

APTIVUS®

Soft Capsules and Oral Solution

Tipranavir

Consumer Medicine Information (CMI)

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This leaflet answers some common questions about Aptivus.

It does not contain all the available information.

It does not take the place of talking to your doctor or pharmacist.

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

Ask your doctor or pharmacist if you have any questions about your medicine or if you have any trouble before, during or after using Aptivus.

This leaflet was last updated on the date at the end of this leaflet. More recent information may be available. The latest Consumer Medicine Information is available from your pharmacist, doctor, or from www.medicines.org.au and may contain important information about the medicine and its use of which you should be aware.

Keep this information with your Aptivus.

You may need to read it again later.

What Aptivus is used for

Aptivus is used in the treatment of the infection caused by the Human Immunodeficiency Virus (HIV-1). HIV-1 is the main virus responsible for the development of Acquired Immunodeficiency Syndrome (AIDS).

Aptivus contains the active ingredient Tipranavir. Tipranavir belongs to a group of antiretroviral medicines called protease inhibitors. Tipranavir helps control HIV infection by

inhibiting or interfering with the protease enzyme that the HIV virus needs to multiply.

Aptivus does not cure or prevent HIV-1 infection or AIDS, but it does hinder the growth of HIV-1.

Aptivus is prescribed for use in combination with low-dose Ritonavir and other antiretrovirals.

When these medicines are taken with Aptivus, the growth of HIV-1 is hindered more effectively.

Aptivus has not been shown to reduce the incidence or frequency of the illnesses caused by AIDS. It is important for you to continue seeing your doctor regularly.

Aptivus does not reduce the risk of or prevent transmission of HIV-1 to others through sexual contact or blood contamination.

Before you take Aptivus

When you must not take Aptivus

Do not take Aptivus if you are allergic to tipranavir or any of the other ingredients in Aptivus.

These ingredients are listed in full at the end of this leaflet. This includes rare inherited conditions of fructose intolerance for the Aptivus capsules.

If you are not sure if you have these allergies, you should raise those concerns with your doctor.

Do not take Aptivus if you have moderate to severe liver problems.

Do not take Aptivus if you are taking certain other medicines which include:

- **amiodarone, bepridil, flecainide, propafenone, quinidine**
 - used to treat irregular heart beats (antiarrhythmics)
- **astemizole, terfenadine**
 - used to treat allergic conditions such as hay fever (antihistamines)
- **dihydroergotamine, ergonovine, ergotamine, methylergonovine**
 - used to treat migraine (ergot derivatives)
- **cisapride**
 - used to treat stomach reflux or gastroparesis
- **pimozide**
 - used to treat chronic psychotic disorders
- **midazolam**
 - used as a sedative during medical procedures
- **triazolam**

- used to treat sleeping problems
- **alfuzosin, sildenafil**
- when used to treat pulmonary arterial hypertension

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

Do not take Aptivus after the expiry date on the carton or bottle has passed.

Do not take Aptivus if the packaging is torn or shows signs of tampering.

Before you start to take Aptivus

It is essential that your doctor knows your medical history before prescribing Aptivus.

Before taking Aptivus, you must tell your doctor if you have, or have had, any of the following conditions:

- liver problem/disease or hepatitis
- haemophilia or other medical condition where the risk of bleeding is increased e.g. trauma, surgery, taking antiplatelet agents or anticoagulants
- diabetes mellitus
- high blood levels of cholesterol or triglycerides
- allergy to sulfonamides (sulfa medicines)

If you are not sure if you have, or have had, any of these conditions, you should raise those concerns with your doctor.

Taking other medicines

Before using Aptivus, it is important to tell your doctor if you are taking any other medicines, obtained with or without a doctor's prescription.

