Contact the specialty pharmacy directly to fill the prescription if one of the following applies:
• Your office knows the patient’s specialty pharmacy
• Your patient knows that the specialty pharmacy is covered in his/her plan and that the pharmacy is in the treatment network
• Your office uses a specialty pharmacy that is in the patient’s network

**SPECIALTY PHARMACY ORDERING PROCESS**

<table>
<thead>
<tr>
<th>The provider’s office</th>
<th>The specialty pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Submits prescriptions to the specialty pharmacy via:</td>
<td>• Verifies the patient’s coverage</td>
</tr>
<tr>
<td>• Submits any supporting documentation to the payer</td>
<td>• Helps with prior authorization if required</td>
</tr>
<tr>
<td></td>
<td>• Can help patients seek co-pay assistance</td>
</tr>
<tr>
<td></td>
<td>• Schedules shipment of product to the patient’s home</td>
</tr>
<tr>
<td></td>
<td>• Bills the payer for the cost of the product</td>
</tr>
<tr>
<td></td>
<td>• Bills the patient for remaining co-pay/coinsurance</td>
</tr>
</tbody>
</table>

**Option 1** Contact the specialty pharmacy directly
(See page 2 for list of specialty pharmacies.)

If option 1 is not applicable, contact Pfizer RxPathways™

Pfizer RxPathways helps eligible patients get access to their Pfizer medicines by offering a range of prescription assistance services:
• Pfizer RxPathways helps insured patients find an appropriate specialty pharmacy
• For uninsured and underinsured patients, Pfizer RxPathways can provide eligible patients with free medicine for up to 12 months

Visit the Pfizer RxPathways Provider Portal at www.PfizerPAP.com to begin the enrollment process for new patients and to manage existing ones or call 1-877-744-5675 Monday to Friday, 8 AM to 8 PM ET

IBRANCE®, INLYTA®, XALKORI®, BOSULIF®, and SUTENT® are not available through traditional retail pharmacies.
Pfizer RxPathways is a joint program of Pfizer Inc and the Pfizer Patient Assistance Foundation™. Pfizer RxPathways is a part of Pfizer’s Global Social Investments portfolio. For more information, please visit www.pfizer.com/responsibility.

Please see full Prescribing Information, including BOXED WARNING and Medication Guide, for SUTENT, starting on page 3. Please see full Prescribing Information for all products at www.pfizerpro.com.
IBRANCE® (palbociclib), INLYTA® (axitinib), XALKORI® (crizotinib), BOSULIF® (bosutinib), and SUTENT® (sunitinib malate)—available through these specialty pharmacies

AcariaHealth™
www.acariahealth.com
Tel: (866) 892-1380
Fax: (866) 892-2363
Hours of operation:
Monday–Friday, 8 AM–10 PM (ET)
Saturday, 9 AM–3 PM (ET)

Accredo® Health Group, Inc.
www.accredore.com
Tel: (877) 732-3431
Fax: (888) 402-1028
Hours of operation:
Monday–Friday, 8 AM–11 PM (ET)
Saturday, 8 AM–5 PM (ET)

Advanced Care Scripts
www.acs-rx.com
Tel: (877) 985-6337
Fax: (866) 679-7131
Hours of operation:
Monday–Friday, 8 AM–7 PM (ET)

Aetna Specialty Pharmacy®
www.aetnaspecialtypharmacy.com
Tel: (866) 782-2779
Fax: (860) 907-3826
Hours of operation:
Monday–Friday, 8 AM–11 PM (ET)
Saturday, 8 AM–5 PM (ET)

Axium Healthcare Pharmacy
www.axiumhealthcare.com
Tel: (888) 315-3395
Fax: (888) 315-3270
Hours of operation:
Monday–Friday, 8 AM–8 PM (ET)

Biologics, Inc.
www.biologicsinc.com
Tel: (800) 850-4306
Fax: (800) 823-4506
Hours of operation:
Monday–Friday, 8 AM–6 PM (ET)

BioPlus® Specialty Pharmacy
www.bioplusrx.com
Tel: (888) 292-0744
Fax: (800) 269-5493
Hours of operation:
Monday–Friday, 8 AM–11 PM (ET)
Saturday–Sunday, 8 AM–5 PM (ET)

