medicines used to treat migraine, including Cafergot, Cafergot S, Ergodryl
- pimozide

In addition, rifampicin (Rifadin*, Rifinah*, Rifacin*) an antibiotic used to treat TB and infections caused by MAC, should not be taken with CRIXIVAN.

Some medicines and CRIXIVAN may interfere with each other. These include:

- rifabutin (Mycobutin*), an antibiotic used to treat TB and infections caused by MAC (*M. avium intracellulare* complex)
- ketoconazole (Nizoral*), used to treat fungal infections
- fluoxetine (Prozac*) and sertraline (Zoloft*), used to treat depression
- erythromycin, an antibiotic used to treat bacterial infections
- diltiazem, nifedipine, and verapamil, used to treat high blood pressure and angina
- phenytoin (Dilantin*), carbamazepine (Tegretol*, Teril*), and phenobarbitone, used to treat epilepsy
- dexamethasone, a corticosteroid medicine
- itraconazole (Sporanox*), used to treat fungal infection
- efavirenz, used to treat HIV infection. The optimal dose of indinavir when given in combination with efavirenz is not known.
- midazolam (Hypnovel*) administered by injection, used as a sedative before surgical procedures

These medicines may be affected by CRIXIVAN, or may affect how well it works. You may need different amounts of your medicine, or you may need to take different medicines.

Taking CRIXIVAN with St. John's wort (*Hypericum perforatum*), an herbal product sold as a dietary supplement, or products containing St. John's wort, is not recommended as it may decrease the effect of CRIXIVAN or other HIV-related medicines.

Some medicines may interfere with the absorption of CRIXIVAN. This includes:

- didanosine (ddI).

Take CRIXIVAN and didanosine at least one hour apart on an empty stomach.

Make sure your doctor and pharmacist know about all of the medicines you are taking, as they have more information on medicines to be careful with or avoid while taking CRIXIVAN.

How to take CRIXIVAN

How much to take

Take CRIXIVAN only when prescribed by your doctor. Your doctor will tell you how many capsules you need to take each day.

The normal adult dose is two 400 mg capsules (that is, 800 mg) taken every eight hours. It is important that you are started and continue on this dose.

However, this dose may be decreased if you have liver disease due to cirrhosis or are taking certain medicines, such as ketoconazole. Your doctor will discuss the risks and benefits of decreasing the dose because dosage reduction may be associated with a decrease in effectiveness against the HIV infection.

Carefully follow all directions given to you by your doctor. They may differ from the information contained in this leaflet.

If you do not understand the instructions on the bottle, ask your doctor or pharmacist for help.

What to take with it

The period around taking your capsules is the 'dose window' - when you must watch what you eat and drink. Remember 3-2-1:
3 hour period made up of:

2 hours before each dose
1 hour after each dose

Swallow CRIXIVAN with a full glass of water or other liquid.

Swallowing CRIXIVAN with water ensures maximum absorption and effectiveness. However, if you do not like water, CRIXIVAN can be swallowed with skim milk, juice (except grapefruit), coffee or tea.

Do not drink grapefruit juice within a dose window.

Grapefruit juice significantly reduces the absorption of CRIXIVAN, therefore decreasing its effectiveness.

If you need to eat within a dose window make sure it's only small amounts of light food.

CRIXIVAN is absorbed well enough with small amounts of light food. Examples of light food are dry toast with jam, juice (except grapefruit) and coffee with skim milk and sugar, or corn flakes with skim milk and sugar.

Taking CRIXIVAN with a meal that is high in calories, fat and protein reduces your body's ability to absorb the medicine and in turn reduces its effectiveness. You can indulge in high energy foods outside the 3-hour dose window.

However, taking CRIXIVAN on an empty stomach improves absorption. This means not eating during the 3-hour dose window.

Ideal practice - do not eat for two hours before and one hour after taking your dose.

Good practice - if you need to eat during a 3-hour dose window make sure it's only small amounts of light food.

Unacceptable practice - do not eat heavy food (high-fat, high-protein, high-calorie) during the 3-hour dose windows.

