Sunitinib: Drug information

(For additional information see "Sunitinib: Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Hepatotoxicity:

Hepatotoxicity has been observed in clinical trials and postmarketing experience. Hepatotoxicity may be severe, and deaths have been reported.

Brand Names: US

Sutent

Brand Names: Canada

Sutent

Pharmacologic Category

Antineoplastic Agent, Tyrosine Kinase Inhibitor; Antineoplastic Agent, Vascular Endothelial Growth Factor (VEGF) Inhibitor

Dosing: Adult

Note: Dosage modifications should be done in increments or decrements of 12.5 mg; individualize based on safety and tolerability.

Gastrointestinal stromal tumor (GIST): Oral: 50 mg once daily for 4 weeks of a 6-week treatment cycle (4 weeks on, 2 weeks off)

GIST off-label dosing: Oral: 37.5 mg once daily, continuous daily dosing (George, 2009, *EJC*)

Pancreatic neuroendocrine tumors, advanced (PNET): Oral: 37.5 mg once daily, continuous daily dosing (maximum daily dose used in clinical trials: 50 mg)

Renal cell cancer, advanced (RCC): Oral: 50 mg once daily for 4 weeks of a 6-week treatment cycle (4 weeks on, 2 weeks off)

Soft tissue sarcoma, non-GIST (off-label use): Oral: 37.5 mg once daily, continuous daily dosing (George, 2009, *JCO*)

Thyroid cancer, refractory (off-label use): Oral: 50 mg once daily for 4 weeks of a 6-week treatment cycle (4 weeks on, 2 weeks off) (Cohen, 2008; Ravaud, 2008)

Dosage adjustment with concurrent CYP3A4 inhibitor: Avoid concomitant administration with strong CYP3A4 inhibitors (eg, clarithromycin, erythromycin, itraconazole, ketoconazole, nefazodone, protease inhibitors, telithromycin, voriconazole); if concomitant administration with a strong CYP3A4 inhibitor cannot be avoided, consider a dose reduction to a minimum of 37.5 mg/day (GIST, RCC) or 25 mg/day

(PNET).

Dosage adjustment with concurrent CYP3A4 inducer: Avoid concomitant administration with strong CYP3A4 inducers (eg, carbamazepine, dexamethasone, phenobarbital, phenytoin, rifampin, St John's wort); if concomitant administration with a strong CYP3A4 inducer cannot be avoided, consider a dosage increase (with careful monitoring for toxicity) to a maximum of 87.5 mg/day (GIST, RCC) or 62.5 mg/day (PNET).

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

Mild, moderate, or severe impairment: No initial adjustment required; subsequent adjustments may be needed based on safety and tolerance.

ESRD on hemodialysis: No initial adjustment required; subsequent dosage **increases** (up to twofold) may be required due to reduced (47%) exposure

Dosing: Hepatic Impairment

Pre-existing hepatic impairment: No adjustment is necessary with mild-to-moderate (Child-Pugh class A or B) hepatic impairment; not studied in patients with severe (Child-Pugh class C) hepatic impairment. Studies excluded patients with ALT or AST >2.5 x ULN, or if due to liver metastases, ALT or AST >5 x ULN.

Hepatotoxicity during treatment: Hepatic adverse events ≥ grade 3 or 4: Withhold treatment; discontinue if hepatotoxicity does not resolve. Do not reinitiate in patients with severe changes in liver function tests or other signs/symptoms of liver failure.

Dosing: Adjustment for Toxicity

Dosage modifications should be done in increments or decrements of 12.5 mg; individualize based on safety and tolerability.

Cardiac toxicity:

Ejection fraction <50% and >20% below baseline without evidence of CHF: Interrupt treatment and/or reduce dose.

LV dysfunction with CHF clinical manifestations: Discontinue treatment.

Dermatologic toxicity:

Signs/symptoms of erythema multiforme (EM), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), including progressive skin rash, often with blisters or mucosal lesions: Discontinue sunitinib; do not restart treatment if SJS or TEN are suspected.

Necrotizing fasciitis: Discontinue sunitinib.

Hypertension, severe: Temporarily interrupt treatment until hypertension is controlled.

Nephrotic syndrome: Discontinue treatment.

Pancreatitis: Discontinue treatment.

Proteinuria:

Urine protein ≥3 g/24 hours: Interrupt treatment and reduce the dose.

Persistent urine protein ≥3 g/24 hours despite dose reductions: Discontinue treatment.

Reversible posterior leukoencephalopathy (RPLS): Temporarily withhold treatment; after resolution, may resume with discretion.

Thrombotic microangiopathy: Discontinue treatment.

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Capsule, Oral:

Sutent: 12.5 mg, 25 mg, 37.5 mg, 50 mg

Generic Equivalent Available (US) No

Medication Guide and/or Vaccine Information Statement (VIS) An FDA-approved patient medication guide, which is available with the product information and at http://www.fda.gov/downloads/Drugs/DrugSafety/UCM219111.pdf, must be dispensed with this medication.

Administration Avoid contact with broken or leaking capsules; if contact occurs, wash immediately with soap and water.

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends single gloving for administration of intact tablets or capsules. If manipulating tablets/capsules (eg, to prepare an oral suspension), NIOSH recommends double gloving, a protective gown, and preparation in a controlled device; if not prepared in a controlled device, respiratory and eye/face protection as well as ventilated engineering controls are recommended. NIOSH recommends double gloving, a protective gown, and (if there is a potential for vomit or spit up) eye/face protection for administration of an oral liquid/feeding tube administration (NIOSH 2016).