In particular, you should tell your doctor if you are taking:

- other anti-HIV medicines
- antacids
- antibiotics (e.g. clarithromycin, disulfiram/metronidazole, rifabutin, rifampicin)
- anticoagulants (e.g. warfarin), antiplatelet agents or medicine used to prevent blood clots (e.g. aspirin)
- antidepressants (e.g. despiramine, trazadone, fluoxetine, paroxetine, sertraline)
- antifungals (e.g. fluconazole, itraconazole, ketoconazole, voriconazole)
- anti-gouts (e.g. colchicine)
- cholesterol lowering medicines (e.g. atorvastatin, lovastatin, simvastatin, rosuvastatin, pravastatin)

- medicines used to treat Type 2 diabetes (e.g. glibenclamide, glimepiride, glipizide, pioglitazone, repaglinide, tolbutamide)
- disulfiram
- fluticasone propionate
- omeprazole
- bosentan, a medicine used to treat hypertension
- salmeterol, a medicine used for asthma
- valaciclovir, a medicine used to treat herpes
- immunosuppressants (e.g. cyclosporin, sirolimus, tacrolimus)
- medicines used to treat erectile dysfunction (e.g. sildenafil, tadalafil, vardenafil)
- loperamide
- methadone
- oral contraceptives
- oestrogens for hormone replacement (Ethinyl estradiol)
- pethidine
- herbal medicines derived from St John's Wort (*Hypericum perforatum*)

- buprenorphine/naloxone
- bupropion
- theophylline
- vitamin E supplements.

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

Your doctor or pharmacist will advise you.

As Aptivus may reduce the effectiveness of oral contraceptives, talk to your doctor about alternative methods of contraception.

Pregnancy

Ask for your doctor's advice if you are pregnant, or likely to become pregnant during your course of medication.

Your doctor will discuss the risks and benefits of taking Aptivus during pregnancy.

Breastfeeding

You should ask for your doctor's advice if you wish to breastfeed during your use of Aptivus.

Breastfeeding is not recommended for a HIV infected woman as there is a risk of passing the HIV-1 virus to your baby.

Children

Aptivus is not recommended for use in children less than 2 years of age.

Safety and effectiveness in children less than 2 years of age have not been established.

Taking Aptivus

It is essential that you take Aptivus with low-dose Ritonavir.

Follow all directions given to you by your doctor carefully.

They may differ from the information contained in this leaflet.

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

Recommended dose

The recommended dose for adults is two Aptivus soft capsules or 5mL Aptivus oral solution, together with 200 mg of ritonavir, twice daily (i.e. at regular 12-hour intervals at about the same time each day - morning and night).

The recommended dose of Aptivus oral solution and ritonavir for children 2 years of age or older will be determined by your doctor based on the weight or size of your child. The determined dose is taken twice daily.

How to take Aptivus

Aptivus Capsules

Aptivus capsules should be swallowed whole. Do not chew the capsules. Aptivus taken with low-dose Ritonavir should be taken with food.

Aptivus Oral Solution

Aptivus oral solution should only be taken by mouth. Aptivus taken with low-dose Ritonavir should be taken with food.

It is important that you use the 5mL dispensing syringe supplied to measure your exact dose of oral solution.

The dispensing syringe is designed to fit into the adapter (inside the bottle) and allow you to measure the right dose of Aptivus oral solution.

How to administer Aptivus oral solution:

- 1. Check the oral solution is clear and no crystals are visible at the bottom of the bottle.**
- 2. Open the bottle by pressing down on the cap and turning in an anti-clockwise direction.**

- 3. Remove the syringe cap covering the tip of the syringe (the cap will not be attached if this is the first time you are using the syringe).**
- 4. Insert the syringe into the adapter (located in the neck of the bottle). Make sure the syringe is tightly inserted.**
- 5. Turn the bottle upside down and gently withdraw the required amount of Aptivus oral solution. (The maximum volume which can be measured using the dispensing syringe is 5mL.)**
- 6. Take the dose of Aptivus oral solution.**
- 7. After use, place the syringe cap securely on the syringe tip and recap the bottle.**

If you forget to take a dose

It is important to take Aptivus as directed.

If you miss a dose, take it as soon as you remember. However, if you remember when it is almost time for your next dose, take only your usual dose at that time.

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

If you are not sure what to do, talk to your doctor or pharmacist.

