The medicine is dispensed with a doctor's prescription only

CAPRELSA 100 mg FILM-COATED TABLETS

Active ingredient:

SANOFI GENZYME 🧳

Each tablet contains: vandetanib 100 mg For inactive ingredients, see section 6.

Read this leaflet carefully in its entirety before using the medicine.

Keep this leaflet, you may need it again. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

If a side effect occurs, if one of the side effect worsens, or if you experience a side effect not mentioned in this leaflet, please refer to your doctor straight away.

In addition to the leaflet, Caprelsa has a Patient safety information card. This card includes important safety information, which you should know and follow before starting and during treatment with Caprelsa. Read the Patient safety information card and the patient leaflet before starting treatment with the preparation. Keep the card for further reference if

1. WHAT IS THE MEDICINE INTENDED FOR?

Caprelsa is intended for the treatment of metastatic medullary thyroid cancer, cancer that cannot be removed by surgery or has spread to other parts of the body.

Caprelsa works by slowing down the growth of new blood vessels in tumors (in cancer), which cuts off the supply of food and oxygen to the tumor. Caprelsa may also act directly on cancer cells to kill them or slow down their growth.

Therapeutic group:

Protein kinase inhibitor.

2. BEFORE USING THE MEDICINE

▼ Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient vandetanib or to any of Caprelsa's ingredients (see section 6).
- You have a congenital heart disorder called 'congenital long QT syndrome' which is seen on an electrocardiogram (ECG)
- You are breastfeeding.
- You are taking any of the following medicines: arsenic, cisapride (to treat heartburn), intravenous erythromycin and moxifloxacin (for the treatment of infectious inflammation), toremifene (to treat breast cancer), mizolastine (to treat allergies), Class IA and Class III antiarrhythmics (used to control heart

Do not use this preparation if any of the above apply to you. If you are not sure, please consult with your doctor.

Special warnings regarding use of Caprelsa:

Before treatment with Caprelsa, tell the doctor if: You are sensitive to the sun.

People taking Caprelsa may be more sensitive to the sun – sensitivity that will manifest as a sunburn. While you are taking Caprelsa, protect yourself from sun exposure and always use sunscreen and wear long clothes to avoid exposure to the sun. · You have high blood pressure.

- You have or have had in the past, an aneurysm (enlargement and weakening
- of a blood vessel wall) or a tear in a blood vessel wall Monitoring of your blood and your heart:

The doctor will perform blood tests to check the levels of potassium, calcium, magnesium, and thyroid-stimulating hormone (TSH), as well as the electrical activity of the heart (ECG). The doctor will perform these tests at the following times: · Before starting treatment with Caprelsa.

- Regularly during Caprelsa treatment.
- 1, 3 and 6 weeks after starting Caprelsa treatment.
- 12 weeks after starting Caprelsa treatment.
- Every 3 months thereafter.
- If the doctor changes your dosage of Caprelsa.
- If you started taking medicines that affect the heart.
- As instructed by your doctor.
- Children and adolescents:

Caprelsa is not intended for children and adolescents under the age of 18.

Tests and follow-up:

See Warnings section. **Drug interactions:**

If you are taking, or have recently taken, other medicines, including non-

prescription medicines and nutritional supplements, tell the doctor or pharmacist. This is because Caprelsa may affect the way certain medicines work and certain medicines may affect the way Caprelsa works.

- In particular, inform the doctor if you are taking any of the following medicines:
 itraconazole, ketoconazole, ritonavir, clarithromycin, rifampicin and moxifloxacine (medicines used to treat infections). · carbamazepine and phenobarbital (used to treat epilepsy).
- ondansetron (to treat nausea and vomiting).
- cisapride (to treat heartburn), pimozide (a psychiatric medicine used to treat repetitive and uncontrolled movements of the body and verbal outbursts)
- halofantrine and lumefantrine (to treat malaria). methadone (to treat addiction), haloperidol, chlorpromazine, sulpiride,
- amisulpride and zuclopenthixol (to treat mental illness). • pentamidine (to treat infection).
- vitamin K antagonists and dabigatran (blood thinners).
- cyclosporine and tacrolimus (for the prevention of transplant rejection), digoxin (for heart rate disorders), metformin (to treat diabetes).
- proton pump inhibitors (to treat heartburn)
- Use of the medicine and food:

The medicine can be taken with or without food.