Use

Gastrointestinal stromal tumor: Treatment of gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib

Pancreatic neuroendocrine tumors, advanced: Treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease

Renal cell carcinoma, advanced: Treatment of advanced renal cell carcinoma

Use: Off-Label

Thyroid cancer; Soft tissue sarcoma (non-GIST)

Medication Safety Issues

Sound-alike/look-alike issues:

SUNItinib may be confused with axitinib, dasatinib, erlotinib, gefitinib, imatinib, lapatinib, nilotinib, PAZOPanib, regorafenib, SORAfenib, vandetanib

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Administration issues:

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)

Adverse Reactions

>10%:

Cardiovascular: Hypertension (27% to 34%, GIST: 8% to 15%; grade 3: 10% to 13%, GIST: 4%), decreased left ventricular ejection fraction (RCC: 16% to 27%, grade 3: 3% to 7%; GIST: 11%, grade 3: 1%), peripheral edema (RCC: 24%), chest pain (RCC: 13%), severe hypertension (4% to 10%; >200 mmHg systolic or 110 mmHg diastolic)

Central nervous system: Fatigue (RCC: 62%, pNET: 33%), glossalgia (pNET: ≤48%; RCC: 11%), mouth pain (pNET: ≤48%; RCC: 6% to 14%), headache (18% to 23%), insomnia (15% to 18%), chills (RCC: 14%), depression (RCC: 11%), dizziness (RCC: 11%)

Dermatologic: Skin discoloration (≤25% to 30%; yellow color), hair discoloration (20% to 29%; GIST: 7%), palmar-plantar erythrodysesthesia (23% to 29%, GIST: 14%; grades 3/4: 4% to 8%), xeroderma (15% to 23%), skin rash (14% to 18%; RCC: 29%), alopecia (5% to 14%), erythema (RCC: 12%), pruritus (RCC: 12%)

Endocrine & metabolic: Increased uric acid (RCC: 46%), decreased serum calcium (34% to 42%), decreased serum albumin (pNET: 41%, RCC: 28%), decreased serum phosphate (31% to 36%), increased serum glucose (RCC: 23%), decreased serum potassium (12% to 21%), decreased serum sodium (RCC: 20%), decreased serum magnesium (pNET: 19%), increased serum potassium (16% to 18%), hypothyroidism (4% to 7%; RCC: 16%), increased serum calcium (RCC: 13%), increased serum sodium (10% to 13%)

Gastrointestinal: Diarrhea (59% to 66%; GIST: 40%), nausea (RCC: 58%; pNET: 45%), increased serum lipase (17% to 25%; RCC: 56%; grades 3/4: 5% to 18%), anorexia (RCC: 48%; GIST: 33%), mucositis (47% to 48%, GIST: 29%; includes aphthous stomatitis, dry mucous membranes, gingival

pain, gingivitis, glossitis, oral discomfort, oral mucosal ulcer, stomatitis, tongue ulceration), dysgeusia (21%; RCC: 47%), vomiting (34% to 39%), abdominal pain (30% to 39%), increased serum amylase (17% to 20%; RCC: 35%; grades 3/4: 4% to 6%), dyspepsia (RCC: 34%; pNET: 15%), constipation (20% to 23%), weight loss (16%), flatulence (RCC: 14%), xerostomia (RCC: 13%), gastroesophageal reflux disease (RCC: 12%)

Hematologic & oncologic: Decreased hemoglobin (RCC: 79%, pNET: 65%, GIST: 26%; grades 3/4: ≤8%), leukocyte disorder (decreased leukocytes; RCC: 78%; grades 3/4: 8%), decreased neutrophils (71% to 77%, GIST: 53%; grades 3/4: 10% to 17%), abnormal absolute lymphocyte count (decreased; RCC: 68%, pNET: 56%, GIST: 38%; grades 3/4: RCC: 18%, pNET: 7%), decreased platelet count (60% to 68%, GIST: 38%, GIST and RCC: grades 3/4: 5% to 9%), hemorrhage (18% to 22%; RCC: 37%; RCC and GIST, grades 3/4: 3% to 4%; includes hematemesis, hematochezia, hematoma, hemoptysis, melena, metrorrhagia)

Hepatic: Increased serum AST (pNET: 72%, RCC: 56%, GIST: ≤39%; grades 3/4: ≤2% to 5%), increased serum ALT (pNET: 61%; RCC: 51%; GIST: ≤39%; grades 3/4: ≤2% to 4%), increased serum alkaline phosphatase (RCC: 46%; GIST: 24%; grades 3/4: 2% to 4%), increased serum bilirubin (16% to 20%; pNET: 37%; RCC and GIST, grades 3/4: 1%), increased indirect serum bilirubin (RCC and GIST: 10% to 13%; grades 3/4: ≤1%)

Neuromuscular & skeletal: Increased creatine phosphokinase (RCC: 49%), limb pain (RCC: 40%; GIST: ≤14%), weakness (22% to 34%), arthralgia (RCC: 30%; pNET: 15%), back pain (RCC: 28%), myalgia (GIST: ≤14%)

Renal: Increased serum creatinine (RCC: 70%; GIST: 12%)

