

Package leaflet: Information for the patient

Fotivda 890 microgram hard capsules Fotivda 1340 microgram hard capsules tivozanib

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Fotivda is and what it is used for
2. What you need to know before you take Fotivda
3. How to take Fotivda
4. Possible side effects
5. How to store Fotivda
6. Contents of the pack and other information

1. What Fotivda is and what it is used for

The active substance in Fotivda is tivozanib, which is a protein kinase inhibitor. Tivozanib reduces the supply of blood to the cancer, which slows down the growth and spread of cancer cells. It works by blocking the action of a protein called vascular endothelial growth factor (VEGF). Blocking the action of VEGF prevents the formation of new blood vessels.

Fotivda is used to treat adults with advanced kidney cancer. It is used where other treatments such as interferon-alpha or interleukin-2 have either not yet been used or have not helped to stop your disease.

2. What you need to know before you take Fotivda

Do not take Fotivda:

- If you are allergic to tivozanib or any of the other ingredients of this medicine (listed in section 6);
- If you are taking St. John's Wort (also known as *Hypericum perforatum*, a herbal remedy used for treatment of depression and anxiety).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking Fotivda:

- if you have **high blood pressure**.
Fotivda can increase your blood pressure. Your doctor will monitor your blood pressure regularly and, if it is too high, may either give you a medicine to lower it, or reduce your dose of Fotivda. However, if your blood pressure remains too high, your doctor may decide to interrupt or to stop treatment with Fotivda. If you are already taking a medicine to treat high blood pressure, and your doctor reduces the dose of Fotivda or interrupts or stops treatment, you will be regularly checked for low blood pressure.

- if you have had problems with **blood clots**.
Treatment with Fotivda may raise the risk of developing a blood clot (thrombus) in your blood vessels that could break loose and be carried by the blood stream to block another blood vessel. Tell your doctor if you have ever had one of the following:
 - a blood clot in your lungs (with cough, chest pain, sudden shortness of breath or coughing up blood),
 - blood clot in your legs or arms, eye, or brain (with pain or swelling in your hands or feet, reduced vision, or changes in your mental state)
 - a stroke, or signs and symptoms of a ‘mini-stroke’ (transient ischaemic attack)
 - a heart attack
 - high blood pressure
 - diabetes
 - major surgery
 - multiple injuries such as broken bones and damage to internal organs
 - inability to move for a long period
 - heart failure which can cause shortness of breath or ankle swelling
 - inability to breathe, bluish colour on your skin, fingertips or lips, restlessness, anxiety, confusion, altered consciousness or sense of awareness, rapid, shallow breathing, a racing heart or excessive sweating.
- if you suffer or have suffered from any of these symptoms or are treated for heart failure:
 - Shortness of breath (dyspnoea) when you exert yourself or when you lie down
 - Feeling weak and tired
 - Swelling (oedema) in your legs, ankles and feet
 - Reduced ability to exercise
 - Persistent cough or wheezing with white or pink blood-tinged phlegm
 Signs and symptoms of heart failure will be monitored whilst you are taking your medicine. If necessary, your doctor may reduce your dose of Fotivda, or interrupt or stop this treatment.
- If you have or are treated for an **abnormal rate and rhythm of the heartbeat (arrhythmia)**. Your doctor will monitor the effect of Fotivda on your heart by recording the electrical activity of your heart (an electrocardiogram) or by measuring your blood calcium, magnesium and potassium levels during your treatment.
- if you have **problems with your liver**.
Your doctor will regularly monitor how well your liver is working before and during treatment with Fotivda (e.g. with blood tests), and if necessary may need to reduce how often you take Fotivda.
- if you have **problems with your thyroid gland or use medicines to treat thyroid disease**.
Treatment with Fotivda may cause your thyroid gland to work less well than usual. Your doctor will regularly monitor how well your thyroid gland is working before and during treatment with Fotivda (e.g. with blood tests).