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

If you have taken too much (overdose)

Immediately telephone your doctor, pharmacist or Poisons Information Centre (telephone 13 11 26) for advice, or go to Emergency at your nearest hospital if you think that you or anyone else may have taken too much Aptivus. Do this even if there are no signs of discomfort or poisoning. You may need urgent medical attention.

While you are taking Aptivus

Things you must do

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

Not all medicines can be safely taken with Aptivus. Some medicines will require a change in dosage or close monitoring if taken with Aptivus.

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

Contact your doctor if you experience any symptoms of liver problems, such as loss of appetite, nausea, vomiting, jaundice (yellowing of the skin and/or eyes), dark coloured urine, pale coloured stools, pain/ache or sensitivity to touch in your right abdominal area (below your ribs).

These could be signs of serious liver dysfunction which your doctor will need to monitor closely and may require stopping treatment with Aptivus.

Patients taking Aptivus (with ritonavir) may develop severe liver disease that can be life-threatening. The chance of developing liver problems is increased if you have chronic hepatitis B or C infection.

If you are taking oral contraceptives (to prevent pregnancy), you should use additional or different type of contraception.

Aptivus may reduce the effectiveness of oral contraceptives.

If you become pregnant while taking Aptivus tell your doctor immediately.

Contact your doctor immediately if you notice any unusual or unexplained bleeding.

There have been reports of bleeding episodes in people with haemophilia while taking protease inhibitors.

Bleeding in the brain, which can lead to permanent disability or death, has occurred in patients treated with Aptivus in clinical trials. A majority of the patients (experiencing bleeding in the brain) also had other medical conditions or were receiving other medications that may have caused or contributed to bleeding in the brain.

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 (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. Some people required adjustments to their diabetes medicines, while others needed new diabetes medicines.

If you have had a previous opportunistic infection, and you notice symptoms of inflammation occurring when you first start taking Aptivus, tell your doctor immediately.

Symptoms of inflammation include redness, swelling, heat and pain. These symptoms have been reported in some patients who have previously had an infection when combination antiretroviral therapy was started.

If you are taking 'statin' medicines to lower your cholesterol level (including atorvastatin), and you notice any muscle pain or weakness not caused by exercise, tell your doctor immediately.

Severe muscle pain and weakness have occurred in people taking protease inhibitors together with cholesterol-lowering medicines called 'statins'.

Things you must not do

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

Do not stop taking Aptivus or change the dose without first checking with your doctor.

Aptivus helps control your HIV infection but does not cure it. Therefore, Aptivus must be taken every day as your doctor prescribed it.

Effects on ability to drive or operate machinery

Be careful driving or operating machinery until you know how Aptivus affects you.

Aptivus soft capsules contain small amounts of alcohol (approximately 7% or 100 mg per capsule).

Side effects

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

It may be difficult to tell whether side effects are the result of taking Aptivus, effects of the HIV disease or side 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 need to change your dose or advise you to stop taking Aptivus.

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

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

Do not be alarmed by the following lists of side effects. You may not experience any of them.

The commonly reported side effects in adults are:

- diarrhoea, loose stools, nausea, vomiting, stomach pain
- bronchitis
- depression
- fever
- headache
- rash - some patients who developed rash also had joint pain or stiffness, throat tightness, or generalised itching.
- tiredness
- changes in blood chemistry including increases in blood lipid (cholesterol and triglycerides) levels and abnormal liver function tests

Less frequently reported side effects in adults include:

- reduction in red/white blood cells or blood platelets
- stomach fullness, flatulence, indigestion, heartburn, decreased appetite, dehydration, weight loss
- diabetes, increased blood level of glucose or pancreas enzymes (such as amylase, lipase), pancreatitis
- flu-like symptoms, generally feeling unwell, cough, breathing difficulties

- dizziness, sleepiness
- trouble sleeping, other sleep disorders
- muscle cramp or pain
- numbness or weakness of the arms and legs
- kidney problems

The most frequently reported side effects in children are similar to those described in adults. The frequency of most side effects tends to be lower in children.

Contact your doctor immediately if you experience symptoms of an allergic reaction. You may require urgent medical attention.