Respiratory: Cough (RCC: 27%), dyspnea (RCC: 26%), epistaxis (pNET: 20%), nasopharyngitis (RCC: 14%), oropharyngeal pain (RCC: 14%), upper respiratory tract infection (RCC: 11%)

Miscellaneous: Fever (RCC: 22%)

1% to 10%:

Cardiovascular: Deep vein thrombosis (≤3%), pulmonary embolism (≤3%)

Endocrine & metabolic: Hypoglycemia (2%; pNET: 10%)

Gastrointestinal: Hemorrhoids (RCC: 10%), pancreatitis (1%)

Respiratory: Flu-like symptoms (RCC: 5%)

<1%, postmarketing, and/or case reports: Acute renal failure, adrenocortical insufficiency, arterial thrombosis (includes cerebral infarction, cerebrovascular accident, transient ischemic attack), cardiac failure, cardiomyopathy, cerebral hemorrhage, cholecystitis (particularly acalculous), erythema multiforme, esophagitis, fistula (sometimes associated with tumor necrosis and/or regression), fulminant necrotizing fasciitis (including of the perineum), gastrointestinal hemorrhage, gastrointestinal perforation, hemolytic uremic syndrome, hepatic failure, hepatotoxicity, hypersensitivity (includes angioedema), hyperthyroidism, ischemic heart disease, myocardial infarction, myopathy (with/without acute renal failure), nephrotic syndrome, neutropenic infection, osteonecrosis of the jaw, preeclampsia (like syndrome with proteinuria and reversible hypertension) (Gallucci 2013; Patel 2008), prolonged Q-T interval on ECG (dose dependent), proteinuria, pulmonary hemorrhage, pyoderma gangrenosum (including positive dechallenges), renal insufficiency, respiratory tract hemorrhage, respiratory tract infection (may be serious), reversible posterior leukoencephalopathy syndrome, rhabdomyolysis

(with/without acute renal failure), seizure, sepsis, septic shock, skin infection (may be serious), Stevens-Johnson syndrome, thrombotic thrombocytopenic purpura, thyroiditis (Feldt 2012), torsades de pointes, toxic epidermal necrolysis, tumor hemorrhage, tumor lysis syndrome, urinary tract hemorrhage, urinary tract infection (may be serious), ventricular arrhythmia, wound healing impairment

Contraindications

There are no contraindications listed in the manufacturer's US labeling.

Canadian labeling: Hypersensitivity to sunitinib or any component of the formulation; pregnancy

Warnings/Precautions

Concerns related to adverse effects:

• Adrenal toxicity: Has been reported; monitor for adrenal insufficiency in patients with stress such as trauma, severe infection, or who are undergoing surgery.

• 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.

• Cardiovascular events: Cardiovascular events (some fatal), including heart failure, cardiomyopathy, myocardial ischemia and myocardial infarction (MI) have been reported. Use with caution in patients at risk for cardiovascular events. May cause a decrease in left ventricular ejection fraction (LVEF), including some grade 3 reductions. Obtain LVEF evaluation prior to treatment. Discontinue with clinical signs and symptoms of heart failure. Interrupt therapy and/or decrease dose with LVEF <50% and >20% reduction from baseline in patients without clinical heart failure signs/symptoms. Patients with cardiac events (MI, bypass grafts, symptomatic heart failure, cerebrovascular accident, transient ischemic attack, and pulmonary embolism) within the previous 12 months were excluded from clinical trials and it is not known if the risk for left ventricular dysfunction is increased in patient with these conditions; assess risks versus benefits; monitor for clinical signs/symptoms of heart failure, in addition to baseline, also obtain periodic LVEF evaluation.

• Dermatologic toxicities: Severe cutaneous reactions, including erythema multiforme (EM), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) have been reported (some fatal); if signs/symptoms of EM, SJS, or TEN (progressive skin rash, often with blisters or mucosal lesions) are present, discontinue sunitinib. Do not restart treatment if SJS or TEN are suspected. Necrotizing fasciitis (with fatalities) has been reported, including perineum necrotizing fasciitis and fasciitis secondary to fistula formation. Discontinue sunitinib in patients who develop necrotizing fasciitis. Sunitinib may cause skin and/or hair depigmentation or discoloration.

• GI complications: Serious and fatal GI complications, including GI perforation, have occurred (rarely). Pancreatitis has been observed in RCC patients; discontinue sunitinib if symptoms are present.

• Hand-foot skin reaction: Hand-foot skin reaction (HFSR) observed with tyrosine kinase inhibitors (TKIs) is distinct from hand-foot syndrome (palmar-plantar erythrodysesthesia) associated with traditional chemotherapy agents; HFSR due to TKIs is localized with defined hyperkeratotic lesions; symptoms include burning, dysesthesia, paresthesia, or tingling on the palms/soles, and generally occur within the first 2 to 4 weeks of treatment; pressure and flexor areas may develop blisters (callus-like), dry/cracked skin, edema, erythema, desquamation, or hyperkeratosis (Appleby, 2011).

The following treatments may be used in addition to the recommended dosage modifications (Lacouture, 2008). Prior to treatment initiation, a pedicure is recommended to remove hyperkeratotic areas/calluses, which may predispose to HFSR; avoid vigorous exercise/activities that may stress hands or feet. During therapy, patients should reduce exposure to hot water (may exacerbate hand-foot symptoms); avoid constrictive footwear and excessive skin friction. Patients may also wear thick cotton gloves or socks and should wear shoes with padded insoles. Grade 1 HFSR may be relieved with moisturizing creams, cotton gloves and socks (at night) and/or keratolytic creams such as urea (20% to 40%) or salicylic acid (6%). Apply topical steroid (eg, clobetasol ointment) twice daily to erythematous areas of grade 2 HFSR; topical anesthetics (eg, lidocaine 2%) and then systemic analgesics (if appropriate) may be used for pain control. Resolution of acute erythema may result in keratotic areas which may be softened with keratolytic agents.