Talk to your doctor, pharmacist or nurse while taking Fotivda:

- if you get **shortness of breath or ankle swelling**
Tell your doctor right away as these may be symptoms of heart failure. Your doctor will monitor this, and depending on the severity may reduce your dose of Fotivda, or interrupt or stop treatment with Fotivda.
- if you have had problems with **bleeding**
Treatment with Fotivda may increase the risk of bleeding. If you get bleeding problems (with painful swollen stomach (abdomen), vomiting blood, coughing up blood, black stools, blood in your urine, headache or changes in your mental state), tell your doctor right away. Treatment with Fotivda may need to be temporarily stopped.

- if laboratory tests show that there is **protein in your urine**
Your doctor will monitor this at the beginning and during your treatment. Depending on the results, your doctor may reduce your dose of Fotivda, or interrupt or stop this treatment.
- if you suffer from a disease of the brain, called **posterior reversible encephalopathy syndrome (PRES)**
Tell your doctor right away if you have symptoms such as headache, seizure (fit), lack of energy, confusion, blindness or other visual and neurologic disturbances such as weakness in an arm or a leg. If PRES is diagnosed, your doctor will stop treatment with Fotivda.
- if the **skin on the palms of your hands and the soles of your feet** become dry, cracked, scaling, or peeling, or is stinging or tingling
These may be symptoms of a condition called hand foot skin reaction. Your doctor will treat the condition and, depending on the severity, the doctor may reduce your dose of Fotivda, or interrupt or stop this treatment.
- if you have symptoms of **gastrointestinal perforation or fistula** formation (developing a hole in the stomach or intestine or abnormal passages forming between parts of the intestine) such as severe stomach pain, chills, fever, nausea, vomiting or painful bowel obstruction, diarrhoea or rectal bleeding.
Your doctor will regularly monitor you for these symptoms during your treatment with Fotivda.
- if you need to have an **operation or another form of surgery**
Your doctor may recommend that you temporarily stop taking Fotivda if you have an operation or surgery, as it could affect wound healing.

The printing ink used on the Fotivda 890 microgram capsule contains tartrazine (E102), which may cause allergic reactions.

Children and adolescents

Do not give Fotivda to children and adolescents under 18 years of age. This medicine has not been studied in children and adolescents.

Other medicines and Fotivda

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes herbal medicines and other medicines you have bought without a prescription.

Fotivda may work less well when taken with some medicines. Tell your doctor if you are taking any of the following medicines; they may decide to change your medication:

- dexamethasone (a corticosteroid to reduce inflammation and treat disorders of the immune system);
- rosuvastatin (a medicine used to help lower cholesterol levels in your blood);
- phenobarbital, phenytoin, carbamazepine (used to treat epilepsy);
- nafcillin, rifampicin, rifabutin, rifapentin (antibiotics);
- St. John's Wort (also known as *Hypericum perforatum*, a herbal remedy used for treatment of depression and anxiety) as this herbal remedy should not be used at the same time as Fotivda.

Pregnancy, breast-feeding and fertility

Do not take Fotivda if you are pregnant. Tell your doctor who will discuss with you the risks of taking Fotivda to you and your child.

Both you and your partner must **use effective contraception**. If you or your partner are taking hormonal contraceptives (the pill, an implant or patch) you **must use an additional barrier method** throughout treatment and for another month after completing treatment.

Do not breast-feed during treatment with Fotivda, as it is not known whether the active ingredient in Fotivda passes into breast-milk. Talk to your doctor if you are already breast-feeding.

Talk to your doctor when planning a baby, as Fotivda may affect the **fertility** of men and women.

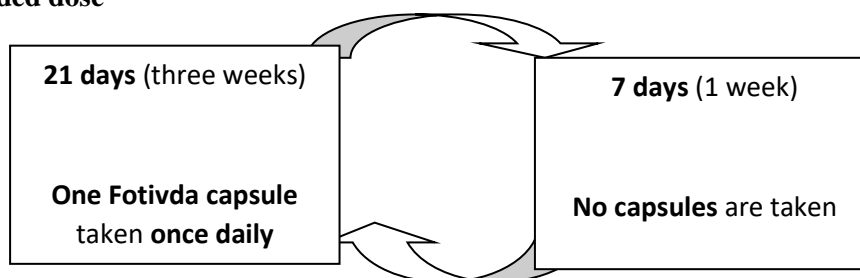
Driving and using machines

Fotivda can have side effects that may affect your ability to drive or use machines. Avoid driving or using machines if you feel weak, tired, or dizzy. See also Section 4 “Possible side effects”.

