Package leaflet: Information for the patient

Everolimus Sandoz® 2,5 mg, tabletten
Everolimus Sandoz® 5 mg, tabletten
Everolimus Sandoz® 10 mg, tabletten

everolimus

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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [Nationally completed name] is and what it is used for

[Nationally completed name] is an anticancer medicine containing the active substance everolimus. Everolimus reduces the blood supply to the tumour and slows down the growth and spread of cancer cells.

[Nationally completed name] is used to treat adult patients with:
- hormone receptor-positive advanced breast cancer in postmenopausal women, in whom other treatments (so called “non-steroidal aromatase inhibitors”) no longer keep the disease under control. It is given together with a medicine called exemestane, a steroidal aromatase inhibitor, which is used for hormonal anticancer therapy.
- advanced tumours called neuroendocrine tumours that originate from the stomach, bowels, lung or pancreas. It is given if the tumours are inoperable and do not overproduce specific hormones or other related natural substances.
- advanced kidney cancer (advanced renal cell carcinoma), where other treatments (so-called “VEGF-targeted therapy”) have not helped stop your disease.

2. What you need to know before you take [Nationally completed name]

[Nationally completed name] will only be prescribed for you by a doctor with experience in cancer treatment. Follow all the doctor's instructions carefully. They may differ from the general information contained in this leaflet. If you have any questions about [Nationally completed name] or why it has been prescribed for you, ask your doctor.

Do not take [Nationally completed name]

- **if you are allergic** to everolimus, to related substances such as sirolimus or temsirolimus, or to any of the other ingredients of this medicine (listed in section 6).

If you think you may be allergic, ask your doctor for advice.

Warnings and precautions
Talk to your doctor before taking [Nationally completed name]:

- if you have any problems with your liver or if you have ever had any disease which may have affected your liver. If this is the case, your doctor may need to prescribe a different dose of [Nationally completed name].
- if you have diabetes (high level of sugar in your blood). [Nationally completed name] may increase blood sugar levels and worsen diabetes mellitus. This may result in the need for insulin and/or oral antidiabetic agent therapy. Tell your doctor if you experience any excessive thirst or increased frequency of urination.
- if you need to receive a vaccine while taking [Nationally completed name].
- if you have high cholesterol. [Nationally completed name] may elevate cholesterol and/or other blood fats.
- if you have had recent major surgery, or if you still have an unhealed wound following surgery. [Nationally completed name] may increase the risk of problems with wound healing.
- if you have an infection. It may be necessary to treat your infection before starting [Nationally completed name].
- if you have previously had hepatitis B, because this may be reactivated during treatment with [Nationally completed name] (see section 4 'Possible side effects').
- if you have received or are about to receive radiation therapy.

[Nationally completed name] may also:

- weaken your immune system. Therefore, you may be at risk of getting an infection while you are taking [Nationally completed name]. If you have fever or other signs of an infection, consult with your doctor. Some infections may be severe and may have fatal consequences
- impact your kidney function. Therefore, your doctor will monitor your kidney function while you are taking [Nationally completed name].
- cause shortness of breath, cough and fever.
- cause mouth ulcers and sores to develop. Your doctor might need to interrupt or discontinue your treatment with [Nationally completed name]. You might need treatment with a mouthwash, gel or other products. Some mouthwashes and gels can make ulcers worse, so do not try anything without checking with your doctor first. Your doctor might restart treatment with [Nationally completed name] at the same dose or at a lower dose.

- cause complications of radiation therapy. Severe complications of radiotherapy (such as shortness of breath, nausea, diarrhoea, skin rashes and soreness in mouth, gums and throat), including fatal cases, have been observed in some patients who were taking everolimus at the same time as radiation therapy or who were taking everolimus shortly after they had radiation therapy. In addition, so-called radiation recall syndrome (comprising skin redness or lung inflammation at the site of previous radiation therapy) has been reported in patients who had radiation therapy in the past.
  Tell your doctor if you are planning to have radiation therapy in the near future, or if you have had radiation therapy before.

Tell your doctor if you experience these symptoms.

You will have regular blood tests during treatment. These will check the amount of blood cells (white blood cells, red blood cells and platelets) in your body to see if [Nationally completed name] is having an unwanted effect on these cells. Blood tests will also be carried out to check your kidney function (level of creatinine) and liver function (level of transaminases) and your blood sugar and cholesterol levels. This is because these can also be affected by [Nationally completed name].