BriovaRx™
www.briovarx.com
Tel: (855) 48ROVA (48-4682)
Hours of operation:
Monday–Friday, 8:30 AM–10 PM (ET)
Saturday, 9 AM–5 PM (ET)

CareMed Pharmaceutical Services
www.caremedps.com
Tel: (877) 227-3405
Fax: (877) 542-2731
Hours of operation:
Monday–Friday, 9 AM–6 PM (ET)

Cigna®
www.cigna.com
Tel: (800) 351-3606
Fax: (800) 351-3616
Hours of operation:
Monday–Friday, 8 AM–9 PM (ET)
Saturday, 9 AM–1 PM (ET)

CVS Caremark Specialty Pharmacy
www.cvscaermarkspecialtypharmacy.com
Tel: (800) 237-2776
Fax: (800) 323-2445
Hours of operation:
Monday–Friday, 7:30 AM–9 PM (ET)

Diplomat Specialty Pharmacy
www.diplomatpharmacy.com
Tel: (877) 977-9118
Fax: (800) 550-6272
Hours of operation:
Monday–Friday, 8 AM–8 PM (ET)
Saturday, 9 AM–4 PM (ET)

Echo Salveo Specialty Pharmacy
www.echospecialty.com
Tel: (718) 391-0400
Fax: (718) 391-0777
Hours of operation:
Monday–Friday, 9 AM–6 PM (ET)
Saturday, 9 AM–4 PM (ET)

Exactus Pharmacy Solutions
www.exactusrx.com
Tel: (866) 658-9246
Fax: (866) 892-8194
Hours of operation:
Monday–Thursday, 8 AM–7 PM (ET)
Friday, 8 AM–6 PM (ET)

Humana RightSource® Specialty Pharmacy
www.rightsourcerx.com/specialty
Tel: (800) 468-2668
Fax: (877) 405-7940
Hours of operation:
Monday–Thursday, 8 AM–7 PM (ET)
Friday, 8 AM–6 PM (ET)

Mission Road Pharmacy/MRP
www.mrpscripts.com
Tel: (323) 227-4646
Fax: (213) 402-3004
Hours of operation:
Monday, Wednesday–Friday, 8 AM–5 PM (PT)
Tuesday, 8 AM–9 PM (PT)

Onco360®
www.onco360.com
Tel: (877) 662-6633
Fax: (877) 662-6355
Hours of operation:
Monday–Friday, 8 AM–7 PM (ET)
Saturday, 9 AM–2 PM (ET)

OncologyRx Care Advantage™
www.mycareadvantage.com
Tel: (888) 479-6337
Fax: (866) 423-2979
Hours of operation:
Monday–Friday, 9 AM–8 PM (ET)

OncoSourceRx
www.oncosourcerx.com
Tel: (888) 662-6779
Fax: (877) 800-4790
Hours of operation:
Monday–Friday, 8:30 AM–5 PM (ET)

OptumRx™
www.optumrx.com
Tel: (888) 293-9309
Fax: (800) 853-3644
Hours of operation:
Monday–Sunday, 24 hours

Prime Therapeutics
www.primetherapeutics.com/specialty
Tel: (877) 627-6337
Fax: (877) 828-3939
Hours of operation:
Monday–Friday, 8 AM–8 PM (ET)

Rite Aid Specialty Pharmacy
www.riteaidspecialtypharmacy.com
Tel: (877) 244-4415
Fax: (877) 273-1414
Hours of operation:
Monday–Friday, 8 AM–6 PM (ET)
Saturday, 9 AM–11 AM (ET)

Safeway Specialty Care
Tel: (877) 466-8028
Fax: (877) 466-8040
Hours of operation:
Monday–Friday, 7 AM–6 PM (PST)

US Bioservices
www.usbioservices.com
Tel: (877) 757-0667
Fax: (888) 899-0067
Hours of operation:
Monday–Friday, 8 AM–8 PM (ET)

Walgreens Specialty Pharmacy
www.walgreenshealth.com
Tel: (888) 347-3416
Fax: (877) 231-8302
Hours of operation:
Monday–Friday, 8 AM–8 PM (ET)
Saturday, 9 AM–5 PM (ET)

Please see full Prescribing Information, including BOXED WARNING and Medication Guide, for SUTENT, starting on page 3.
Please see full Prescribing Information for all products at www.pfizerpro.com.
WARNING: HEPATOXICITY
See full prescribing information for complete boxed warning.