• Hepatotoxicity: **[US Boxed Warning]: Hepatotoxicity, which may be severe and/or fatal, has been observed in clinical trials and in postmarketing surveillance.** Signs of liver failure include jaundice, elevated transaminases, and/or hyperbilirubinemia, in conjunction with encephalopathy, coagulopathy and/or renal failure. Monitor liver function tests at baseline, with each treatment cycle and if clinically indicated. Withhold treatment for grade 3 or 4 hepatotoxicity; discontinue if hepatotoxicity does not resolve. Do not reinitiate in patients with severe changes in liver function tests or other signs/symptoms of liver failure. Sunitinib has not been studied in patients with ALT or AST >2.5 times ULN (or >5 times ULN if due to liver metastases).

• Hypertension: May cause hypertension; monitor and control with antihypertensives if needed; interrupt therapy until hypertension is controlled for severe hypertension. Use caution and closely monitor in patients with underlying or poorly controlled hypertension.

• Hypoglycemia: Symptomatic hypoglycemia has been associated with sunitinib; may result in loss of consciousness or require hospitalization. Hypoglycemia occurred infrequently in patients with renal cell cancer and gastrointestinal stromal tumors (GIST); however, the incidence is higher (~10%) in patients with pancreatic neuroendocrine tumors (PNET); preexisting glucose homeostasis abnormalities were not always present in hypoglycemic patients with PNET. Blood glucose decreases may be worse in patients with diabetes. Monitor blood glucose levels regularly during and following discontinuation of treatment. Dose modifications of antidiabetic medications may be necessary to minimize the risk of hypoglycemia.

• Osteonecrosis of the jaw: Osteonecrosis of the jaw (ONJ), also referred to as medication-related osteonecrosis of the jaw (MRONJ), has been reported with sunitinib. Concurrent bisphosphonate use or dental disease may increase the risk for ONJ. According to a position paper by the American Association of Maxillofacial Surgeons (AAOMS), MRONJ has been associated with bisphosphonates and other antiresorptive agents (denosumab), and antiangiogenic agents (eg, bevacizumab, sunitinib) used for the treatment of osteoporosis or malignancy. Antiangiogenic agents, when given concomitantly with antiresorptive agents, are associated with an increased risk of ONJ. Other risk factors for MRONJ include dentoalveolar surgery (eg, tooth extraction, dental implants), preexisting inflammatory dental disease, and concomitant corticosteroid use. Consider a dental examination and preventive dentistry prior to initiation of sunitinib (and during therapy); if possible, avoid invasive dental procedures in patients with current or prior bisphosphonate use. The AAOMS suggests that if medically permissible, initiation of antiangiogenic agents for cancer therapy should be delayed until optimal dental health is attained (if extractions are required, antiangiogenesis therapy should delayed until the extraction site has mucosalized or until after adequate osseous healing). Once antiangiogenic therapy for oncologic disease is initiated, procedures that involve direct osseous injury and placement of dental implants should be avoided.

Patients developing ONJ during therapy should receive care by an oral surgeon (AAOMS [Ruggiero 2014]).

• Proteinuria/nephrotic syndrome: Proteinuria and nephrotic syndrome have been reported; some cases have led to renal failure and fatal outcomes. Monitor for new onset or worsening proteinuria with baseline and periodic urinalysis and follow up with 24-hour urine protein if clinically indicated. If urine protein is ≥3 g/24 hours, interrupt treatment and reduce the dose. Discontinue treatment in patients with nephrotic syndrome or persistent urine protein ≥3 g/24 hours despite dose reductions. The safety of continuing treatment with sunitinib in patients with moderate to severe proteinuria has not been evaluated.

• QTc prolongation: QTc prolongation and torsade de 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. A baseline and periodic 12-lead ECG should be obtained; correct electrolyte abnormalities prior to treatment and monitor and correct potassium, calcium, and magnesium levels during therapy.

• Reversible posterior leukoencephalopathy syndrome (RPLS): Has been reported (rarely, some fatal). Symptoms of RPLS include confusion, headache, hypertension, lethargy, seizure, blindness and/or other vision, or neurologic disturbances; interrupt treatment and begin management of hypertension.

• Thyroid disorders: Thyroid dysfunction (eg, hypothyroidism, hyperthyroidism, and 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. Patients not receiving thyroid hormone replacement therapy at sunitinib initiation should be monitored (TSH) every 4 weeks for 4 months and then every 2 to 3 months; those patients already receiving levothyroxine prior to initiating sunitinib should have TSH monitored every 4 weeks until levels and levothyroxine dose are stable, then monitor every 2 months (Hamnvik 2011).

• Thrombotic microangiopathy: Thrombotic microangiopathy (including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome), sometimes leading to renal failure or fatality, has been reported with sunitinib, both as monotherapy and in combination with bevacizumab. Discontinue if thrombotic microangiopathy develops; effects may be reversible after discontinuation.

• Tumor lysis syndrome: Tumor lysis syndrome (TLS), including fatalities, has been reported, predominantly in patients with RCC 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.

