Sunitent® 12.5/25/50 Sunitinib Hard gelatin capsule

• Read this entire leaflet carefully before you start taking this medicine.
• 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
• If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.
• To make sure you can safely take sunitinib, tell your doctor if you have any of these other conditions:
• liver or kidney disease;
• heart disease, high blood pressure, heart rhythm disorder;
• seizures;
• a bleeding or blood-clotting disorder;
• a disorder of your thyroid or adrenal gland;
• a personal or family history of Long QT syndrome; or a history of stroke, heart attack, congestive heart failure, a blood clot, or coronary artery disease.
• If you need surgery or a dental procedure, tell the surgeon or dentist ahead of time that you are using sunitinib. You may need to stop using the medicine for a short time.
• Tell your doctor about all medicines you use, and those you start or stop using during your treatment with sunitinib even supplements and herbal medicines.
• Be informed that yellowish skin discoloration may occur because of the color of drug.

CATEGORY

Antineoplastic agent

INDICATIONS

Sunitinib is an oral medicinal product used in the treatment of 3 types of cancer:
1. Gastrointestinal Stromal Tumor (GIST)
Sunitinib is indicated for the treatment of Gastrointestinal Stromal Tumor (GIST) after failure of imatinib mesylate treatment due to resistance or intolerance.
2. Advanced or Metastatic Renal Cell Carcinoma (MRCC)
Sunitinib is indicated for the treatment of metastatic renal cell carcinoma of clear cell histology.
3. Advanced Pancreatic Neuroendocrine Tumor (pancreatic NET)
Sunitinib is indicated for the treatment of patients with unresectable locally advanced or metastatic, well-differentiated pancreatic neuroendocrine tumours whose disease is progressive.

DOSAGE & ADMINISTRATION

You should follow the doses and instructions given by your doctor.
General dosing information:
► The recommended dose of sunitinib for Gastrointestinal Stromal Tumor (GIST) and advanced Renal Cell Carcinoma (RCC) is one 50 mg capsule taken once daily, on a schedule of 4 weeks on treatment followed by 2 weeks off.
► The recommended dose of sunitinib for advanced pancreatic neoroendocrine tumor is one 37.5 mg capsule taken once daily continuously without a scheduled off treatment period.
Proper use of this medication:
► Sunitinib may be taken with or without food. Administer with food if GI upset occurs.
► Do not drink grapefruit juice or eat grapefruit while taking sunitinib. It may increase the amount of sunitinib in the blood.
► Do not crush, chew, or open a sunitinib capsule. Swallow it whole. The medicine from a crushed or broken pill can be dangerous if it gets on your skin. If this occurs, wash your skin with soap and water and rinse thoroughly.
► In case of missed dose, take the missed capsule as soon as possible. Do not take it if it is almost time for next scheduled dose. Do not double.
► Sunitinib therapy should continue until disease progression or unacceptable toxicity occurs.

PATIENT MONITORING

CBCs and serum chemistries (including liver function tests, creatinine, electrolytes, magnesium, calcium, phosphate, amylase, and lipase) should be performed at the beginning of each treatment cycle for patients receiving treatment with sunitinib. Baseline laboratory measurement of thyroid function is recommended in all patients. During sunitinib treatment, routine monitoring of thyroid function should be performed every 3 months. Monitor patients for hypertension and for the development of proteinurin. Baseline ECG should be conducted prior to starting sunitinib, and ECGs should be performed periodically during therapy. Sunitinib should generally not be prescribed to patients with abnormally long baseline QT/QTc intervals or AV block. If there are symptoms suggestive of arrhythmia or if the QT/QTc interval becomes markedly prolonged while the patient is on sunitinib, the drug should be discontinued. Blood glucose levels should be checked regularly in all patients. For patients receiving anti-diabetic drugs, drug dosages may need to be adjusted to minimize the risk of hypoglycemia.

MECHANISM OF ACTION

Sunitinib specifically targets the activity of certain enzymes called tyrosine kinases that play a major role in transmitting the chemical signals required for critical cellular processes. Sunitinib prevents the growth of blood vessels from surrounding tissue to a solid tumour, and prevents the proliferation of cancer cells.

PHARMACOKINETICS

Following oral administration, peak plasma concentration of sunitinib generally occur within 6-12 hours. Food has no effect on bioavailability of sunitinib. Steady-state concentrations of the primary drug and primary metabolite are achieved within 10 to 14 days. Plasma protein binding is 95%. Sunitinib and its active metabolite are metabolized in the liver by CYP3A4. Elimination in the feces is 61% and in the renal is 16%. Terminal half-life of sunitinib and the primary metabolite are 40 to 60 hours and 80 to 110 hours, respectively.