Hepatotoxicity has been observed in clinical trials and post-marketing experience. This hepatotoxicity may be severe, and deaths have been reported. [See Warnings and Precautions (5.1)]

RECENT MAJOR CHANGES

Warnnings and Precautions, Cardiovascular Events (5.3) 4/2015
Warnnings and Precautions, Thrombotic Microangiopathy (5.8) 4/2015
Warnnings and Precautions, Proteinuria (5.9) 6/2015
Warnnings and Precautions, Dermatologic Toxicities (5.10) 6/2014
Warnnings and Precautions, Hypoglycemia (5.12) 12/2014

INDICATIONS AND USAGE

SUTENT is a kinase inhibitor indicated for the treatment of:
- Gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate. (1.1)
- Advanced renal cell carcinoma (RCC). (1.2)
- Progressive, well-differentiated pancreatic neuroendocrine tumors (pNET) in patients with unresectable locally advanced or metastatic disease. (1.3)

Dosage and Administration

GIST and RCC:
- 50 mg orally once daily, with or without food, 4 weeks on treatment followed by 2 weeks off. (2.1)
- 37.5 mg orally once daily, with or without food, continuously without a scheduled off-treatment period. (2.2)

Dose Modification:
- Dose interruptions and/or dose adjustments of 12.5 mg recommended based on individual safety and tolerability. (2.3)

Dosage Forms and Strengths

Capsules: 12.5 mg, 25 mg, 37.5 mg, 50 mg (3)

Contraindications

None (4)

Warnings and Precautions

Hepatotoxicity, including liver failure, has been observed. Monitor liver function tests before initiation of treatment, during each cycle of treatment, and as clinically indicated. SUTENT should be interrupted for Grade 3 or 4 drug-related hepatic adverse events and discontinued if there is no resolution. Do not restart SUTENT if patients subsequently experience severe changes in liver function tests or have other signs and symptoms of liver failure. (5.1)
- Women of childbearing potential should be advised of the potential hazard to the fetus and to avoid becoming pregnant. (5.2)

- Cardiovascular events including myocardial ischemia, myocardial infarction, left ventricular ejection fraction declines to below the lower limit of normal and cardiac failure including death have occurred. Monitor patients for signs and symptoms of congestive heart failure. (5.3)
- Prolonged QT intervals and Torsade de Pointes have been observed. Use with caution in patients at higher risk for developing QT interval prolongation. When using SUTENT, monitoring with on-treatment electrocardiograms and electrolytes should be considered. (5.4)
- Hypertension may occur. Monitor blood pressure and treat as needed. (5.5)
- Hemorrhagic events including tumor-related hemorrhage have occurred. Perform serial complete blood counts and physical examinations. (5.6)
- Cases of Tumor Lysis Syndrome (TLS) have been reported primarily in patients with RCC and GIST with high tumor burden. Monitor these patients closely and treat as clinically indicated. (5.7)
- Thrombotic microangiopathy, including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome, sometimes leading to renal failure or a fatal outcome, has been reported in clinical trials and in post-marketing experience of SUTENT. (5.8)
- Proteinuria: Monitor urine protein. Interrupt treatment for 24-hour urine protein >3 grams. Discontinue for repeat episodes of protein >3 grams despite dose reductions or nephrotic syndrome. (5.9)
- Discontinue SUTENT if necrotizing fasciitis, erythema multiforme, Stevens-Johnson Syndrome or toxic epidermal necrolysis occurs. (5.10)
- Thyroid dysfunction may occur. Patients with signs and/or symptoms suggestive of hypothyroidism or hyperthyroidism should have laboratory monitoring of thyroid function performed and be treated as per standard medical practice. (5.11)
- Hypoglycemia may occur. Check blood glucose levels regularly and assess if anti-diabetic drug dose modifications are required. (5.12)
- Osteonecrosis of the jaw has been reported. Consider preventive dentistry prior to treatment with SUTENT. If possible, avoid invasive dental procedures, particularly in patients receiving intravenous bisphosphonate therapy. (5.13)
- Wound Healing: Impaired wound healing has occurred with SUTENT. Temporary interruption of therapy with SUTENT is recommended in patients undergoing major surgical procedures. (5.14)
- Adrenal hemorrhage was observed in animal studies. Monitor adrenal function in case of stress such as surgery, trauma or severe infection. (5.15)