• 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.

Disease-related concerns:

• Renal insufficiency: An increased incidence of fatigue, thyroid dysfunction and treatment-induced hypertension was reported in patients with renal insufficiency (CrCl ≤60 mL/minute) who received sunitinib for the treatment of renal cell cancer (Gupta 2011).

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Other warnings/precautions:

• Administration: 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).

Metabolism/Transport Effects

Substrate of CYP3A4 (major); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential; **Inhibits** BCRP

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Androgens: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. **Exceptions:** Danazol. *Risk C: Monitor therapy*

Antidiabetic Agents: May enhance the hypoglycemic effect of Hypoglycemia-Associated Agents. *Risk C: Monitor therapy*

Antifungal Agents (Azole Derivatives, Systemic): May decrease the metabolism of SUNItinib. Applicable Isavuconazonium considerations are addressed in separate monographs. **Exceptions:** Isavuconazonium Sulfate. *Risk D: Consider therapy modification*

Aprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Bevacizumab: SUNItinib may enhance the adverse/toxic effect of Bevacizumab. Specifically, the risk for a specific form of anemia, microangiopathic hemolytic anemia (MAHA), may be increased. Bevacizumab may enhance the hypertensive effect of SUNItinib. *Risk X: Avoid combination*

Bisphosphonate Derivatives: Systemic Angiogenesis Inhibitors may enhance the adverse/toxic effect of Bisphosphonate Derivatives. Specifically, the risk for osteonecrosis of the jaw may be increased. *Risk C: Monitor therapy*

Bosentan: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

CYP3A4 Inducers (Moderate): May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inducers (Strong): May decrease the serum concentration of SUNItinib. Management: Avoid when possible. If such a combination cannot be avoided, consider increasing sunitinib dose and monitor clinical response and toxicity closely. *Risk D: Consider therapy modification*

CYP3A4 Inhibitors (Moderate): May decrease the metabolism of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inhibitors (Strong): May decrease the metabolism of CYP3A4 Substrates. *Risk D: Consider therapy modification*

Dabrafenib: May decrease the serum concentration of CYP3A4 Substrates. Management: Seek alternatives to the CYP3A4 substrate when possible. If concomitant therapy cannot be avoided, monitor clinical effects of the substrate closely (particularly therapeutic effects). *Risk D: Consider therapy modification*

Dasatinib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Deferasirox: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Dexamethasone (Systemic): May decrease the serum concentration of SUNItinib. *Risk D: Consider therapy modification*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Enzalutamide: May decrease the serum concentration of CYP3A4 Substrates. Management: Concurrent use of enzalutamide with CYP3A4 substrates that have a narrow therapeutic index should be avoided. Use of enzalutamide and any other CYP3A4 substrate should be performed with caution and close monitoring. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Fosaprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Fusidic Acid (Systemic): May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Grapefruit Juice: May increase the serum concentration of SUNItinib. Management: Advise patients to avoid consuming grapefruit and grapefruit juice during sunitinib treatment. *Risk D: Consider therapy modification*

Herbs (Hypoglycemic Properties): May enhance the hypoglycemic effect of Hypoglycemia-Associated Agents. *Risk C: Monitor therapy*

Highest Risk QTc-Prolonging Agents: QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying) may enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. Management: Avoid such combinations when possible. Use should be accompanied by close monitoring for evidence of QT prolongation or other alterations of cardiac rhythm. *Risk D: Consider therapy modification*

Hypoglycemia-Associated Agents: May enhance the hypoglycemic effect of other Hypoglycemia-Associated Agents. *Risk C: Monitor therapy*

Idelalisib: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

MAO Inhibitors: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. *Risk C: Monitor therapy*

MiFEPRIStone: May increase the serum concentration of CYP3A4 Substrates. Management: Minimize doses of CYP3A4 substrates, and monitor for increased concentrations/toxicity, during and 2 weeks following treatment with mifepristone. Avoid cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus. *Risk D: Consider therapy modification*

MiFEPRIStone: May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying). Management: Though the drugs listed here have uncertain QT-prolonging effects, they all have some possible association with QT prolongation and should generally be avoided when possible. *Risk D: Consider therapy modification*

Mitotane: May decrease the serum concentration of CYP3A4 Substrates. Management: Doses of CYP3A4 substrates may need to be adjusted substantially when used in patients being treated with mitotane. *Risk D: Consider therapy modification*

Moderate Risk QTc-Prolonging Agents: QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying) may enhance the QTc-prolonging effect of Moderate Risk QTc-Prolonging Agents. *Risk C: Monitor therapy*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Netupitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

NiCARdipine: May increase the serum concentration of SUNItinib. *Risk C: Monitor therapy*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Palbociclib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Pegvisomant: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. *Risk C: Monitor therapy*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Prothionamide: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. *Risk C: Monitor therapy*

Quinolone Antibiotics: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. Quinolone Antibiotics may diminish the therapeutic effect of Blood Glucose Lowering Agents.