CONTRAINDICATION

Except under special circumstances, this medication should not be used when the following conditions exists:
► Hypersensitivity to sunitinib or any of its components.
► Pregnancy

WARNING & PRECAUTIONS

Patients receiving therapy with sunitinib should be monitored by a qualified physician experienced in the use of anti-cancer agents.
• Sunitinib may cause severe and sometime life-threatening skin rashes such as Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). If signs or symptoms of SJS or TEN are present, sunitinib treatment should be discontinued. If diagnosis of SJS or TEN is confirmed, treatment must not be restarted.
These adverse reactions have been reported during treatment by sunitinib that will be life-threatening:
• Tumor Hemorrhage: These events may occur suddenly.
• Decreases in left ventricular ejection fraction
• Hypertension
• QT Interval Prolongation, including fatality
• Myopathy and/or rhabdomyolysis, including fatality
• Cardiomyopathy, including fatal cases
• Pulmonary embolism, including fatal cases
• Renal failure, including fatal cases
• Fatal Hepatotoxicity
• Reversible Posterior Leukoencephalopathy Syndrome, including fatal cases
• Hypothyroidism
Pediatrics:
The safety and efficacy of sunitinib in pediatric patients have not been established

PREGNANCY

FDA pregnancy category D
Adequate and well controlled studies with sunitinib in pregnant woman have not been done. Women of childbearing potential should be advised to avoid pregnancy while receiving sunitinib therapy. Adequate contraceptive methods should be use during therapy.

LACTATION

It is not known whether sunitinib is distributed into breast milk. Breast-feeding while taking sunitinib is not recommended.

DRUG INTERACTIONS

► *Bevacizumab:* Concurrent use of sunitinib and bevacizumab may result in unexpected severe toxicity. Coadministration is not recommended.
► *CYP3A4 inducers (eg, carbamazepine, phenobarbital, phenytoin, rifampin, rifapentine, St. John's wort):* May reduce sunitinib levels, decreasing the therapeutic effect. Consider a dosage increase for sunitinib to a max of sunitinib 87.5 mg daily if sunitinib must be coadministered with a CYP3A4 inducer. Monitor for toxicity. St. John's wort may decrease sunitinib plasma concentrations unpredictably. Coadministration is not recommended.
► *CYP3A4 inhibitors (eg, atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, voriconazole):* May elevate sunitinib levels, increasing the pharmacologic effects and risk of adverse reactions, including ventricular arrhythmias. Consider a dose decrease for sunitinib to a minimum of sunitinib 37.5 mg daily if sunitinib must be coadministered with a strong CYP3A4 inhibitor.
► *Drugs that prolong the QT interval (eg, antiarrhythmic agents [eg, amiodarone, procainamide, quinidine, sotalol], chloroquine, chlorpromazine, cisapride, dolasetron, doxepin, haloperidol, lithium, methadone, pentamidine, pimozide, romidepsin, tacrolimus, thioridazine, tyrosine kinase inhibitors [eg, dasatinib, lapatinib], ziprasidone):* Prolongation of the QT interval with possible development of cardiac arrhythmias, including torsades de pointes, should be considered when sunitinib is coadministered with these agents.
► *Grapefruit juice:* May elevate sunitinib levels, increasing the pharmacologic and adverse effects. Patients taking sunitinib should avoid grapefruit products, including grapefruit juice.
• The above list of potentially interacting drugs is not comprehensive. Current scientific literature should be consulted for more information.

SIDE EFFECTS

Like all medicines, sunitinib can have side effects which are usually mild to moderate.
► Very common side effects (these are likely to affect more than 10 in every 100 people):
- tiredness
- decreased white blood cell and platelet counts
- increased blood pressure
- mouth pain/irritation, mouth soreness, taste disturbances, upset stomach, nausea, vomiting, diarrhea, constipation, abdominal pain, dry mouth, bleeding.
- skin discoloration due to the color of sunitinib malate (yellow), hair color change, rash or blisters on the palms of the hands and soles of the feet, dry skin
- headache

► Common side effects (these are likely to affect between 1 and 10 in every 100 people):
dizziness, weakness, loss of appetite, infection, heartburn, hypothyroidism
• If any of the side effects get serious or if you notice any side effect not listed in this leaflet, please tell your doctor.
• This is not a complete list of side effects. For any unexpected effects while taking sunitinib, contact your doctor or pharmacist.

OVERDOSE

If you think you may have accidentally taken too many sunitinib capsules, talk to your doctor immediately or contact a poison control center.

STORAGE:

► Store below 30°C, protect from moisture and light.
► Keep out of the reach and sight of children.
► Keep in the original container until use.

PACKAGING

► 30 capsules of 12.5 mg sunitinib (as Malate) in a plastic container with a leaflet in a cardboard box.
► 30 capsules of 25 mg sunitinib (as Malate) in a plastic container with a leaflet in a cardboard box.
► 30 capsules of 50 mg sunitinib (as Malate) in a plastic container with a leaflet in a cardboard box.

REFERENCE

AHFS, DRUG INFORMATION 2012
Sutent® package leaflet, information for user, Pfizer, 2014
www.drugs.com

AN: Sunitent® 203

OSVE Pharmaceutical Co.
You are kindly requested to contact us in case of any comments or advices.
PO Box: 13185-1554
Email: info@osvahpharma.com
www.osvahpharma.com
Tehran-Iran

Sunitent BRO | 170x120 mm
OSVE Pharmaceutical Co.
Date: 95/7/19

Parman Graphic Group

Print description: Pantone No.: 293 C | Black