PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

TULODIV, 600 mg, 50 mg, 300 mg, film-coated tablets

Abacavir, Dolutegravir, Lamivudine

Contains sugar: Mannitol 145,400 mg (per tablet)

Read all of this leaflet carefully before you start taking TULODIV

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- TULODIV has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

IMPORTANT - Hypersensitivity reactions

- **TULODIV contains abacavir.** Some people who take abacavir may develop a **hypersensitivity reaction** (a serious allergic reaction), which can be life-threatening if they continue to take abacavir.
- You must carefully read all the information under 'Hypersensitivity reactions' in Warnings and precautions and section 4.
- The TULODIV pack includes an **Alert Card**, to remind you and medical staff about abacavir hypersensitivity. **Detach this card and keep it with you at all times.**

What is in this leaflet

1. What TULODIV is and what it is used for

TULODIV is a medicine that contains three active ingredients used to treat HIV infection: abacavir, lamivudine and dolutegravir. Abacavir and lamivudine belong to a group of anti-retroviral medicines (medicines used to treat HIV infection) called nucleoside analogue reverse transcriptase inhibitors (NRTIs), and dolutegravir belongs to a group of anti-retroviral medicines called integrase inhibitors (INIs).

TULODIV is used to treat HIV (human immunodeficiency virus) infection in adults and adolescents aged 18 years and older.

TULODIV does not cure HIV infection; it reduces the amount of virus in your body and keeps it at a low level.

Not everyone responds to treatment with TULODIV in the same way. Your doctor will monitor the effectiveness of your treatment.

2. What you need to know before you take TULODIV

Do not take TULODIV:

- if you are allergic (hypersensitive) to abacavir, dolutegravir or lamivudine, or any of the other ingredients of TULODIV (listed in section 6).
  Carefully read all the information about hypersensitivity reactions in Warnings and precautions, and Section 4.
- if you have liver problems.
- if you have kidney problems.
- if you are taking another medicine called dofetilide or pilsicanide (to treat heart conditions) or metformin (to treat diabetes).
- if you are pregnant and are within your first trimester of pregnancy or are breastfeeding.

Warnings and precautions

Hypersensitivity to abacavir

TULODIV contains abacavir.

About 5 in every 100 people who take abacavir develop a hypersensitivity reaction (a serious allergic reaction), which can be life-threatening if they continue to take abacavir.

Who gets these reactions?

Anyone taking TULODIV could develop a hypersensitivity reaction to abacavir.

You are more likely to develop such a reaction if you have a gene called HLA-B*5701 (but you can get a reaction even if you don't have this gene). If possible, you will have been tested for this gene before TULODIV was prescribed for you. If you know you have this gene, tell your doctor before you take TULODIV.

What are the symptoms?

The most common symptoms are:

- fever (high temperature) and skin rash.

Other common symptoms are:

nausea (feeling sick), vomiting (being sick), diarrhoea, abdominal (stomach) pain, severe tiredness, shortness of breath, cough, headache, muscle pain and discomfort.

Other less common symptoms can include:

- pain in the joints, swelling of the neck, serious breathing problems, sore throat
- occasionally, inflammation of the eye (conjunctivitis), mouth ulcers, low blood pressure, tingling or numbness of the hands or feet.

If you continue to take TULODIV, the symptoms will get worse and may be life-threatening.

When do these reactions happen?

Hypersensitivity reactions can start at any time during treatment with TULODIV, but are more likely during the first 6 weeks of treatment.

Occasionally, reactions have developed in people who start taking abacavir again and had only one symptom on the Alert Card before they stopped taking it.

Very rarely, reactions have developed in people who start taking abacavir again, but who had no symptoms before they stopped taking it.

Contact your doctor immediately:

1. if you get a skin rash, OR
2. if you get symptoms from at least 2 of the following groups:
    - fever
    - shortness of breath, sore throat or cough
    - nausea or vomiting, diarrhoea or stomach pain
    - severe tiredness or achiness, or generally feeling ill.

Your doctor may advise you to stop taking TULODIV.

Always carry your Alert Card while you are taking TULODIV.