Specifically, if an agent is being used to treat diabetes, loss of blood sugar control may occur with quinolone use. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Salicylates: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. *Risk C: Monitor therapy*

Sarilumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Selective Serotonin Reuptake Inhibitors: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. *Risk C: Monitor therapy*

Siltuximab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Simeprevir: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

St John's Wort: May decrease the serum concentration of SUNItinib. *Risk X: Avoid combination*

Stiripentol: May increase the serum concentration of CYP3A4 Substrates. Management: Use of stiripentol with CYP3A4 substrates that are considered to have a narrow therapeutic index should be avoided due to the increased risk for adverse effects and toxicity. Any CYP3A4 substrate used with stiripentol requires closer monitoring. *Risk D: Consider therapy modification*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Temsirolimus: May enhance the adverse/toxic effect of SUNItinib. *Risk X: Avoid combination*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at

least 3 months after immunosuppressants. *Risk X: Avoid combination*

Food Interactions Grapefruit juice may increase the levels/effects of sunitinib. Food has no effect on the bioavailability of sunitinib. Management: Avoid grapefruit juice.

Pregnancy Risk Factor D (show table)

Pregnancy Implications Animal reproduction studies have demonstrated teratogenicity, embryotoxicity, and fetal loss. Because sunitinib inhibits angiogenesis, a critical component of fetal development, adverse effects on pregnancy would be expected. Women of childbearing potential should be advised to avoid pregnancy if receiving sunitinib.

Breast-Feeding Considerations It is not known if sunitinib is excreted in human milk. Due to the potential for serious adverse reactions in the nursing infant, the decision to discontinue breast-feeding or discontinue sunitinib should take into account the benefits of treatment to the mother.

Dietary Considerations Avoid grapefruit juice.

Monitoring Parameters LVEF, baseline (and periodic with cardiac risk factors), ECG (12-lead; baseline and periodic), blood pressure; adrenal function CBC with differential and platelets (prior to each treatment cycle), liver function tests (baseline, with each cycle and if clinically indicated), serum chemistries including magnesium, phosphate, and potassium (prior to each treatment cycle), blood glucose levels (regularly during and following discontinuation of treatment), urinalysis (for proteinuria development or worsening); consider dental exam prior to treatment initiation; symptoms of hypothyroidism, hyperthyroidism, or thyroiditis; signs/symptoms of hypoglycemia

Thyroid function testing (Hamnvik, 2011):

Preexisting levothyroxine therapy: Obtain baseline TSH levels, then monitor every 4 weeks until levels and levothyroxine dose are stable, then monitor every 2 months

Without preexisting thyroid hormone replacement: TSH at baseline, then every 4 weeks for 4 months, then every 2-3 months

Mechanism of Action Exhibits antitumor and antiangiogenic properties by inhibiting multiple receptor tyrosine kinases, including platelet-derived growth factors (PDGFRα and PDGFRβ), vascular endothelial growth factors (VEGFR1, VEGFR2, and VEGFR3), FMS-like tyrosine kinase-3 (FLT3), colony-stimulating factor type 1 (CSF-1R), and glial cell-line-derived neurotrophic factor receptor (RET).

Pharmacodynamics/Kinetics

Distribution: V_d/F: 2230 L

Protein binding: Sunitinib: 95%; SU12662: 90%

Metabolism: Hepatic; primarily metabolized by CYP3A4 to the N-desethyl metabolite SU12662 (active)

Half-life elimination: Terminal: Sunitinib: 40 to 60 hours; SU12662: 80 to 110 hours

Time to peak, plasma: 6 to 12 hours

Excretion: Feces (61%); urine (16%)

Pricing: US

Capsules (Sutent Oral)

12.5 mg (28): $5371.60

25 mg (28): $10743.20

37.5 mg (28): $16114.82

50 mg (28): $18702.42

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Sunitix (BD, LK); Sutene (KR); Sutent (AE, AR, AT, AU, BE, BG, BH, BR, BZ, CH, CL, CN, CO, CR, CY, CZ, DE, DK, DO, EC, EE, ES, FI, FR, GB, GR, GT, HK, HN, HR, HU, ID, IE, IL, IS, IT, JO, JP, KW, LB, LK, LT, LU, LV, MT, MY, NI, NL, NO, NZ, PA, PE, PH, PL, PT, QA, RO, RU, SA, SE, SG, SI, SK, SV, TH, TR, TW, UA, UY, VE, VN)

REFERENCES

1. *Appleby L, Morrissey S, Bellmunt J, et al, "Management of Treatment-Related Toxicity With Targeted Therapies for Renal Cell Carcinoma: Evidence-Based Practice and Best Practices," Hematol Oncol Clin North Am, 2011, 25(4):893-915. [PubMed 21763973]*
2. *Arnaud L, Schartz NE, Bousquet G, et al, "Transient Sunitinib-Induced Coma in a Patient With Fibromyxoid Sarcoma," J Clin Oncol, 2008, 26(9):1569-71. [PubMed 18349416]*
3. *Castellano D, del Muro XG, Pérez-Gracia JL, et al, "Patient-Reported Outcomes in a Phase III, Randomized Study of Sunitinib Versus Interferon-{alpha} as First-Line Systemic Therapy for Patients With Metastatic Renal Cell Carcinoma in a European Population," Ann Oncol, 2009, 20(11):1803-12. [PubMed 19549706]*
4. *Cella D, Michaelson MD, Bushmakin AG, et al, "Health-Related Quality of Life in Patients With Metastatic Renal Cell Carcinoma Treated With Sunitinib vs Interferon-Alpha in a Phase III Trial: Final Results and Geographical Analysis," Br J Cancer, 2010, 102(4):658-64. [PubMed 20104222]*
5. *Chu TF, Rupnick MA, Kerkela R, et al, "Cardiotoxicity Associated With Tyrosine Kinase Inhibitor Sunitinib," Lancet, 2007, 370(9604):2011-9. [PubMed 18083403]*
6. *Cohen EE, Needles BM, Cullen KJ, et al, "Phase 2 Study of Sunitinib in Refractory Thyroid Cancer," J Clin Oncol, 2008, 26(Supp):6025 [abstract 6025 from 2008 ASCO Annual Meeting].*
7. *Costero O, Picazo ML, Zamora P, et al, "Inhibition of Tyrosine Kinases by Sunitinib Associated With Focal Segmental Glomerulosclerosis Lesion in Addition to Thrombotic Microangiopathy," Dial Nephrol Transplant, 2010, 25(3):1001-3. [PubMed 20019017]*
8. *Demetri GD, van Oosterom AT, Garret CR, et al, "Efficacy and Safety of Sunitinib in Patients With Advanced Gastrointestinal Stromal Tumour After Failure of Imatinib: A Randomised Controlled Trial," Lancet, 2006, 368(9544):1329-38. [PubMed 17046465]*
9. *Desai J, Yassa L, Marqusee E, et al, "Hypothyroidism After Sunitinib Treatment for Patients With Gastrointestinal Stromal Tumors," Ann Intern Med, 2006, 145(9):660-4. [PubMed 17088579]*

