KITENT® CAPSULE

KITENT®
SUNITINIB

KITENT® (SUNITINIB) CAPSULE FOR ORAL USE
Read this patient information carefully before you start taking Kitent® because it answers some common questions about Kitent®. 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 +982166433514 or send email to medical@kimia-pharma.co

Read this patient information carefully before you start taking Kitent® 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 capsule Kitent® 12.5 mg contains: sunitinib (as malate) 12.5 mg.
Each capsule Kitent® 25 mg contains: sunitinib (as malate) 25 mg.
Each capsule Kitent® 50 mg contains: sunitinib (as malate) 50 mg.

Mechanism of action
Sunitinib is a small molecule that inhibits multiple receptor tyrosine kinases (RTKs).

Pharmacokinetic
Absorption
Following oral administration of Kitent®, the time to maximum plasma concentration (T_{max}) ranged from 6 to 12 hours.
Distribution
The apparent volume of distribution (Vd/F) for Kitent® is 2230 L. Binding of Kitent® and its primary active metabolite to human plasma protein in vitro is 95% and 90%, respectively.
Metabolism
Kitent® is metabolized primarily by CYP3A4 to its primary active metabolite, which is further metabolized by CYP3A4.
Excretion
After a radiolabeled dose of Kitent®, approximately 61% of the dose was recovered in feces and 16% in urine.
Elimination
Following administration of a single oral dose in healthy subjects, the terminal half-lives of Kitent® and its primary active metabolite are approximately 40 to 60 hours and 80 to 110 hours, respectively.

Indication
Kitent® is a kinase inhibitor indicated for:
- treatment of adult patients with gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate.
- treatment of adult patients with advanced renal cell carcinoma (RCC).
- adjuvant treatment of adult patients at high risk of recurrent RCC following nephrectomy.
- treatment of progressive, well-differentiated pancreatic neuroendocrine tumors (pNET) in adult patients with unresectable locally advanced or metastatic disease.

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

Dosage and Administration
Gastrointestinal Stromal Tumor (GIST) and Advanced Renal Cell Carcinoma (RCC):
The recommended dosage is 50 mg once daily for 4 weeks, followed by a 2-week treatment-free period to complete 6-week cycle (Schedule 4/2).
Adjuvant Treatment of RCC:
The recommended dosage is 50 mg orally once daily for the first 4 weeks of a 6-week cycle (Schedule 4/2) for a maximum of 9 cycles.
Pancreatic neuroendocrine tumors (pNET):
The recommended dosage is 37.5 mg orally once daily

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 Kitent®. For more information, ask your healthcare provider or pharmacist.

Kitent® can cause serious side effects, including:
- **Severe liver problems that can be life-threatening. Tell your healthcare provider right away if you develop any of the following signs and symptoms of liver problems during treatment with Kitent®:**
  - o pain or discomfort in the right upper stomach area
  - o dark urine
  - o yellow eyes or skin
  - o itching

  Your healthcare provider should do blood tests to check your liver function before you start taking and during treatment with Kitent®. Your healthcare provider may temporarily stop, reduce your dose, or permanently stop treatment with Kitent® if you develop liver problems.
- **Heart problems.** Heart problems may include heart failure, heart attack and heart muscle problems (cardiomyopathy) that can be life-threatening. Tell your healthcare provider if you feel very tired, are short of breath, or have swollen feet and ankles.
- **Abnormal heart rhythm changes. Changes in the electrical activity of your heart called QT prolongation can cause irregular heartbeats that can be life threatening.** Your healthcare provider may do electrocardiograms and blood tests (electrolytes) to watch for these problems during your treatment with Kitent®. Tell your healthcare provider right away if you feel dizzy, faint, or have abnormal heartbeats during your treatment with Kitent®.
  - o you feel faint or lightheaded, or you pass out
  - o feel your heart beat is irregular or fast
  - o dizziness
- **High blood pressure.** High blood pressure is common with Kitent® and may sometimes be severe. Follow your healthcare provider's instructions about having your blood pressure checked regularly. Call your healthcare provider if your blood pressure is high, or if you have any of the following signs or symptoms of high blood pressure:
  - o severe headache
  - o lightheadedness
  - o dizziness
  - o change in vision