If you have stopped taking TULODIV because of a hypersensitivity reaction, you must NEVER AGAIN take TULODIV, or any other medicine containing abacavir. If you do, within hours, your blood pressure could fall dangerously low, which could result in death.

Tell your doctor:

- if you experience any of the following: rash, fever, tiredness, swelling of the face or mouth (angioedema), causing difficulty in breathing, muscle or joint pain, blisters, mouth sores or pink eye. These are signs or symptoms of a hypersensitivity (allergic) reaction that be due to dolutegravir, one of the active ingredients in TULODIV. Your doctor may decide to carry out tests on your liver, kidneys or blood, and may tell you to stop taking TULODIV.
- if you have heart problems, if you smoke, or have other illnesses that may increase your risk of heart disease such as high blood pressure or diabetes. Some studies have shown an increase in the risk of having a heart attack in people taking abacavir, one of the active ingredients in TULODIV. Do not stop taking TULODIV unless your doctor advises you to do so.
- if you notice changes in your body shape such as loss of fat from the arms legs or face, extra fat build up around the stomach, breasts or on the back of the neck. Your doctor may need to examine you and conduct some blood tests.
- if you notice signs of infection or inflammation. People with advanced HIV infection or AIDS have weak immune systems, and are more likely to develop serious infections (opportunistic infections). Such infections may have been “silent” and not detected by the weak immune system before treatment was started. After starting treatment, the immune system becomes stronger, and may attack the infections, which can cause symptoms of infection or inflammation. Symptoms usually include fever, plus some of the following:
  - headache
  - stomach ache
  - difficulty breathing.
- if you experience palpitations (rapid or irregular heartbeat) or tremor, hyperactivity (excessive restlessness and movement) or weakness beginning in the hands and feet and moving up towards the trunk of the body. In rare cases, as the immune system becomes stronger, it can also attack healthy body tissue (autoimmune disorders). These symptoms of autoimmune disorders may develop many months after you start taking medicine to treat your HIV infection.
- if you have stiffness in the joints, aches and pains (especially in the hip, knee or shoulder) or difficulty moving. These are symptoms of a condition called osteonecrosis where parts

of the bone tissue die because of reduced blood supply to the bone. People may be more likely to get this condition:
  - if they have been taking combination therapy for a long time
  - if they are also taking anti-inflammatory medicines called corticosteroids
  - if they drink alcohol
  - if their immune systems are very weak
  - if they are overweight.
- if you experience deep, rapid breathing, drowsiness, nausea, vomiting and stomach pain. These are signs and symptoms of lactic acidosis (excess of lactic acid in your blood) that may occur after you start taking TULODIV. This does not occur frequently, but has occasionally been fatal. While you are being treated with TULODIV, your doctor will monitor you closely for any signs that you may be developing lactic acidosis. If you think you may have lactic acidosis, contact your doctor immediately.
- if you have stomach pain, nausea or vomiting as these are symptoms of your pancreas being inflamed (pancreatitis).
- if you have or had liver disease, including hepatitis B or C. If you are infected with HIV and hepatitis B virus your doctor will carefully consider the best treatment for you. Your doctor may also conduct regular blood tests to monitor your liver function.
- if you are taking any other medicines including vitamins and supplements (see Other medicines and TULODIV).

You may continue to develop opportunistic infections and other complications of HIV infection, and therefore you should remain under close observation by healthcare provider who will conduct regular monitoring of your viral load and CD4 counts.

HIV infection is spread by sexual contact with someone who has the infection, or by transfer of infected blood (for example, by sharing injection needles). You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy, so it is important you take your medicine exactly as your doctor has told you. Discuss with your doctor the precautions needed to avoid infecting other people.

Other medicines and TULODIV

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Do not take TULODIV with these medicines:

- dofetilide or pilsicainide, used to treat heart conditions.

- metformin, used to treat diabetes.