Pregnancy and breastfeeding:

- Do not take Caprelsa if you are pregnant. Consult the doctor before starting treatment with Caprelsa if you are pregnant, breastfeeding, think you are pregnant or are planning a pregnancy. This is because Caprelsa may harm the unborn child. The doctor will explain the risks and benefits of Caprelsa treatment at this time to you. Women of child-bearing age must use effective contraception when taking Caprelsa and for at least four months after you stopped taking Caprelsa.
- To keep your baby safe, do not breastfeed during treatment with Caprelsa.
- **Driving and operating machinery:** Exercise caution when driving a car or using machines and machinery, since

3. HOW SHOULD YOU USE THE MEDICINE?

The dosage and treatment regimen will be determined by the doctor only.

The usual dosage of Caprelsa is generally 300 mg each day. Do not exceed the recommended dosage.

Method of administration: Be sure to take the tablets at the same time each day.

There is no information regarding crushing or halving the tablets.

If you have trouble swallowing the tablet: The tablet can be mixed with water as follows:

• Take half a glass of water (non-carbonated); only use water, and do not use any other liquids.

· Place the tablet in the water.

10 minutes

- · Drink straight away. In order to make sure that no remnants of the medicine remain in the glass,
- the medicine and drink

If you have accidentally taken a higher dosage: If you have accidentally taken an overdose or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency

If you experience any side effects, please inform the doctor. Your doctor may tell you to take a lower dosage of Caprelsa. Your doctor may also prescribe other medicines to treat the side effects. See the list of side effects in section 4.

Take action according to the time left until your next dose. • If 12 hours or more remain until the time for the next dose, take the missed

dose as soon as you remember. Then take the next dose at the normal time. • If less than 12 hours remain until it is time for the next dose, skip the missed dose. Then take the next dose at the normal time.

Do not take a double dose to make up for a forgotten dose. Adhere to the treatment regimen as recommended by the doctor. Even if there

is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

doctor or pharmacist.

4. SIDE EFFECTS As with any medicine, use of Caprelsa may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them. If

• Severe diarrhoea.

you have a side effect, your doctor may tell you to take a lower dosage of Caprelsa. Your doctor may also prescribe you other medicines to treat the side effects. Refer to the doctor straight away if you experience any of the following side effects – you may need urgent medical treatment:

in the electrical activity of your heart. These effects have been seen in 8% of

patients taking Caprelsa for metastatic medullary thyroid cancer. Your doctor may recommend you take Caprelsa at a lower dosage or to stop taking Caprelsa. Caprelsa has uncommonly been associated with life-threatening changes in heart rhythm.

- Always use the preparation exactly as your doctor has instructed you to. Check with your doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

• Stir the tablet until it has dispersed into the water. This may take up to about

add approximately half a glass of water to the empty glass with the remains of

room and bring the package of the medicine with you. If you experience a side effect:

If you forget to take the medicine:

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them. If you have further questions regarding use of the medicine, consult the

• Fainting, dizziness or heart rhythm changes. These may be signs of a change

 Severe skin reaction affecting large areas of the body. The signs may include redness, pain, ulcers, blisters and shedding of the skin. The lips, nose, eyes and genitals may also be affected. This effect may be common (occurring in less than 1 in 10 users) or uncommon (occurring in less than 1 in 100 users), depending on the type of skin reaction.

- Swallow the tablet with water.
- Caprelsa may cause tiredness, weakness or blurred vision.
- Inability to control bowel movements
- Pneumonia caused by the respiration of a foreign substance into the lungs · Bowel obstruction
- Bowel perforation
- Abnormal color of urine Lack of urine
- Impaired ability to heal properly Inflammation of the pancreas (pancreatitis)
- · Blistering of skin (bullous dermatitis) Side effects of unknown frequency (effects whose frequency has not yet

wall (aneurysm and artery dissection)

• Serious breathlessness, or sudden worsening of breathlessness, possibly accompanied by a cough or high fever. This may be caused by an inflammation

Seizures, headache, confusion or difficulty concentrating. These may be signs of a syndrome called RPLS (Reversible Posterior Leukoencephalopathy Syndrome). This syndrome generally passes when stopping treatment with Caprelsa. RPLS is uncommon (occurs in less than 1 in 100 users).

Inform the doctor immediately if you experience any of the side effects listed

Diarrhoea. Your doctor may prescribe a medicine to treat the diarrhoea, but

• High blood pressure. Your doctor may prescribe a medicine to treat blood

• Stones or calcium deposits in the kidneys or urinary tract (nephrolithiasis)

· Blurred vision, including mild changes in the eyes which can lead to blurred

• Sensitivity of the skin to sunlight. While using Caprelsa, protect yourself from

• Stroke, cerebral insufficieency or another condition in which the blood flow

• A type of rash that affects the hands and feet (hand foot syndrome)

exposure to the sun and always use sunscreen and long clothes when going

in less than 1 in 100 users) but can be life-threatening.

