VANDESA® (VANDETANIB) F.C. TABLET

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Read this patient information carefully before you start taking Vandesa® because it answers some common questions about vandesa®. This medication is prescribed for your current condition, therefore do not use it, in similar cases and do not recommend it to others. To report SUSPECTED ADVERSE REACTIONS, contact Noavaran Daroui Kimia Co. at +982166435789 or send email to medical@kimia-pharma.co

Read this patient Information carefully before you start taking Vandesa® because it contains important information for you. This leaflet does not take the place of talking with your healthcare provider about your medical condition or treatment.

Composition

Each film-coated tablet Vandesa® 100 mg contains: 100 mg vandetanib.
Each film-coated tablet Vandesa® 300 mg contains: 300 mg vandetanib.

Mechanism of action

In vitro studies have shown that Vandesa® inhibits the tyrosine kinase activity of the EGFR and VEGFR families, RET, BRK, TIE2, and members of the EPH receptor and Src kinase families.

Pharmacokinetic

Absorption

Absorption is slow with peak plasma concentrations typically achieved at a median of 6 hours, range 4-10 hours, after dosing. Vandesa® accumulates approximately 8-fold on multiple dosing with steady state achieved in approximately 3 months.

Distribution

Vandesa® binds to human plasma with in vitro protein binding being approximately 90%. In ex vivo plasma samples from colorectal cancer patients at steady state exposure after 300 mg once daily, the mean percentage protein binding was 94%.

Metabolism

Following oral dosing, unchanged Vandesa® and metabolites Vandesa® were detected in plasma, urine and feces. Vandesa® is primarily metabolized by CYP3A4 and flavin–containing monooxygenase enzymes FMO1 and FMO3. A glucuronide conjugate was seen as a minor metabolite in excreta only.

Excretion

Within a 21-day collection period after a single dose of ^{14}C-Vandesa®, approximately 69% was recovered with 44% in feces and 25% in urine.

Indication

Vandesa® is prescribed for:

- The treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease.
- Use Vandesa® in patients with indolent, asymptomatic or slowly progressing disease only after careful consideration of the treatment related risks of Vandesa®.

It is not known if Vandesa® is safe and effective in children.

Dosage and administration

- The recommended dose of Vandesa® is 300 mg taken orally once daily with or whitout food, until disease progression or unacceptable toxicity occurs.
- Vandesa® is not recommended for use in patients with moderate and severe hepatic impairment, as safety and efficacy have not been established.

Side effects / Adverse reactions

It should be noted that these side effects do not occur in all patients. These are not all the possible side effects of Vandesa®. Call your doctor for medical advice about side effects.

Vandesa® may cause serious side effects including:

- **QT Prolongation and Torsades de Pointes.** Vandesa® can prolong the QT interval in a concentration-dependent manner. Torsades de pointes, ventricular tachycardia and sudden deaths have occurred in patients treated with Vandesa®. An electrocardiogram (ECG), serum potassium, calcium, magnesium and thyroid-stimulating hormone (TSH) should be tested before starting treatment with Vandesa®, 2-4 weeks and 8-12 weeks after, and every 3 months thereafter. Patients should contact their healthcare provider in the event of syncope, pre-syncopal symptoms, and cardiac palpitations. Electrolytes and ECGs should be monitored more frequently in patients who experience diarrhea.
- **Serious skin reactions.** Vandesa® can cause a serious skin reaction, such as toxic epidermal necrolysis and called Stevens-Johnson syndrome or other serious skin reactions that may affect any part of body. These serious skin reactions may be life threatening and the patient may need to be treated in a hospital. The symptoms include: skin rash or acne, dry skin, itching, blisters on skin, blisters or sores in mouth, peeling of skin, fever, muscle or joint aches, redness or swelling of face, hands, or soles of feet.
- **Breathing problems (interstitial lung disease).** Vandesa® may cause a breathing problem called interstitial lung disease (ILD) that can lead to death. Patients may experience sudden onset or worsening of breathlessness, persistent cough or fever.
- **Stroke.** Strokes have been reported in some Vandesa® treating patients and in some cases have caused death. If the patient has symptoms of a stroke which may include: numbness or weakness of the face, arm or leg, especially on one side of the body, sudden confusion, trouble speaking or understanding, sudden trouble seeing in one or both eyes, sudden trouble walking, dizziness, loss of balance or coordination, sudden, severe headache, taking Vandesa® should be stopped.
- **Bleeding.** Severe bleeding can happen during treatment with Vandesa®.
- **Heart failure.** Vandesa® can cause heart failure that can lead to death. You may have to stop taking Vandesa® if you have heart failure. Heart failure may not be reversible after stopping Vandesa®. Your healthcare provider should monitor you for signs and symptoms of heart failure.
- **Diarrhea.** Diarrhea is often a symptom of medullary thyroid cancer. Vandesa® can also cause diarrhea or make diarrhea worse. Your healthcare provider should check your blood levels to monitor your electrolytes more frequently if you have diarrhea. If diarrhea occurs, serum electrolytes and ECGs should be carefully monitored to reduce the risk and enable early detection of QT prolongation resulting from dehydration.
- **Thyroid hormones.** You can have changes in your thyroid hormone when taking Vandesa®. Your healthcare provider should monitor your thyroid hormone levels while taking Vandesa®.
- **High blood pressure (hypertension).** If you develop high blood pressure or your high blood pressure gets worse, your healthcare provider may lower your dose of Vandesa® or tell you to stop taking Vandesa® until your blood pressure is under control. Your healthcare provider may prescribe another medicine to control your high blood pressure.
- **Reversible Posterior Leukoencephalopathy Syndrome (RPLS).** A condition called reversible posterior leukoencephalopathy syndrome can happen while taking Vandesa®. Call your healthcare provider right away if you have: headaches, seizures, confusion, changes in vision, problems thinking.
- **Possible wound healing problems.** Vandesa® has the potential to adversely affect wound healing. If the patient plan to have any surgery before starting and during treatment with Vandesa®, the healthcare provider should be informed right away. Taking Vandesa® should withheld at least 1 month before planned surgery. Administering Vandesa® should be avoided for at least 2 weeks following major surgery and adequate wound healing. The safety of resumption of treatment with Vandesa® after resolution of wound healing complications has not been established. The healthcare provider should tell when the patient may start taking Vandesa® again after surgery.

Call your healthcare provider right away if you have aforementioned symptoms.

The most common side effects

The most common side effects in patients who take Vandesa® include:

- Diarrhea • Rash • Acne • Nausea and vomiting • High blood pressure (hypertension)
- Headache • Feeling tired • Loss of appetite • Upper respiratory tract infections
- Stomach (abdominal) pain • Eye disorders • Vision disorders

Drug interaction

- **CYP3A4 inducers:** Rifampicin, a strong CYP3A4 inducer, decreased Vandesa® plasma concentrations. Avoid concomitant use of known strong CYP3A4 inducers during Vandesa® therapy. Avoid concomitant use of St. John's wort because it can decrease Vandesa® exposure unpredictably.
- **OCT2 transporter:** Vandesa® increased plasma concentrations of metformin that is transported by the organic cation transporter type 2 (OCT2). Use caution and closely monitor for toxicities when administering Vandesa® with drugs that are transported by OCT2.
- **Digoxin:** Vandesa® increased plasma concentrations of digoxin .Use caution and closely monitor for toxicities when administering Vandesa® with digoxin.
- **Drugs that prolong the QT Interval:** Avoid concomitant use of Vandesa® with agents that may prolong the QT interval. The administration of Vandesa® with anti-arrhythmic drugs (including, but not limited to amiodarone, disopyramide, procainamide, sotalol, dofetilide) and other drugs that may prolong the QT interval (including but not limited to chloroquine, clarithromycin, dolasetron, granisetron, haloperidol, methadone, moxifloxacin, and pimozide) should be avoided.
- Do not use in patients with congenital long QT syndrome.