3. How to take Fotivda

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

Recommended dose



The recommended dose is one Fotivda 1340 microgram capsule, taken once daily for 21 days (3 weeks), followed by a 7-day (1-week) period when no capsules are taken. This schedule is repeated in cycles of 4 weeks.

Your doctor will check you regularly, and you will normally continue to take Fotivda as long as it is working, and you do not suffer unacceptable side effects.

Reduced dose

In case you experience severe side effects, your doctor may decide to interrupt Fotivda therapy and/or lower the dose to:

One Fotivda 890 microgram capsule, taken once daily for 21 days (3 weeks), followed by a 7-day (1-week) period when no capsules are taken.

This schedule is repeated in cycles of 4 weeks.

Liver problems

If you have **liver problems**, your doctor may reduce how often you take your dose to every other day (i.e. one 1340 microgram capsule every other day).

Taking with food and drink

Fotivda must be taken with a glass of water and can be taken either with or without food. Swallow the capsule whole. Do not chew, dissolve or open the capsule before swallowing.

If you take more Fotivda than you should

Tell your doctor straightaway if you have taken more than your prescribed dose of 1 capsule per day. Taking too much Fotivda makes side effects more likely or to become more severe, especially high blood pressure. Get **medical help straightaway** if you experience confusion, changes in your mental state or headaches. These are all symptoms of high blood pressure.

If you forget to take Fotivda

If you have missed taking a capsule do **not** take a replacement capsule. Continue to take your next

dose at the usual time.

Do not take a double dose to make up for a forgotten capsule.

If you vomit after taking Fotivda, do **not** take a replacement capsule. Continue to take your next dose at the usual time.

If you stop taking Fotivda

Do not stop taking this medicine unless your doctor tells you to. If you stop taking the capsules your condition may get worse.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects

High blood pressure is the most serious and a very common side effect (see also in section 2 “*Warnings and Precautions*”).

Tell your doctor immediately if you think you have **high blood pressure**. Symptoms include severe headaches, blurred vision, shortness of breath, changes in your mental state, such as feeling anxious, confused or disorientated

Your doctor will check your blood pressure regularly during treatment with Fotivda. If you develop high blood pressure, your doctor may prescribe a medicine to treat your high blood pressure, lower your dose of Fotivda, or stop your treatment with Fotivda.

Other side effects

Very common (may affect more than 1 in 10 people)

- Difficulty speaking
- Diarrhoea
- Loss of appetite; weight loss.
- Headache
- Difficult breathing; shortness of breath during exercise; coughing.
- Tiredness; unusual weakness; pain (including in the mouth, bone, extremities, side of the body, groin, tumour).
- Inflammation of the mouth; slight mouth pain or discomfort; feeling sick; pain, discomfort and tightness in the stomach.
- Hand-foot-syndrome with skin reddening, swelling, numbness and skin peeling on palms and soles.
- Back pain
- Tiredness and lack of energy.

Common (may affect up to 1 in 10 people)

- Underactive thyroid gland which may cause symptoms such as tiredness, lethargy, muscle weakness, slow heart rate, weight gain.
- Unable to sleep.
- Nerve damage including numbness, pins and needles, sensitive skin or numbness and weakness in the arms and legs.
- Sight problems including blurred vision.
- Rapid heart rate; tightness of the chest; heart attack/reduced blood flow to heart; blood clot in an artery (blood vessel).