ADVERSE REACTIONS

- The most common adverse reactions (≥20%) are fatigue, asthenia, fever, diarrhea, nausea, mucositis/stomatitis, vomiting, dyspepsia, abdominal pain, constipation, hypertension, peripheral edema, rash, hand-foot syndrome, skin discoloration, dry skin, hair color changes, altered taste, headache, back pain, arthralgia, extremity pain, cough, dyspepsia, anorexia, and bleeding. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer, Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- CYP3A4 Inhibitors: Consider dose reduction of SUTENT when administered with strong CYP3A4 inhibitors. (7.1)
- CYP3A4 Inducers: Consider dose increase of SUTENT when administered with CYP3A4 inducers. (7.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

* Sections or subsections omitted from the full prescribing information are not listed.
1 INDICATIONS AND USAGE

1.1 Gastrointestinal Stromal Tumor (GIST)
SUTENT is indicated for the treatment of gastrointestinal stromal tumor disease after progression on or intolerance to imatinib mesylate.

1.2 Advanced Renal Cell Carcinoma (RCC)
SUTENT is indicated for the treatment of advanced renal cell carcinoma.

1.3 Advanced Pancreatic Neuroendocrine Tumors (pNET)
SUTENT is indicated for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dose for GIST and RCC
The recommended dose of SUTENT for gastrointestinal stromal tumor (GIST) and advanced renal cell carcinoma (RCC) is 50 mg oral dose taken once daily

2.2 Recommended Dose for pNET
The recommended dose of SUTENT for pancreatic neuroendocrine tumors (pNET) is 50 mg oral dose taken once daily.

3 WARNINGS AND PRECAUTIONS

3.1 Hepatotoxicity

Hepatotoxicity has been observed in clinical trials and post-marketing experience. This hepatotoxicity is generally severe, and deaths have been reported. (See Warnings and Precautions [5.1]).

3.2 Incomplete Remission

In the presence of clinical manifestations of congestive heart failure (CHF), discontinuation of SUTENT may be considered.

3.3 Cardiovascular Events

In the presence of cardiovascular events, treatment with SUTENT may be considered.

3.4 Post-Marketing Experience

Post-marketing experience in patients treated with SUTENT for MRCC, GIST and metastatic neuroendocrine tumors has been obtained.

5.2 Pregnancy

Pregnancy: Pregnant women shown to be pregnant prior to the initiation of SUTENT therapy should discontinue treatment with SUTENT.

5.3 Hemorrhagic Events

Hemorrhagic events in post-marketing experience, some of which were fatal, included GI, respiratory, tumor, urinay tract and brain hemorrhages.

5.4 QT Interval Prolongation and Torsade de Pointes

Torsade de Pointes has been observed in <0.1% of SUTEN-treated patients.

6 FULL PRESCRIBING INFORMATION

WARNING: HEPATOXICITY

Hepatotoxicity has been observed in clinical trials and post-marketing experience. This hepatotoxicity is generally severe, and deaths have been reported. (See Warnings and Precautions [5.1]).

1 INDICATIONS AND USAGE

1.1 Gastrointestinal Stromal Tumor (GIST)
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1.3 Advanced Pancreatic Neuroendocrine Tumors (pNET)
SUTENT is indicated for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dose for GIST and RCC
The recommended dose of SUTENT for gastrointestinal stromal tumor (GIST) and advanced renal cell carcinoma (RCC) is 50 mg oral dose taken once daily, on a schedule of 4 weeks on treatment followed by 2 weeks off (Schedule 4/2). SUTENT may be taken with or without food.