Children and adolescents
[Nationally completed name] is not to be used in children or adolescents (age below 18 years).

Other medicines and [Nationally completed name]
[Nationally completed name] may affect the way some other medicines work. If you are taking other medicines at the same time as [Nationally completed name], your doctor may need to change the dose of [Nationally completed name] or the other medicines.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

The following may increase the risk of side effects with [Nationally completed name]:
- ketoconazole, itraconazole, voriconazole, or fluconazole and other antifungals used to treat fungal infections.
- clarithromycin, telithromycin or erythromycin, antibiotics used to treat bacterial infections.
- ritonavir and other medicines used to treat HIV infection/AIDS.
- verapamil or diltiazem, used to treat heart conditions or high blood pressure.
- dronedarone, a medicine used to help regulate your heart beat.
- ciclosporin, a medicine used to stop the body from rejecting organ transplants.
- imatinib, used to inhibit the growth of abnormal cells.
- angiotensin-converting enzyme (ACE) inhibitors (such as ramipril) used to treat high blood pressure or other cardiovascular problems.
- nefazodone, used to treat depression.
- cannabidiol (uses amongst others include treatment of seizures).

The following may reduce the effectiveness of [Nationally completed name]:

- rifampicin, used to treat tuberculosis (TB).
- efavirenz or nevirapine, used to treat HIV infection/AIDS.
- St. John's wort (*Hypericum perforatum*), a herbal product used to treat depression and other conditions.
- dexamethasone, a corticosteroid used to treat a wide variety of conditions including inflammatory or immune problems.
- phenytoin, carbamazepine or phenobarbital and other anti-epileptics used to stop seizures or fits.

These medicines should be avoided during your treatment with [Nationally completed name]. If you are taking any of them, your doctor may switch you to a different medicine, or may change your dose of [Nationally completed name].

[Nationally completed name] with food and drink
Avoid grapefruit and grapefruit juice while you are on [Nationally completed name]. It may increase the amount of [Nationally completed name] in the blood, possibly to a harmful level.

Pregnancy, breast-feeding and fertility

Pregnancy
[Nationally completed name] could harm your unborn baby and is not recommended during pregnancy. Tell your doctor if you are pregnant or think that you may be pregnant. Your doctor will discuss with you whether you should take this medicine during your pregnancy.

Women who could potentially become pregnant should use highly effective contraception during treatment and for up to 8 weeks after ending treatment. If, despite these measures, you think you may have become pregnant, ask your doctor for advice **before** taking any more [Nationally completed name].

Breast-feeding
[Nationally completed name] could harm your breast-fed baby. You should not breast-feed during treatment and for 2 weeks after the last dose of [Nationally completed name]. Tell your doctor if you are breast-feeding.

Female fertility
Absence of menstrual periods (amenorrhoea) has been observed in some female patients receiving [Nationally completed name].

[Nationally completed name] may have an impact on female fertility. Talk to your doctor if you wish to have children.

Male fertility
[Nationally completed name] may affect male fertility. Talk to your doctor if you wish to father a child.

Driving and using machines

If you feel unusually tired (fatigue is a very common side effect), take special care when driving or using machines.

[Nationally completed name] contains lactose
[Nationally completed name] contains lactose (milk sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take [Nationally completed name]

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

The recommended dose is 10 mg, taken once a day. Your doctor will tell you how many tablets of [Nationally completed name] to take.

If you have liver problems, your doctor may start you on a lower dose of [Nationally completed name] (2.5, 5 or 7.5 mg per day).

If you experience certain side effects while you are taking [Nationally completed name] (see section 4), your doctor may lower your dose or stop treatment, either for a short time or permanently.

Take [Nationally completed name] once a day, at about the same time every day, consistently either with or without food.

Swallow the tablet(s) whole with a glass of water. Do not chew or crush the tablets.

If you take more [Nationally completed name] than you should
- If you have taken too much [Nationally completed name], or if someone else accidentally takes your tablets, see a doctor or go to a hospital immediately. Urgent treatment may be necessary.
- Take the carton and this leaflet, so that the doctor knows what has been taken.

If you forget to take [Nationally completed name]
If you miss a dose, take your next dose as scheduled. Do not take a double dose to make up for the forgotten tablets.