- Blood clot in the lung. Symptoms include cough, chest pain, sudden shortness of breath or coughing up blood.
- Blood clot in a deep vein such as in the leg.
- Very high blood pressure leading to a stroke; flushed skin.
- Nose bleed; runny nose; blocked nose.
- Flatulence; heartburn; difficult and painful swallowing; sore throat; bloated stomach; swollen and painful tongue; inflamed painful and/or bleeding gums.
- Taste changes or loss of taste.
- Dizziness; ringing in the ears; dizziness and a spinning sensation (vertigo).
- Bleeding, e.g. in the brain, from the mouth, gums, lungs, stomach, gut ulcers, female genitals, anus, adrenal gland.
- Coughing up blood; vomiting up blood.
- Paleness and tiredness from excess bleeding.
- Being sick; indigestion; constipation; dry mouth.
- Itchy skin; rash; itching of the body; skin peeling; dry skin; hair loss; redness of the skin including the hands and body; acne.
- Fever; chest pain; swelling of feet and legs; chills and low body temperature.
- Joint pain; muscle pain.
- Increased amount of protein in the urine.
- Abnormal blood test results for liver, pancreas, kidney, and thyroid.
- Inflammation of the pancreas causing severe stomach pain which may spread to your back.

Uncommon (may affect up to 1 in 100 people)

- Rashes with pus; fungal infections.
- Bruising easily, bleeding into the skin.
- overactive thyroid gland (which may cause symptoms like increased appetite, loss of weight, intolerance to heat, increased sweating, tremors, rapid heart rate); enlarged thyroid gland.
- Increase in number of red blood cells.
- Memory loss.
- Temporary reduced blood flow to the brain.
- Watery eyes.
- Blocked ears.
- Lack of blood flow through the heart blood vessels.
- Peptic ulcer in the small intestines.
- Red, swollen and sore skin; blistering skin; excessive sweating; hives.
- Muscle weakness.
- Swelling or irritation of the mucous membranes.
- Abnormal electrocardiogram (ECG), rapid and/or irregular heart beat.
- Heart failure. Symptoms include shortness of breath or ankle swelling. Swelling in the lungs caused by fluid build-up.

Rare (may affect up to 1 in 1,000 people)

- Posterior reversible encephalopathy syndrome (PRES). Symptoms include headache, seizure, lack of energy, confusion, blindness or other visual and neurologic disturbances.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

Ireland

HPRA Pharmacovigilance

Earlsfort Terrace

IRL - Dublin 2

Tel: +353 1 6764971

Fax: +353 1 6762517

Website: www.hpra.ie

e-mail: medsafety@hpra.ie

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Fotivda

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and bottle after EXP. The expiry date refers to the last day of that month.

Keep the bottle tightly closed in order to protect from moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Fotivda contains

Fotivda 890 microgram hard capsules

The active substance is tivozanib. Each capsule contains tivozanib hydrochloride monohydrate equivalent to 890 microgram of tivozanib.

The other ingredients are:

- *Capsule content*: mannitol, magnesium stearate.
- *Capsule shell*: gelatin, titanium dioxide (E171), indigo carmine (E132), yellow iron oxide (E172).
- *Printing ink, yellow*: shellac, propylene glycol, strong ammonia solution, titanium dioxide (E171), tartrazine aluminium lake (E102).
- *Printing ink, blue*: shellac, propylene glycol, strong ammonia solution, indigo carmine aluminium lake (E132).

Fotivda 1340 microgram hard capsules

The active substance is tivozanib. Each capsule contains tivozanib hydrochloride monohydrate equivalent to 1340 microgram of tivozanib.

The other ingredients are:

- *Capsule content*: mannitol, magnesium stearate.
- *Capsule shell*: gelatin, titanium dioxide (E171), yellow iron oxide (E172).
- *Printing ink, blue*: shellac, propylene glycol, strong ammonia solution, indigo carmine aluminium lake (E132).

What Fotivda looks like and contents of the pack

Fotivda 890 microgram hard capsules have a dark blue opaque cap and bright yellow opaque body, printed with yellow ink “TIVZ” on the cap and with dark blue ink “LD” on the body.

Fotivda 1340 microgram hard capsules have a bright yellow opaque cap and bright yellow opaque body, printed with dark blue ink “TIVZ” on the cap and with dark blue ink “SD” on the body.

Fotivda 890 microgram and Fotivda 1340 microgram are available as packs of 21 capsules in HDPE-bottles with child-resistant closure.

Marketing Authorisation Holder

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Johannes Vermeerplein 11
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Amsterdam
Netherlands

Manufacturer

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United Kingdom

This leaflet was last approved in 15.02.2019.

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>.