Some of the symptoms of an allergic reaction may include:

- Skin rash, hives or itching
- Swelling of the face, lips or tongue
- Wheezing or difficulty in breathing

Cases of hepatitis and severe life-threatening liver dysfunction (such as liver failure) have been reported in patients being treated with Aptivus.

Contact your doctor immediately if you experience any symptoms of liver problems, such as loss of appetite, nausea, vomiting, jaundice (yellowing of the skin and/or eyes), dark coloured urine, pale coloured stools, pain/ache

or sensitivity to touch in your right abdominal area (below your ribs).

In some patients, combination antiretroviral therapy may cause changes in body shape due to changes in fat distribution. These may include:

- loss of fat from legs, arms and face
- increased fat in the abdomen and other internal organs
- breast enlargement
- fatty lumps on the back of the neck.

In patients with haemophilia type A and B, there have been reports of increased bleeding while taking protease inhibitors.

Bleeding in the brain has been reported rarely.

Tell your doctor as soon as possible if you experience any side effects during or after taking Aptivus, so that these may be properly treated.

Other side effects not listed above may also occur in some patients.

You should tell your doctor or pharmacist if you notice anything unusual, during or after taking Aptivus.

After taking Aptivus

Storage

Keep your Aptivus where children cannot reach it.

Bottles of Aptivus soft capsules should be stored in the refrigerator where the temperature stays between 2°C and 8°C. Do not freeze the capsules.

After opening the bottle, the capsules may be stored below 25°C but must be used within 60 days. You should write the date of opening the bottle on the bottle label or outer carton.

Any capsules remaining after 60 days should be returned to your pharmacist for disposal.

Bottles of Aptivus oral solution should be stored between 15°C and 30°C. Do not refrigerate or freeze the oral solution.

After opening the bottle, the oral solution must be used within 60 days. You should write the date of opening the bottle on the bottle label or outer carton.

Any oral solution remaining after 60 days should be returned to your pharmacist for disposal.

Disposal

If your doctor tells you to stop taking this medicine or the expiry date has passed, the unused medicine should be

returned to your pharmacist so that it can be disposed of safely.

Product Description

What is Aptivus

Aptivus is the brand name of your medicine and is available in two dosage forms:

Aptivus Capsules

The capsules are pink, oblong, soft gelatin capsules with a black imprint of "TPV 250".

The capsules are supplied in a plastic bottle containing 120 capsules. Each bottle is labelled with the Australian Registration Number AUST R 118104.

Aptivus Oral Solution

The oral solution is a yellow, viscous, clear liquid.

The oral solution is supplied in an amber glass bottle containing 95mL. Each bottle is labelled with the Australian Registration Number AUST R 154888.

Ingredients

Aptivus Capsules

Each capsule contains 250 mg tipranavir (active ingredient).

The other ingredients are:

- PEG-35 castor oil
- Ethanol absolute
- glyceryl caprylate/caprates
- propylene glycol
- purified water
- trometamol
- nitrogen
- propyl gallate

The capsule shell consists of:

- gelatin
- iron oxide red CI77491
- propylene glycol
- purified water
- Sorbitol Special Glycerin Blend (sorbitol, 1, 4-sorbitan, mannitol and glycerin)
- titanium dioxide CI77891
- black printing ink containing: SDA 35 alcohol, propylene glycol, iron oxide black CI77499, polyvinyl acetate phthalate, purified water, isopropyl alcohol, macrogol 400 and ammonia solution concentrated 28%.

Aptivus Oral Solution

Each 1mL of the oral solution contains 100mg tipranavir (active ingredient).

The other ingredients are:

- macrogol 400
- propylene glycol
- glyceryl caprylate/caprates
- tocopherol
- ascorbic acid
- purified water
- sucralose
- butter toffee flavour
- buttermint flavour

Manufacturer

Aptivus soft capsules and oral solution are made in the United States of America (USA).

They are supplied in Australia by:

BOEHRINGER INGELHEIM PTY LIMITED

ABN 52 000 452 308

78 Waterloo Road

North Ryde NSW 2113

This leaflet was updated

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