When to take it

Take CRIXIVAN at regular eight-hour intervals, at about the same time each day. Keeping to the 8-hour interval between doses of CRIXIVAN is important because keeping a constant level of CRIXIVAN in the body helps prevent resistance. Resistance means that the medicine may lose its effectiveness over time.

How long to take it

Continue to take CRIXIVAN for as long as your doctor prescribes. CRIXIVAN helps control your HIV infection but does not cure it. Therefore CRIXIVAN must be taken every day.

Do not stop taking CRIXIVAN or change the dose without first checking with your doctor. Do not let yourself run out of medicine over weekends or on holidays. If you have a break in therapy or reduce your dose temporarily, the virus may develop resistance and therefore CRIXIVAN may no longer be effective.

If you forget to take it

If you miss a dose, but remember within two hours, then take the missed dose, otherwise skip it and then go back to taking your capsules as you would normally.

If you are not sure whether to skip the dose, talk to your doctor or pharmacist.

Do not take a double dose to make up for the dose that you missed.

If you have trouble remembering to take your capsules, ask your pharmacist for some hints.

If you take too much (overdose)

Immediately telephone your doctor or the National Poisons Centre (telephone 0800 POISON or 0800 764 766) for advice, or go to accident and emergency at your nearest hospital, if you think that you or anyone else may have taken too much CRIXIVAN. Do this

even if there are no signs of discomfort or poisoning.

While you are using CRIXIVAN

Things you must do

It is important for adults to drink at least six (6) full glasses of liquid a day (1.5 litres) to keep your kidneys flushed and your urine pale.

This is to help reduce the possibility of kidney stones, which may be caused by the capsules. What you drink throughout the day depends on whether you are inside or outside your dose windows. Outside your dose windows you can indulge in any drink to help keep your fluids up. But remember, too much tea, coffee and alcohol can cause dehydration. Try to get used to ordering a glass of water to drink with them. Remember, you have to drink even more fluid if you are exercising, dancing or are in a hot climate.

If you have diabetes, tell your doctor if you notice symptoms of high blood glucose levels. There have been some reports of diabetes and increased blood glucose, also called hyperglycaemia, in people treated with protease inhibitors. In some of these people this led to ketoacidosis, a serious condition resulting from poorly controlled blood glucose. Before starting protease inhibitors, some people already had diabetes, others did not. Some people required adjustments to their diabetes medicines, while others needed new diabetes medicines.

Report any changes in your condition to your doctor immediately. This is to make sure that any infections which occur due to your low immunity (called opportunistic infections) are treated promptly.

Continue to use safer sexual practices. CRIXIVAN has not been shown to decrease

the chance of transmitting HIV to a sexual partner.

If you are about to be started on any new medicine tell your doctor and pharmacist that you are taking CRIXIVAN.

Tell all the doctors, dentists and pharmacists who are treating you that you are taking CRIXIVAN.

If you become pregnant while taking CRIXIVAN tell your doctor.

Things you must not do

Do not stop taking CRIXIVAN or change the dose without first checking with your doctor. Do not let yourself run out of medicine over weekends or on holidays. If you have a break in therapy or reduce your dose temporarily, the virus may develop resistance and therefore CRIXIVAN may no longer be effective.

Do not give CRIXIVAN to anyone else, even if they have the same condition as you.

Things to be careful of

Be careful driving or operating machinery until you know how CRIXIVAN affects you. CRIXIVAN generally does not cause problems with your ability to drive a car or operate machinery. However, as with many medicines, CRIXIVAN may cause dizziness in some people. Make sure you know how you react to CRIXIVAN before you drive a car or operate machinery.

Be careful of what you eat and drink during dose windows.

Adverse Effects

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are taking CRIXIVAN.

CRIXIVAN helps most people with HIV infection, but it may have unwanted adverse

effects. All medicines can have adverse effects. Sometimes they are serious, most of the time they are not. You may need medical treatment if you get some of the adverse effects.

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.

Frequently it is difficult to tell whether adverse effects are the result of taking CRIXIVAN, effects of the HIV disease or adverse effects of other medicines you may be taking. For this reason it is very important to inform your doctor of any change in your condition. Your doctor may want to change your dose or advise you to stop taking CRIXIVAN.