Warnings

Before you take Vandesa®, tell your healthcare provider if you:

- have any heart problems, including a condition called congenital long QT syndrome
- have an irregular heartbeat
- take or have stopped taking a medicine that causes QT prolongation
- have low blood levels of potassium, calcium, or magnesium
- have high blood levels of thyroid-stimulating hormone
- have high blood pressure
- have skin problems
- have a history of breathing problems
- have a recent history of coughing up blood or bleeding
- have diarrhea
- have liver problems
- have kidney problems
- have seizures or are being treated for seizures
- are pregnant or plan to become pregnant
- are breastfeeding or plan to breastfeed
- plan to have surgery or have had a recent surgery

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Vandesa® and other medicines may affect each other causing side effects.

Especially tell your healthcare provider if you take:

- St. John's wort. You should not take St. John's wort while taking Vandesa®.
- certain medicines that can affect how your liver breaks down medicine.
- a medicine for your heart.

Ask your healthcare provider if you are not sure if your medicine is one listed above. Do not take other medicines while taking Vandesa® until you have talked with your healthcare provider or pharmacist.

Hypothyroidism. Changes in thyroid hormone may occur when taking Vandesa®. If signs or symptoms of hypothyroidism occur, thyroid hormone levels should be examined and thyroid replacement therapy should be adjusted accordingly.

Missed dose

If you miss a dose and your next dose is in:

- Less than 12 hours, take your next dose at the normal time. Do not make up for the missed dose.
- 12 hours or more, take the missed dose as soon as you remember. Take the next dose at the normal time.

Overdose

Call your healthcare provider right away if you take too much Vandesa®.

Pregnancy and lactation

Vandesa® can cause fetal harm when administered to a pregnant woman. Talk to your healthcare provider if you are pregnant or plan to become pregnant. Females of reproductive potential should use effective contraception during treatment and for at least 4 months following the last dose of Vandesa®.

It is not known if Vandesa® passes into breast milk. If you are breastfeeding or plan to breastfeed, you and your healthcare provider should decide if you will take Vandesa® or breastfeed. You should not do both.

Patient information

- Take Vandesa® exactly as your healthcare provider tells you to take it. Do not change your dose or stop taking Vandesa® unless your healthcare provider tells you to.
- Vandesa® may be taken with or without food.
- Swallow Vandesa® tablets whole with water.
- Do not crush or chew Vandesa® tablets. If Vandesa® tablets are accidentally crushed, contact with skin should be avoided. If contact occurs, wash affected areas well with water.
- If you cannot swallow Vandesa® tablets whole:
  - Place your dose of Vandesa® in a glass that contains 2 ounces of noncarbonated water (no other liquids should be used).
  - Stir the Vandesa® tablet(s) and water mixture for about 10 minutes or until the tablet(s) are in very small pieces (the tablets will not completely dissolve).
  - Swallow Vandesa® and water mixture right away.
  - If any Vandesa® and water mixture remains in the glass, mix with an additional 4 ounces of noncarbonated water and swallow the mixture to make sure that you take your full dose of Vandesa®.
- Limit exposure to the sun. Vandesa® can make your skin sensitive to the sun. While taking Vandesa® and for 4 months after stopping your Vandesa® treatment, use sun block and wear clothes that cover your skin, including your head, arms and legs when you go outdoors.
- Use caution before driving or using machinery. Keep in mind Vandesa® may make you feel tired, weak, or cause blurred vision.
- Your healthcare provider should check your blood pressure regularly and heart during your treatment with Vandesa®.

Storage

- Store Vandesa® tablets below 30°C.
- Safely throw away medicine that is out of date or that you no longer need. Ask your pharmacist how to safely throw away Vandesa® tablets.
- Keep out of the reach of children.
- Keep away from light and moisture.
- Use appropriate precautions for handling and disposal of cytotoxic drugs.

Packaging

Bottle of 30 F.C. Tablets.

References

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/022405s016lbl.pdf
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