  Your healthcare provider may prescribe medicine for you to treat high blood pressure, if needed.
- **Bleeding problems.** Bleeding is common with Kitent®, but Kitent® can also cause severe bleeding problems that can be life-threatening. Your healthcare provider will monitor you for bleeding and may do blood tests if needed. Call your healthcare provider right away if you have any of these symptoms or a serious bleeding problem during treatment with Kitent®, including:
  - o vomiting blood
  - o coughing up blood
  - o black, sticky stools
  - o bloody urine
  - o change in your mental status
  - o headache
  - o painful, swollen stomach (abdomen)
- **Serious stomach and intestinal problems that can be life-threatening.** Some people have had tears in their stomach or intestine (perforation), or have developed an abnormal opening between the stomach and intestine (fistula). Get medical help right away if you get stomach-area (abdominal) pain that does not go away or is severe during treatment with Kitent®.
- **Tumor lysis syndrome (TLS).** TLS is caused by the fast breakdown of cancer cells and can cause kidney failure and the need for dialysis treatment, abnormal heart rhythm, and seizure that may be life-threatening.
- **Abnormal changes in the brain (Reversible Posterior Leukoencephalopathy Syndrome [RPLS]).** RPLS can cause a collection of symptoms including headache, confusion, and vision loss. Some people who have taken Kitent® have developed RPLS that can be life-threatening.
- **Thrombotic microangiopathy (TMA) including thrombotic thrombocytopenia purpura (TTP) and hemolytic uremic syndrome (HUS).** TMA is a condition that involves injury to the smallest blood vessels, and blood clots that can happen while taking Kitent®. TMA is accompanied by a decrease in red cells and cells that are involved with clotting. TMA may harm your body's organs such as the brain and kidneys, and can sometimes be life-threatening.
- **Protein in your urine.** Some people who have taken Kitent® have developed protein in their urine, and in some cases, kidney problems that can be life-threatening. Your healthcare provider will check you for this problem.
- **Serious skin and mouth reactions.** Treatment with Kitent® has caused severe skin reactions that can be life-threatening, including:
  - o severe rash with blisters or peeling of the skin.
  - o tissue damage (necrotizing fasciitis).
  - o painful sores or ulcers on the skin, lips or inside the mouth.

  If you have any signs or symptoms of severe skin reactions, stop taking Kitent® and call your healthcare provider or get medical help right away.
- **Thyroid problems.** Your healthcare provider may do tests to check your thyroid function during Kitent® treatment. Tell your healthcare provider if you have any of the following signs and symptoms during your treatment with Kitent®:
  - o tiredness that gets worse and does not go away
  - o loss of appetite
  - o sweating
  - o feeling nervous or agitated, tremors
  - o problems with heat
  - o diarrhea
  - o weight gain or weight loss
  - o fast heart rate
  - o headache
  - o feeling depressed
  - o nausea or vomiting
  - o hair loss
  - o irregular menstrual periods or no menstrual periods
- **Low blood sugar (hypoglycemia).** Low blood sugar can happen with Kitent®, and may cause you to become unconscious, or you may need to be hospitalized. Low blood sugar with Kitent® may be worse in people who have diabetes and take antidiabetic medicines. Your healthcare provider should check your blood sugar levels regularly during treatment with Kitent® and may need to adjust the dose of your antidiabetic medicines. Call your healthcare provider right away if you have any of the following signs or symptoms of low blood sugar during your treatment with Kitent®:
  - o headache
  - o irritability
  - o drowsiness
  - o hunger
  - o weakness
  - o fast heart beat
  - o dizziness
  - o sweating
  - o confusion
  - o feeling jittery
- **Jawbone problems (osteonecrosis).** Severe jawbone problems have happened in some people who take Kitent®. Certain risk factors such as taking a bisphosphonate medicine or having dental disease may increase your risk of getting osteonecrosis. Your healthcare provider may tell you to see your dentist before you start taking Kitent®. Your healthcare provider may tell you to avoid dental procedures, if possible, during your treatment with Kitent®, especially if you are receiving a bisphosphonate medicine into a vein (intravenous). Tell your healthcare provider if you plan to have any dental procedures before or during treatment with Kitent®.
  - o You should stop taking Kitent® at least 3 weeks before planned dental procedures.
  - o Your healthcare provider should tell you when you may start taking Kitent® again after dental procedures.
- **Pancreatitis.** Increases in serum lipase and amylase activities were observed in patients with various solid tumors who received Kitent®. Increases in lipase activities were transient and were generally not accompanied by signs or symptoms of pancreatitis in subjects with various solid tumors. Cases of serious pancreatic events, some with fatal outcome, have been reported. If symptoms of pancreatitis are present, patients should have Kitent® discontinued and be provided with appropriate supportive care.
- **Wound healing problems.** Wound healing problems have happened in some people who take Kitent®. Tell your healthcare provider if you plan to have any surgery before or during treatment with Kitent®.
  - o You should stop taking Kitent® at least 3 weeks before planned surgery.
  - o Your healthcare provider should tell you when you may start taking Kitent® again after surgery.

Your healthcare provider may temporarily stop, reduce your dose, or permanently stop treatment with Kitent® if you develop serious side effects.