If you stop taking [Nationally completed name]
Do not stop taking [Nationally completed name] unless your doctor tells you to.

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

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

STOP taking [Nationally completed name] and seek medical help immediately if you experience any of the following signs of an allergic reaction:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps

Serious side effects of [Nationally completed name] include:

Very common *(may affect more than 1 in 10 people)*
- Increased temperature, chills (signs of infection)
- Fever, coughing, difficulty breathing, wheezing (signs of inflammation of the lung, also known as pneumonitis)

Common *(may affect up to 1 in 10 people)*
- Excessive thirst, high urine output, increased appetite with weight loss, tiredness (signs of diabetes)
- Bleeding (haemorrhage), for example in the gut wall
- Severely decreased urine output (sign of kidney failure)

Uncommon *(may affect up to 1 in 100 people)*
- Fever, skin rash, joint pain and inflammation, as well as tiredness, loss of appetite, nausea, jaundice (yellowing of the skin), pain in the upper right abdomen, pale stools, dark urine (may be signs of hepatitis B reactivation)
- Breathlessness, difficulty breathing when lying down, swelling of the feet or legs (signs of heart failure)
- Swelling and/or pain in one of the legs, usually in the calf, redness or warm skin in the affected area (signs of blockade of a blood vessel (vein) in the legs caused by blood clotting)
- Sudden onset of shortness of breath, chest pain or coughing up blood (potential signs of pulmonary embolism, a condition that occurs when one or more arteries in your lungs become blocked)
- Severely decreased urine output, swelling in the legs, feeling confused, pain in the back (signs of sudden kidney failure)
- Rash, itching, hives, difficulty breathing or swallowing, dizziness (signs of serious allergic reaction, also known as hypersensitivity)

Rare *(may affect up to 1 in 1,000 people)*
- Shortness of breath or rapid breath (signs of acute respiratory distress syndrome)

If you experience any of these side effects, tell your doctor immediately as this might have life-threatening consequences.

Other possible side effects of [Nationally completed name] include:

Very common *(may affect more than 1 in 10 people)*
- High level of sugar in the blood (hyperglycaemia)

- Loss of appetite
- Disturbed taste (dysgeusia)
- Headache
- Nose bleeds (epistaxis)
- Cough
- Mouth ulcers
- Upset stomach including feeling sick (nausea) or diarrhoea
- Skin rash
- Itching (pruritus)
- Feeling weak or tired
- Tiredness, breathlessness, dizziness, pale skin, signs of low level of red blood cells (anaemia)
- Swelling of arms, hands, feet, ankles or other part of the body (signs of oedema)
- Weight loss
- High level of lipids (fats) in the blood (hypercholesterolaemia)

Common *(may affect up to 1 in 10 people)*
- Spontaneous bleeding or bruising (signs of low level of platelets, also known as thrombocytopenia)
- Breathlessness (dyspnoea)
- Thirst, low urine output, dark urine, dry flushed skin, irritability (signs of dehydration)
- Trouble sleeping (insomnia)
- Headache, dizziness (sign of high blood pressure, also known as hypertension)
- Swelling of part or all of your arm (including fingers) or leg (including toes), feeling of heaviness, restricted movement, discomfort (possible symptoms of lymphoedema)
- Fever, sore throat, mouth ulcers due to infections (signs of low level of white blood cells, leukopenia, lymphopenia and/or neutropenia)
- Fever
- Inflammation of the inner lining of the mouth, stomach, gut
- Dry mouth
- Heartburn (dyspepsia)
- Being sick (vomiting)
- Difficulty in swallowing (dysphagia)
- Abdominal pain
- Acne
- Rash and pain on the palms of your hands or soles of your feet (hand-foot syndrome)
- Reddening of the skin (erythema)
- Joint pain
- Pain in the mouth
- Menstruation disorders such as irregular periods
- High level of lipids (fats) in the blood (hyperlipidaemia, raised triglycerides)
- Low level of potassium in the blood (hypokalaemia)
- Low level of phosphate in the blood (hypophosphataemia)
- Low level of calcium in the blood (hypocalcaemia)
- Dry skin, skin exfoliation, skin lesions

- Nail disorders, breaking of your nails
- Mild loss of hair
- Abnormal results of liver blood tests (increased alanine and aspartate aminotransferase)
- Abnormal results of renal blood tests (increased creatinine)
- Swelling of the eyelid
- Protein in the urine