Very common side effects (occur in more than 1 in 10 users):

if the diarrhoea gets worse, please tell your doctor straight away

Additional side effects

Abdominal pain

Skin rash or acne

• Abdominal pain (indigestion)

• Loss of appetite (anorexia)

• Trouble sleeping (insomnia)

Inflammation of the nasal passages

• Upper respiratory tract infections

· Abnormal sensation in the skin

• Numbness or tingling sensation in the skin

• Edema (swelling caused by excess fluids)

Inflammation of the main air passages to the lungs

Common side effects (occur in less than 1 in 10 users):

• Toxins in the blood - a complication of infection

• Inflammation of the follicles, especially hair follicles

· Inflammation of the urinary bladder

• Inflammation of the larynx/voice box

• Skin pustular infection ("furuncle")

Loss of body fluids (dehydration)

· Inflammation of the lung tissue

• Increased pressure in the eye (glaucoma)

• Inflammation of the lining of the stomach (gastritis)

Inflammation of the sinuses

Weakness (asthenia)

• Tiredness (fatigue)

• Urinary tract infection

Depression

Nail problems

 Tiredness Nausea

Vomiting

pressure

Headache

 Dizziness Pain

outside.

Dehydration

· Weight loss

Dry mouth

• Pneumonia

Fungal infection

Kidney infection

• Drowsiness, sleepiness

· Difficulty swallowing

Gastrointestinal bleeding

• Gallstones (cholelithiasis)

• Frequent and urgent urination

 Eye irritation (conjunctivitis) Visual impairment Halo vision

· Corneal defect (keratopathy) • A type of diarrhoea (colitis)

· Seeing flashes of light (photopsia)

• Loss of hair from the head and body (alopecia) • Changes in sense of taste (dysgeusia)

Inflammation of the appendix (appendicitis)

• Involuntary muscle contractions (convulsion)

Uncommon side effects (occur in less than 1 in 100 users):

• Rapidly alternating muscular contraction and relaxation (clonus)

signs include breathlessness and swelling of the ankle)

• Heart failure (a condition in which the heart cannot pump the blood well;

• Inflammation of the diverticula (diverticula - small bulging pouches that can

Painful urination

• Nose bleed (epistaxis)

Bacterial infection

Malnutrition

form in the digestive system)

· Clouding of the lens of the eye

· Bacterial skin infections Abdominal wall abscess

• Swelling of the brain

· Heart rhythm disorders

· Reduced heart function

Lung function disorders

• Kidney failure

Fever

• Dry eyes

Feeling unsteady

· Bloody cough

Constipation

Anxiety

Tremor

Fainting

• Flu

· Severe high blood pressure

the brain is inadequate

• Sore mouth (stomatitis)

of the lungs called interstitial lung disease. This effect is uncommon (occurs

Side effects that may be seen in laboratory tests:

• Abnormal liver and pancreatic function which are seen in blood tests. Usually

- without symptoms, but your doctor may want to monitor these values • Decreased levels of calcium in the blood. The doctor may prescribe or change
- Decreased levels of potassium in the blood • Increased levels of calcium in the blood
- · Increased red blood cell levels
- straight away.

"Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il), which directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il 5. HOW SHOULD THE MEDICINE BE STORED?

• Avoid poisoning! This medicine and any other medicine, should be stored in a safe place, out of the reach of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

• Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month. • Do not discard medicines in the household waste bin or waste water. Ask your

pharmacist how to dispose of medicines you no longer need. These measures will help protect the environment. 6. FURTHER INFORMATION

Composition of the preparation:

What the medicine looks like and contents of the package: White, round, film-coated tablets with "Z100" imprinted on one side.

In addition to the active ingredient, the medicine also contains:

sanofi-aventis Israel ltd., 10 Beni Gaon Street, P.O.B. 8090, Netanya

Manufacturer: Genzyme Europe B.V., Amsterdam, Netherlands

Revised in March 2020

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 149 23 33769

• Protein or blood in the urine (seen in a urine test) Heart rhythm changes (shown in an ECG). Your doctor may tell you to stop taking Caprelsa or to take a lower dosage of Caprelsa

- Increased levels of glucose (sugar) in the blood · Decreased levels of sodium in the blood • Decrease in thyroid function
- If a side effect occurs, if one of the side effect worsens, or if you suffer from a side effect not mentioned in this leaflet, please refer to your doctor
- Side effects can be reported to the Ministry of Health by clicking on the link

• Store the preparation in a cool place below 30°C.

Caprelsa comes in a blister pack of 30 tablets. License holder:

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, please ask your doctor.