Tell your doctor if you are taking:

- zalcitabine, emtricitabine, etravirine, efavirenz, nevirapine or tipranavir/ritonavir, used to treat HIV infection.
- other medicines containing lamivudine, used to treat HIV infection or hepatitis B infection.
- cladribine, used to treat hairy cell leukaemia.
- rifampicin, to treat tuberculosis (TB) and other bacterial infections.
- trimethoprim/sulfamethoxazole co-trimoxazole), an antibiotic to treat bacterial infections.
- phenytoin and phenobarbital, to treat epilepsy.
- oxcarbazepine and carbamazepine, to treat epilepsy and bipolar disorder.
- methadone, used as a heroin substitute. Abacavir increases the rate at which methadone is removed from the body. If you are taking methadone, you will be checked for any withdrawal symptoms. Your methadone dose may need to be changed.
- St. John's wort (*Hypericum perforatum*), a herbal remedy to treat depression.
- medicines called antacids, to treat indigestion and heartburn. Do not take an antacid during the 6 hours before you take TULODIV, or for at least 2 hours after you take it (see also section 3).
- supplements or multivitamins containing calcium, iron or magnesium. If you take TULODIV with food, you can take supplements or multivitamins containing calcium, iron or magnesium at the same time as TULODIV. If you do not take TULODIV with food, do not take supplements or multivitamins containing calcium, iron or magnesium during the 6 hours before you take TULODIV, or for at least 2 hours after you take it (see also section 3).
- medicines (usually liquids) containing sorbitol and other sugar alcohols (such as xylitol, mannitol, lactitol or maltitol), if taken regularly.

Tell your doctor or pharmacist if you are taking any of these. Your doctor may decide to adjust your dose or that you need extra checkups.

TULODIV with food and drink

TULODIV can be taken with or without food.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking TULODIV.

Taking TULODIV at the time of becoming pregnant or during the first six weeks of pregnancy, may increase the risk of a type of birth defect, called neural tube defect, such as spina bifida (malformed spinal cord).

If you could get pregnant while receiving TULODIV, talk to your doctor and discuss whether there is a need for contraception, such as condom or pills.

Tell your doctor immediately if you become pregnant or are planning to become pregnant. Your doctor will review your treatment. Do not stop taking TULODIV without consulting your doctor, as this may harm you and your unborn child.

It is recommended women who are HIV-positive do not breastfeed because HIV infection can be passed on to the baby in breast milk.

A small amount of the ingredients in TULODIV can also pass into your breast milk.

Driving and using machines
TULODIV can make you dizzy and have other side effects that make you less alert. Do not drive or use machines unless you are sure you are not affected.

3. How to take TULODIV
Do not share medicines prescribed for you with any other person.

Always take TULODIV exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose is of TULODIV in adults and in adolescents weighing more than 40 kg is one combined tablet (50 mg dolutegravir, 600 mg abacavir, 300 mg lamivudine) taken once a day.

If you weigh less than 40 kg, you cannot take TULODIV, because the dose of each component of this medicine cannot be adjusted to your weight. Your doctor might prescribe the components separately for you.

Swallow the tablet with some liquid.

TULODIV can be taken with or without food.

Antacid medicines
Antacids, to treat indigestion and heartburn, can stop TULODIV being absorbed into your body and make it less effective.

Do not take an antacid during the 6 hours before you take TULODIV, or for at least 2 hours after you take it. Other acid-lowering medicines like ranitidine and omeprazole can be taken at the same time as TULODIV. Talk to your doctor for further advice on taking acid-lowering medicines with TULODIV.

Calcium, iron or magnesium containing supplements/multivitamins
Supplements or multivitamins containing calcium, iron or magnesium can stop TULODIV being absorbed into your body and make it less effective.

Do not take supplements or multivitamins containing calcium, iron or magnesium during the 6 hours before you take TULODIV, or for at least 2 hours after you take it. If you take food with TULODIV, then you can take supplements or multivitamins containing calcium, iron or magnesium at the same time as TULODIV.

Your doctor will tell you how long your treatment with TULODIV will last. Do not stop treatment unless your doctor advises you to do so.

If you take more TULODIV than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take TULODIV
If you miss a dose, take it as soon as you remember, but if it is within 4 hours of your next dose, skip the dose you missed and take the next one at the usual time. Then continue your treatment as before. Do not take a double dose to make up for forgotten individual doses.