10. *Edeline J, Laguerre B, Rolland Y, et al, "Aortic Dissection in a Patient Treated by Sunitinib for Metastatic Renal Cell Carcinoma," Ann Oncol, 2010, 21(1):186-7. [PubMed 19875754]*
11. *Faivre S, Delbaldo C, and Vera K, "Safety, Pharmacokinetic, and Antitumor Activity of SU11248, a Novel Oral Multitarget Tyrosine Kinase Inhibitor, in Patients With Cancer," J Clin Oncol, 2006, 24(1):25-35. [PubMed 16314617]*
12. *Feldman DR, Baum MS, Ginsberg MS, et al, "Phase I Trial of Bevacizumab Plus Escalated Doses of Sunitinib in Patients With Metastatic Renal Cell Carcinoma," J Clin Oncol, 2009, 27(9):1432-9. [PubMed 19224847]*
13. *Feldman DR, Ginsberg MS, Baum M, et al, "Phase I Trial of Bevacizumab Plus Sunitinib in Patients With Metastatic Renal Cell Carcinoma," J Clin Oncol, 2008, 26(Supp):5100 [abstract 5100 from 2008 ASCO Annual Meeting].*
14. *Feldman DR, Martorella AJ, Robbins RJ, et al, "Re: Hypothyroidism in Patients With Metastatic Renal Cell Carcinoma Treated With Sunitinib," J Natl Cancer Inst, 2007, 99(12):974-5. [PubMed 17565156]*
15. *Feldt S, Schüssel K, Quinzler R, et al. Incidence of thyroid hormone therapy in patients treated with sunitinib or sorafenib: a cohort study. Eur J Cancer. 2012;48(7):974-981. [PubMed 22382202]*
16. *Gallucci G, Tartarone A, Tocchetti CG, et al. Role of preeclampsia-related angiogenic factors in sunitinib cardiotoxicity: two cases and review of the literature. Future Oncol. 2013;9(1):127-133. [PubMed 23252570]*
17. *Garcia-Donas J, Esteban E, Leandro-Farcia LJ, et al, "Single Nucleotide Polymorphism Associations With Response and Toxic Effects in Patients With Advanced Renal-Cell Carcinoma Treated With First-Line Sunitinib: a Multicentre, Observational, Prospective Study," Lancet Oncol, 2011, 12(12):1143-50. [PubMed 22015057]*
18. *George S, Blay JY, Casali PG, et al, "Clinical Evaluation of Continuous Daily Dosing of Sunitinib Malate in Patients With Advanced Gastrointestinal Stromal Tumour After Imatinib Failure," Eur J Cancer, 2009, 45(11):1959-68. [PubMed 19282169]*
19. *George S, Merriam P, Maki RG, et al, "Multicenter Phase II Trial of Sunitinib in the Treatment of Nongastrointestinal Stromal Tumor Sarcomas," J Clin Oncol, 2009, 27(19):3154-60. [PubMed 19451429]*
20. *Goulart B, Carr L, Martins RG, et al, "Phase II Study of Sunitinib in Iodine Refractory, Well-Differentiated Thyroid Cancer (WDTC) and Metastatic Medullary Thyroid Carcinoma (MTC)," J Clin Oncol, 2008, 26(Supp):6062 [abstract 6062 from 2008 ASCO Annual Meeting].*
21. *Gupta S, Parsa VB, Heilbrun LK, et al, "Safety and Efficacy of Molecularly Targeted Agents in Patients With Metastatic Kidney Cancer With Renal Dysfunction," Anticancer Drugs, 2011, 22(8):794-800. [PubMed 21799472]*
22. *Hamnvik OP, Larsen PR, and Marqusee E, "Thyroid Dysfunction From Antineoplastic Agents," J Natl Cancer Inst, 2011, 103(21):1572-87. [PubMed 22010182]*
23. *Khakoo AY, Kassiotis CM, Tannir N, et al, "Heart Failure Associated With Sunitinib Malate," Cancer, 2008, 112(11):2500-8. [PubMed 18386829]*
24. *Lacouture ME, Wu S, Robert C, et al, "Evolving Strategies for the Management of Hand-Foot Skin Reaction Associated With the Multitargeted Kinase Inhibitors Sorafenib and Sunitinib," Oncologist, 2008, 13(9):1001-11. [PubMed 18779536]*
25. *Motzer RJ, Hutson TE, Olsen MR, et al, "Randomized Phase II Trial of Sunitinib on an Intermittent Versus Continuous Dosing Schedule As First-Line Therapy for Advanced Renal Cell Carcinoma.," J Clin Oncol, 2012, 30(12):1371-7. [PubMed 22430274]*
26. *Motzer RJ, Hutson TE, Tomczak P, et al, "Sunitinib Versus Interferon Alfa in Metastatic Renal-Cell Cancer," N Engl J Med, 2007, 356(2):115-24. [PubMed 17215529]*
27. *Motzer RJ, Michaelson MD, and Redman BG, "Activity of SU11248, a Multitargeted Inhibitor of Vascular Endothelial Growth Factor Receptor, in Patients With Metastatic Renal Cell Cancer," J Clin Oncol, 2006, 24(1):16-24. [PubMed 16330672]*
28. *Navid F, Christensen R, Minkin P, et al, "Stability of Sunitinib in Oral Suspension," Ann Pharmacother, 2008, 42(7):962-6. [PubMed 18577759]*
29. *Niccoli P, Raoul J, Bang Y, et al, "Updated Safety and Efficacy Results of the Phase III Trial of Sunitinib (SU) Versus Placebo (PBO) for Treatment of Pancreatic Neuroendocrine Tumors (NET)," J Clin Oncol, 2010, 28(15s):4000 [abstract 4000 from 2010 ASCO Annual Meeting].*
30. *O'Farrell AM, Foran JM, Fiedler W, et al, "An Innovative Phase I Clinical Study Demonstrates Inhibition of FLT3 Phosphorylation by SU11248 in Acute Myeloid Leukemia Patients," Clin Cancer Res, 2003, 9(15):5465-76. [PubMed 14654525]*