Uncommon *(may affect up to 1 in 100 people)*
- Weakness, spontaneous bleeding or bruising and frequent infections with signs such as fever, chills, sore throat or mouth ulcers (signs of low level of blood cells, also known as pancytopenia)
- Loss of sense of taste (ageusia)
- Coughing up blood (haemoptysis)
- Menstruation disorders such as absence of periods (amenorrhoea)
- Passing urine more often during daytime
- Chest pain
- Abnormal wound healing
- Hot flushes
- Discharge from the eye with itching and redness, pink eye or red eye (conjunctivitis)

Rare *(may affect up to 1 in 1,000 people)*
- Tiredness, breathlessness, dizziness, pale skin (signs of low level of red blood cells, possibly due to a type of anaemia called pure red cell aplasia)
- Swelling of the face, around the eyes, mouth, and inside the mouth and/or throat, as well as the tongue and difficulty breathing or swallowing (also known as angioedema), may be signs of an allergic reaction

Not known *(frequency cannot be estimated from the available data)*
- Reaction at the site of previous radiation therapy, e.g. skin redness or lung inflammation (so-called radiation recall syndrome)
- Worsening of radiation treatment side effects

If these side effects get severe please tell your doctor and/or pharmacist. Most of the side effects are mild to moderate and will generally disappear if your treatment is interrupted for a few days.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store [Nationally completed name]

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 blister foil after EXP. The expiry date refers to the last day of that month.

Do not store above 30°C.

Store in the original package in order to protect from light and moisture.

Open the blister just before taking the tablets.

Do not use this medicine if any pack is damaged or shows signs of tampering.

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 [Nationally completed name] contains
- The active substance is everolimus.

[Nationally completed name] 2.5 mg tablets
- Each tablet contains 2.5 mg of everolimus.

[Nationally completed name] 5 mg tablets
- Each tablet 5 mg of everolimus.

[Nationally completed name] 10 mg tablets
- Each tablet contains 10 mg of everolimus.

- The other ingredients are butylhydroxytoluene (E 321), magnesium stearate, lactose, hypromellose, crospovidone type A.
  See section 2 "[Nationally completed name] contains lactose".

What [Nationally completed name] looks like and contents of the pack
[Nationally completed name] 2.5 mg tablets
White to slightly yellowish, elongated tablets approximately 10.1 x 4.1 mm with a bevelled edge and no score. They are engraved with "LCL" on one side and "NVR" on the other

[Nationally completed name] 5 mg tablets
White to slightly yellowish, elongated tablets approximately 12.1 x 4.9 mm with a bevelled edge and no score. They are engraved with "5" on one side and "NVR" on the other

[Nationally completed name] 10 mg tablets
White to slightly yellowish, elongated tablets approximately 15.1 x 6.0 mm with a bevelled edge and no score. They are engraved with “UHE” on one side and “NVR” on the other

The tablets are packed in aluminium/polyamide/aluminium/PVC blisters and inserted in a carton.

Pack sizes:
Blister: 10, 30, 90 tablets
Unit dose blister: 10x1, 30x1, 90x1 tablets

Not all pack sizes or strengths may be marketed in your country.

Houder van de vergunning voor het in de handel brengen en fabrikant

Houder van de vergunning voor het in de handel brengen
Sandoz B.V., Hospitaaldreef 29, 1315 RC Almere, Nederland

Fabrikant
Novartis Pharma GmbH
Roonstrasse 25
D-90429 Nürnberg
Duitsland

Salutas Pharma GmbH
Otto-von-Guericke-Allee 1
39179 Barleben
Duitsland

Sandoz S.R.L.
Livezeni street Nr. 7A
Targu Mures, 540472
Roemenië

In het register ingeschreven onder:
RVG 122426 - Everolimus Sandoz 2,5 mg, tabletten
RVG 122427 - Everolimus Sandoz 5 mg, tabletten
RVG 122428 - Everolimus Sandoz 10 mg, tabletten

Dit geneesmiddel is geregistreerd in lidstaten van de EEA onder de volgende namen:

Duitsland	Everolimus 1 A Pharma 2,5/ 5/ 10 mg Tabletten
Italië	Everolimus Sandoz GmbH
Nederland	Everolimus Sandoz 2,5/ 5/ 10 mg, tabletten

Deze bijsluiter is voor het laatst goedgekeurd in september 2024.