If you stop taking TULODIV
Take TULODIV for as long as your doctor recommends. Don’t stop unless your doctor advises you to.
If you have stopped taking TULODIV for any reason, particularly because you think you are having side effects or for other illness, it is important that you contact your doctor before

restarting. In some cases your doctor will ask you to restart TULODIV in a place where you will be able to get ready access to medical care if needed.

If you have hepatitis B infection, don't stop TULODIV without your doctor's advice, as your hepatitis may come back.

4. Possible side effects

TULODIV can have side effects.

Not all side effects reported for TULODIV are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking TULODIV, please consult your healthcare provider for advice.

If any of the following happens, stop taking TULODIV and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fever,
- shortness of breath,
- sore throat or cough,
- nausea, vomiting, diarrhoea, abdominal pain,
- severe tiredness, aches and pains, generally feeling ill,
- peeling and/or blistering of the skin.

These are all very serious side effects. If you have them, you may have had a serious reaction to TULODIV. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- unexplained bleeding or bruising, which may be due to changes in the numbers of certain cells in the blood which may affect blood clotting or lead to anaemia,
- changes in numbers of certain cells in the blood which may affect your ability to fight infection some signs of infection include: any fever, sore throat, mouth ulcers and tiredness,
- rapid or irregular heartbeat, tremor, excessive restlessness and movement, or weakness beginning in the hands and feet and moving up towards the trunk of the body,

- recurrent nausea or vomiting, abdominal pain or rapid breathing (lactic acidosis),
- suicidal thoughts or suicide attempt (particularly in patients who have had depression or mental health problems before),
- inflamed pancreas (pancreatitis) with symptoms such as stomach pain, nausea or vomiting,
- inflammation of the liver or liver failure with symptoms such as fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, yellowing of the skin or whites of the eyes,
- breakdown of muscle tissue with symptoms such as dark, reddish urine, a decreased amount of urine, weakness and muscle aches.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:

- difficulty in sleeping, abnormal dreams or nightmares, depression, anxiety,
- headache, dizziness, feeling drowsy, lack of energy,
- tiredness, muscle weakness,
- joint or muscle pain,
- irritated or runny nose,
- flatulence (wind), stomach discomfort, bloating, abdominal, heartburn, indigestion, loss of appetite,
- hair loss.

Less frequent side effects:

- low red blood cell count (anaemia) with some symptoms such as tiredness, dizziness, light-headedness, paleness,
- sensation of weakness in the limbs,
- numbness, tingly feelings in the skin (pins and needles).

Side effects that may show up in blood tests:
Frequent:

- increase in liver enzymes,
- increase in an enzyme called creatine phosphokinase (indicative of muscle disorders).

Less frequent:

- increase in sugar (glucose) in the blood,
- increase in triglycerides (type of fat) in the blood,

- increase in bilirubin (a test of liver function),
- increase in an enzyme called amylase (used to diagnose inflammation of the pancreas).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of TULODIV.

5. How to store TULODIV

- Store all medicines out of reach of children.
- Store at or below 30 °C.
- Do not store in a bathroom.
- Do not use after the expiry date stated on the carton.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What TULODIV contains

The active ingredients are 600 mg of abacavir (as abacavir sulphate), 50 mg of dolutegravir (as dolutegravir sodium) and 300 mg of lamivudine.

The other ingredients are:

Tablet core: magnesium stearate, mannitol, microcrystalline cellulose, povidone, sodium starch glycolate

Film coating: ferrosoferric oxide/black iron oxide (E172), iron oxide red (E172), iron oxide yellow (E172), macrogol/polyethylene glycol (E1521), polyvinyl alcohol – part hydrolysed (E1203), talc (E553b), titanium dioxide (E171)

What TULODIV looks like and contents of the pack

Beige coloured, oval shaped, biconvex film-coated tablets debossed with ‘H’ on one side and ‘A60’ on the other side.

28, 30, 84, 90 and 180 film-coated tablets are packed in high density polyethylene (HDPE) containers with a silica gel canister and closed with a child-resistant plastic cap with a pulp liner.

10 x 10 tablets are packed in blister strips composed of PVC/aluminium and plain aluminium lidding foil.

Not all packs and pack sizes may be marketed.

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This leaflet was last revised in

17 June 2025

Registration number

57/20.2.8/0108