Kitent® Capsule
Sunitinib

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Composition
Each capsule Kitent® 12.5mg contains: sunitinib (As malate) 12.5mg
Each capsules Kitent® 25mg contains: sunitinib (As malate) 25mg
Each capsules Kitent® 50mg contains: sunitinib (As malate) 50mg

Description
Exhibits antitumor and antiangiogenic properties by inhibiting multiple receptor tyrosine kinases, including platelet-derived growth factors (PDGFR-alpha and PDGFR-beta), vascular endothelial growth factors (VEGFR1, VEGFR2, and VEGFR3), FMS-like tyrosine kinase-3 (FLT3), colony-stimulating factor type 1 receptor (CSF-1R), and glial cell-line derived neurotropic factor receptor (RET).

Pharmacokinetic
Absorption
Peak plasma: 6 to 12 hours.
Distribution
• Protein binding Sunitinib: 95%.
• Protein binding SU12662: 90%.
Metabolism
Hepatic; primarily metabolized by cytochrome P450 (CYP-450) 3A4 to the N-desethyl metabolite SU12662 (active).
Excretion
Feces (61%); urine (16%).
Half-life elimination, terminal:
• Sunitinib: 40 to 60 hours.
• SU12662: 80 to 110 hours.

Dosage and Administration
Adult
Pancreatic neuroendocrine tumors, advanced
Usual dosage: 37.5 mg once daily continuously without a scheduled off treatment period.
Maximum dose: 50 mg daily.
Dosage adjustment: Dose interruption and/or dose modification in 12.5 mg increments or decrements is recommended based on individual safety and tolerability.
Gastrointestinal stromal tumor- Renal cell carcinoma, advanced
Usual dosage: 50 mg once daily on a schedule of 4 weeks on treatment followed by 2 weeks off (schedule 4/2).
Dosage adjustment: Dose interruption and/or dose modification in 12.5 mg increments or decrements is recommended based on individual safety and tolerability.

Monitor
LVEF; baseline,
ECG (12-lead; baseline and periodic with cardiac risk factor),
blood pressure; (prior to each treatment cycle), liver function tests (baseline, with each cycle and if clinically indicated), serum including magnesium, phosphate, and potassium (prior to each treatment cycle), urinalysis (for proteinuria development or worsening); consider dental exam prior to treatment initiation;
Symptoms of Hypothyroidism, hyperthyroidism, or thyroiditis.

Warnings /Precautions
1. Hepatotoxicity:
   Hepatotoxicity, which may be severe and/or result in fatal liver failure. Signs of liver failure include jaundice, elevated transaminases, and/or hyper bilirubinemia, in conjunction with encephalopathy, coagulopathy, and/or renal failure.
2. Left ventricular dysfunction/heart failure:
   May cause a decrease in left ventricular ejection fraction (LVEF), including grade 3 reductions; consider obtaining LVEF evaluation prior to treatment. Mean onset of symptomatic
   Heart failure is 22 days from treatment initiation. Cardiovascular events (some fatal), including symptomatic heart failure, myocardial disorders, and cardiomyopathy have been reported with use. Use with caution in patients with cardiac dysfunction.
3. QT interval prolongation:
   QTc prolongation and torsade's pointes have been observed (dose dependent); use caution in patients with a history of QTc prolongation, with medications known to increase sunitinib levels or prolong the QT-interval, or patients with preexisting (relevant) cardiac disease, bradycardia, or electrolyte imbalance. Obtain a baseline and periodic 12-lead electrocardiogram (ECG).
4. Hypertension:
   May cause hypertension; monitor and control with antihypertensive if needed. Interrupt therapy until hypertension is controlled for severe hypertension.
5. Bleeding:
   Hemorrhagic events have been reported including epistaxis, rectal, gingival, upper GI, wound bleeding, urinary tract, genital, brain, tumor-related, and hemoptysis/pulmonary hemorrhage; may be serious and/or fatal.
6. Osteonecrosis of the jaw:
   Osteonecrosis of the jaw (ONJ) has been observed with sunitinib. Concurrent bisphosphonate use or dental disease may increase the risk for ONJ. If possible, avoid invasive dental procedures in patients with current or prior bisphosphonate use. Consider a dental exam and appropriate prophylactic dentistry prior to treatment initiation.
7. Tumor lysis syndrome:
   Tumor lysis syndrome (TLS), including fatalities, has been reported, predominantly in patients with renal cell cancer or GIST. Risk for TLS is higher in patients with a high tumor burden prior to treatment; monitor closely. Correct clinically significant dehydration and treat high uric acid levels prior to initiation of treatment.
8. GI complications:
   Serious and fatal GI complications, including GI perforation, have occurred (rarely). Pancreatitis has been observed in renal cell cancer patients; discontinue sunitinib if symptoms are present.
9. Thyroid disorders:
   Thyroid dysfunction (eg, hypothyroidism, hyperthyroidism, Thyroiditis) may occur; the risk for hypothyroidism appears to increase with therapy duration. Hyperthyroidism, sometimes followed by hypothyroidism, has also been reported. Monitor thyroid function at baseline and if symptomatic.
10. Wound healing complications:
    Impaired wound healing has been reported with sunitinib; temporarily withhold treatment for patients undergoing major surgical procedures. The optimal time to resume treatment after a procedure has not been determined.
11. Adrenal toxicity:
    Has been reported; monitor for adrenal insufficiency in patients with stress such as surgery, trauma, or severe infection.
12. Depigmentation:
    May cause skin and/or hair depigmentation or discoloration.
13. Hazardous agent:
    Use appropriate precautions for handling and disposal.
14. Renal toxicity:
    Proteinuria and (rare) cases of nephrotic syndrome have been reported; discontinue treatment in patients with nephrotic syndrome.
15. Reversible posterior leukoencephalopathy syndrome:
    Has been reported (rarely, some fatal). Symptoms of reversible posterior leukoencephalopathy syndrome include confusion, headache, hypertension, lethargy, seizure, blindness and/or other vision, or neurologic disturbances; interrupt treatment and begin management of hypertension.