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

The most common side effects of Kitent® include:
- tiredness
- weakness
- diarrhea
- nausea
- loss of appetite
- indigestion
- vomiting
- taste changes
- stomach-area (abdominal) pain
- high blood pressure
- low platelet counts
- pain, swelling or sores inside of your mouth
- blisters or rash on the palms of your hands and soles of your feet

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

Drug interaction
Since the drug interactions with Kitent® are not limited to the following medicines tell your healthcare provider or pharmacist if you are taking, have recently taken or might take any other medicines. This includes herbal medicines and other medicines you bought without a prescription.
Tell your healthcare provider before taking Kitent® if you are taking any of the following medicines.
- ketoconazole, itraconazole – used to treat fungal infections
- erythromycin, clarithromycin, rifampicin –used to treat infections
- ritonavir –used to treat HIV
- dexamethasone – a corticosteroid used for various conditions (such as allergic/breathing disorders or skin diseases)
- phenytoin, carbamazepine, phenobarbital – used to treat epilepsy and other neurological conditions
- herbal preparations containing St. John's Wort (*Hypericum perforatum*) – used to treat depression and anxiety
- medications known to prolong the QT interval

Kitent® with food and drink
You should avoid drinking grapefruit juice while on treatment with Kitent®.

Warnings
Before taking Kitent® tell your healthcare provider about all of your medical conditions, including if you:
- have any heart problems
- having lung or breathing problems. Tell your doctor if you develop cough, chest pain, sudden onset of shortness of breath, or coughing up blood. These may be symptoms of a condition called pulmonary embolism that occurs when blood clots travel to your lungs.
- have high blood pressure
- have thyroid problems
- have a history of low blood sugar or diabetes
- have kidney function problems (other than cancer)
- have liver problems
- have any bleeding problem
- Plan to have surgery or have had a recent surgery. You should stop taking Kitent® at least 3 weeks before planned surgery. Tell all of your healthcare providers and dentists that you are taking Kitent®. They should talk to the healthcare provider who prescribed Kitent® for you, before you have **any** surgery, or medical or dental procedure.
- have seizures
- have or have had pain in the mouth, teeth or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth
- are pregnant or plan to become pregnant. Kitent® can harm your unborn baby.
- are breastfeeding or plan to breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription medicines and over-the-counter medicines, vitamins, and herbal supplements. Using Kitent® with certain other medicines can cause serious side effects.

- You may have an increased risk of severe jaw bone problems (osteonecrosis) if you take Kitent® and a bisphosphonate medicine. **Especially tell** your healthcare provider if you are taking or have taken an osteoporosis medicine.
- The medicine in Kitent® is yellow, and it may make your skin look yellow. Your skin and hair may get lighter in color. Kitent® may also cause other skin problems including: dryness, thickness or cracking of the skin.
- Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

Missed dose
If you miss a dose of Kitent® by less than 12 hours, take the missed dose right away. If you miss a dose of Kitent® by more than 12 hours, just take your next dose at your regular time. Do not make up the missed dose. Tell your healthcare provider about any missed dose.

Overdose
If you take too much Kitent® call your healthcare provider or go to the nearest hospital emergency room right away.

Pregnancy and lactation
Kitent® can harm your unborn baby. Tell your healthcare provider right away if you are pregnant, or if you become pregnant or think you are pregnant during treatment with Kitent®.
In females who are able to become pregnant:
- Your healthcare provider should do a pregnancy test before you start treatment with Kitent®.
- You should use effective birth control (contraception) during treatment and for at least 4 weeks after your last dose of Kitent®.

Males with female partners who are able to become pregnant:
- You should use effective birth control (contraception) during treatment and for 7 weeks after your last dose of Kitent®.
- Kitent® may cause fertility problems in males and females. Tell your healthcare provider if this is a concern for you.

Do not breastfeed during treatment with Kitent® and for at least 4 weeks (1 month) after the last dose.

Patient information
- Take Kitent® exactly the way your healthcare provider tells you.
- Take Kitent® 1 time each day with or without food.
- If you take Kitent® for GIST or RCC, you will usually take your medicine for 4 weeks (28 days) and then stop for 2 weeks (14 days). This is 1 cycle of treatment. You will repeat this cycle for as long as your healthcare provider tells you to.
- If you take Kitent® for pNET, take it 1 time each day until your healthcare provider tells you to stop.
- Do not drink grapefruit juice or eat grapefruit during your treatment with Kitent®. They may cause you to have too much Kitent® in your body.
- Your healthcare provider may do blood tests before each cycle of treatment to check you for side effects.
- If you experience dizziness or you feel unusually tired, take special care when driving or using machines.

Storage
- Keep away from light and moisture. Store below 30°C.
- Keep out of the reach of children.
- Keep the desiccant in the bottle. Do not eat or throw away the desiccant pack.
- Keep in the original container.
- Ask your healthcare provider or pharmacist about the right way to throw away expired or unused Kitent®.
- Use appropriate precautions for handling and disposal of cytotoxic drugs.

Packaging
Bottle of 30 Capsules.

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References
https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/021938s039lbledt.pdf
https://www.ema.europa.eu/en/documents/product-information/sutent-epar-product-information_en.pdf
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