Ask your doctor or pharmacist to answer any questions you may have.

Tell your doctor if you have any of the following and they worry you:

- heartburn
- low red blood cell count
- stomach pain, discomfort, or swelling
- nausea, vomiting, diarrhoea, wind
- tiredness, weakness
- dizziness, headache
- skin problems such as dry skin, itching, rash, change in skin colour
- increased fat appearing in areas such as the back of the neck, breasts, stomach and back
- loss of body fat from areas such as face, arms and legs
- hair loss or thinning
- dry mouth, change in your taste
- difficulty sleeping
- swollen glands
- ingrown toenails with or without infection of the nail bed

These are usually mild adverse effects.

Tell your doctor immediately or go to accident and emergency at your nearest hospital if you develop any of the following:

- sudden severe back pain, with or without blood in the urine, which may be caused by an inflammation of the kidneys or kidney stones, infection of the kidneys or decreased kidney function
- crystal formations appearing in your urine
- tingling or numbness of the mouth
- swelling of the face, lips, mouth, throat or tongue which may cause difficulty in swallowing or breathing
- any severe skin reaction
- pinkish, itchy swellings on the skin, also called hives or nettlerash
- high blood glucose levels, which may cause excessive thirst and/or eating, and passing large amounts of urine
- yellowing of the skin and/or eyes which may be caused by liver problems
- a serious form of anaemia that includes symptoms such as fatigue, yellowing of the skin and/or eyes, being short of breath when exercising, and looking pale
- severe muscle pain and weakness, especially in conjunction with statins (cholesterol lowering medication)
- pain in your chest and/or pain radiating down your left arm which may be caused by problems with your heart
- numbness or weakness of the arms or legs, headache, dizziness and confusion, visual disturbance, difficulty swallowing, slurred speech and loss of speech which may indicate you are having a stroke.

Because these adverse effects are serious, you may need urgent medical attention.

If you have haemophilia, tell your doctor immediately if you notice any increased bleeding. There have been some reports of bleeding episodes in people with haemophilia who are taking CRIXIVAN or other protease inhibitors.

Other adverse effects not listed above may also occur in some patients. The long-term

effects of CRIXIVAN are unknown at this time. Tell your doctor if you notice any other effects.

Do not be alarmed by this list of possible adverse effects. You may not experience any of them.

After using CRIXIVAN

Storage

Keep your capsules in the original bottle until it is time to take them. If you take the capsules out of the bottle they may not keep well, as they are affected by moisture. The original bottle contains a desiccant (silica gel in a small container) to help remove the moisture. Do not remove the desiccant from the bottle.

Keep CRIXIVAN in a cool dry place where the temperature stays below 30°C. Do not store it or any other medicine in the bathroom or near a sink. Do not leave it in the car or on window sills. Heat and dampness can destroy some medicines.

Keep it where children cannot reach it. A locked cupboard at least one-and-a-half metres above the ground is a good place to store medicines.

Disposal

If your doctor tells you to stop taking the capsules, or the capsules have passed their expiry date, ask your pharmacist what to do with any that are left over.

Product description

What it looks like

CRIXIVAN comes in two strengths:

- 200 mg - semi-translucent white capsule with CRIXIVAN™ 200 mg marked in blue on the capsule

- 400 mg - semi-translucent white capsule with CRIXIVAN™ 400 mg marked in green on the capsule

A bottle of CRIXIVAN 200 mg contains 360 capsules.

A bottle of CRIXIVAN 400 mg contains 180 capsules.

Ingredients

Active ingredient:

- indinavir sulfate

Inactive ingredients:

- lactose
- magnesium stearate
- gelatin
- titanium dioxide
- silicon dioxide
- sodium lauryl sulfate

CRIXIVAN does not contain gluten, sucrose, tartrazine or any other azo dyes.

Supplier

CRIXIVAN is supplied in New Zealand by:

Merck Sharp & Dohme (New Zealand)
Limited
P O Box 99 851
Newmarket
Auckland
NEW ZEALAND
Tel: 0800 500 673

This leaflet was prepared in May 2009

CP-CRX-0409(150509)

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* Trade name