31. *Patel TV, Morgan JA, Demetri GD, et al. A preeclampsia-like syndrome characterized by reversible hypertension and proteinuria induced by the multitargeted kinase inhibitors sunitinib and sorafenib. J Natl Cancer Inst. 2008;100(4):282-284. [PubMed 18270341]*

32. *Ravaud A, de la Fouchardiere C, Courbon F, et al, "Sunitinib in Patients With Refractory Advanced Thyroid Cancer: The THYSU Phase II Trial," J Clin Oncol, 2008, 26(Supp):6058 [abstract 6058 from 2008 ASCO Annual Meeting].*

33. *Raymond E, Dahan L, Raoul JL, et al, "Sunitinib Malate for the Treatment of Pancreatic Neuroendocrine Tumors," N Engl J Med, 2011, 364(6):501-13. [PubMed 21306237]*

34. *Rini BI, Choueiri TK, Elson P, et al, "Sunitinib-Induced Macrocytosis in Patients With Metastatic Renal Cell Carcinoma," Cancer, 2008, 113(6):1309-14. [PubMed 18618496]*

35. *Rini BI, Tamaskar I, Shaheen P, et al, "Hypothyroidism in Patients With Metastatic Renal Cell Carcinoma Treated With Sunitinib," J Natl Cancer Inst, 2007, 99(1):81-3. [PubMed 17202116]*

36. *Ruggiero SL, Dodson TB, Fantasia J, et al; American Association of Oral and Maxillofacial Surgeons. American Association of Oral and Maxillofacial Surgeons position paper on medication-related osteonecrosis of the jaw--2014 update. J Oral Maxillofac Surg. 2014;72(10):1938-1956. doi: 10.1016/j.joms.2014.04.031. [PubMed 25234529]*

37. *Schutz FA, Je Y, Richards CJ, et al, "Meta-Analysis of Randomized Controlled Trials for the Incidence and Risk of Treatment-Related Mortality in Patients With Cancer Treated With Vascular Endothelial Growth Factor Tyrosine Kinase Inhibitors," J Clin Oncol, 2012, 30(8):871-7. [PubMed 22312105]*

38. *Seidel C, Janssen S, Karstens JH, et al, "Recall Pneumonitis During Systemic Treatment With Sunitinib," Ann Oncol, 2010, 21(10):2119-20. [PubMed 20720089]*

39. *Sutent (sunitinib) [prescribing information]. New York, NY: Pfizer Labs; April 2015.*

40. *Sutent (sunitinib) [product monograph]. Kirkland, Quebec, Canada: Pfizer Canada Inc; December 2014.*

41. *Telli ML, Witteles RM, Fisher GA, et al, "Cardiotoxicity Associated With the Cancer Therapeutic Agent Sunitinib Malate," Ann Oncol, 2008, 19(9):1613-8. [PubMed 18436521]*

42. *US Department of Health and Human Services; Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. http://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf. Updated September 2016. Accessed October 5, 2016.*

43. *van Erp NP, Baker SD, Zandvliet AS, et al, "Marginal Increase of Sunitinib Exposure by Grapefruit Juice," Cancer Chemother Pharmacol, 2011, 67(3):695-703. [PubMed 20512335]*

44. *Zastrow S, Froehner M, Platzek I, et al, "Treatment of Metastatic Renal Cell Cancer With Sunitinib During Chronic Hemodialysis," Urology, 2009, 73(4):868-70. [PubMed 19167044]*

Topic 10305 Version 162.0