Dose adjustment:
• Cardiovascular
• Heart Failure
Reduce dose or temporarily interrupt therapy; when symptoms resolve, resume therapy at reduced doses.
• Congestive heart failure
Discontinue therapy.
• Severe hypertension
• Temporarily interrupt therapy until hypertension is controlled.
• GI
• symptomatic pancreatitis
• Discontinue therapy.
• Hepatic grade 3 or 4 hepatic adverse reactions;
Interrupt dose discontinue therapy if there is no resolution. Do not restart sunitinib if patients subsequently experience changes in liver function tests or have other signs and symptoms of liver failure.
• Hepatic failure;
Discontinue therapy.
• Hematologic
Thrombotic microangiopathy Suspend therapy; following resolution, treatment may be resumed with discretion.
• Neurologic
Reversible posterior leukoencephalopathy syndrome
Temporarily suspend therapy. Following resolution, therapy may be resumed with discretion.
• Renal
Nephrotic syndrome
Discontinue therapy.
• Dental
dental check-up before initiating
treatment, risk of osteonecrosis of the jaw.

Contraindication
Hypersensitivity
Renal impairment.

Adverse Effects
>10%
Also abdominal pain, diarrhoea, constipation, anorexia, taste disturbance,dehydration; hypertension, oedema; dyspnoea,cough; fatigue, dizziness, headache, insomnia, peripheral neuropathy, paraesthesia; hypothyroidism;arthralgia, myalgia; increased lacrimation; epistaxis;
skin, hair, and urine discoloration, hand-foot syndrome, dry skin, and rash; gastro-intestinal perforation, fistula formation (interrupt treatment if occurs) pancreatitis, osteonecrosis of the jaw, hepatic failure, proteinuria (rarely nephrotic syndrome) and seizures reported.

HOW TO USE
Discuss specific use of drug and side effects with patients as it relates to treatment. Patients may experience asthenia, nausea, diarrhea, stomatitis, rash, anemia, leukopenia, thrombocytopenia, constipation, hypertension,dyspepsia, headache, jaundice, changes in hair and skin color, alopecia, xeroderma, edema, insomnia, or bleeding, Have patients report immediately to prescriber signs of infection, angina, dyspnea, illogical thinking, sudden vision changes, ecchymosis, temperature sensitivity, wound that will not heal, discolored urine, jaundice, or severe skin irritation. Educate patients about signs of a significant reaction (eg, wheezing; chest tightness; fever; itching; bad cough; blue skin color; seizures; swelling of face, lips, tongue, or throat).
Note: This is not a comprehensive list of all side effects. Patients should consult prescriber for additional questions.

Pregnancy & Lactation
Category D.
Advise women of childbearing potential to avoid pregnancy if receiving sunitinib.
Lactation: discontinue breast-feeding.

Administration
May be administered with or without food. Dosing schedules vary by indication; some treatment regimens are continuous daily dosing; other treatment schedules are daily dosing for 4 weeks of a 6-week cycle (4 weeks on, 2 weeks off).

Storage
keep away from light and moisture, Store below 30°C temperature. Do not store in the bathroom. Keep all medications away from children and pets.

Presentation Kitent®
Bottle of 30 Capsules

Refrence:
BNF 68, part 8.1.5, other antineoplastic drug , page 607.
Drug fact, Tyrosine kinase inhibitor, pages 3784-3788

Manufactured By:
Noavaran Daroui Kimia Co., Tehran, Iran.
Telefax: +982188012946