2.2 Recommended Dose for pNET
The recommended dose of SUTENT for pancreatic neuroendocrine tumors (pNET) is 50 mg oral dose taken once daily. SUTENT may be taken with or without food.

2.3 Dose Modification

Dose interruption and/or dose modification in 12.5 mg increments or decrements is recommended based on individual safety and tolerability. The maximum dose administered in GI, RCC, and pNET was 125 mg daily.

Strong CYP3A4 inhibitors such as ketoconazole may increase sunitinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal enzyme induction potential is recommended for SUTENT to a maximum of 75 mg (GIST and RCC) or 62.5 mg (pNET) daily should be considered if SUTENT must be co-administered with a CYP3A4 inducer. If dose is increased, the patient should be monitored carefully for toxicity (see Drug Interactions [7.2] and Clinical Pharmacology [12.3]).

CYP3A4 inducers such as rifampin may decrease sunitinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal enzyme induction potential is recommended for SUTENT to a maximum of 75 mg (GIST and RCC) or 62.5 mg (pNET) daily should be considered if SUTENT must be co-administered with a CYP3A4 inducer. If dose is increased, the patient should be monitored carefully for toxicity (see Drug Interactions [7.2] and Clinical Pharmacology [12.3]).

3 DOSAGE FORMS AND STRENGTHS

12.5 mg capsules
Hard gelatin capsule with orange cap and orange body, printed with white ink “Pfizer” on the cap and “STN 12.5 mg” on the body.

25 mg capsules
Hard gelatin capsule with caramel cap and orange body, printed with white ink “Pfizer” on the cap and “STN 25 mg” on the body.

37.5 mg capsules
Hard gelatin capsule with yellow cap and yellow body, printed with black ink “Pfizer” on the cap and “STN 37.5 mg” on the body.

50 mg capsules
Hard gelatin capsule with caramel top and caramel body, printed with white ink “Pfizer” on the cap and “STN 50 mg” on the body.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Hepatotoxicity

Hepatotoxicity has been associated with hepatotoxicity, which may result in liver failure or death. Liver failure has been observed in clinical trials (7/2281 [0.3%]) and post-marketing experience. Liver failure signs include jaundice, elevated transaminases and/or hyperbilirubinemia.

5.2 Incomplete Remission

In the presence of clinical manifestations of congestive heart failure (CHF), discontinuation of SUTENT may be considered.

5.3 Cardiovascular Events

In the presence of cardiovascular events, treatment with SUTENT may be considered.

5.4 Post-Marketing Experience

Post-marketing experience in patients treated with SUTENT for MRCC, GIST and metastatic neuroendocrine tumors has been obtained.

6 FULL PRESCRIBING INFORMATION

WARNING: HEPATOXICITY

Hepatotoxicity has been observed in clinical trials and post-marketing experience. This hepatotoxicity is generally severe, and deaths have been reported. (See Warnings and Precautions [5.1]).

1 INDICATIONS AND USAGE

1.1 Gastrointestinal Stromal Tumor (GIST)
SUTENT is indicated for the treatment of gastrointestinal stromal tumor disease after progression on or intolerance to imatinib mesylate.

1.2 Advanced Renal Cell Carcinoma (RCC)
SUTENT is indicated for the treatment of advanced renal cell carcinoma.

1.3 Advanced Pancreatic Neuroendocrine Tumors (pNET)
SUTENT is indicated for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dose for GIST and RCC
The recommended dose of SUTENT for gastrointestinal stromal tumor (GIST) and advanced renal cell carcinoma (RCC) is 50 mg oral dose taken once daily, on a schedule of 4 weeks on treatment followed by 2 weeks off (Schedule 4/2). SUTENT may be taken with or without food.

2.2 Recommended Dose for pNET
The recommended dose of SUTENT for pancreatic neuroendocrine tumors (pNET) is 50 mg oral dose taken once daily. SUTENT may be taken with or without food.

2.3 Dose Modification

Dose interruption and/or dose modification in 12.5 mg increments or decrements is recommended based on individual safety and tolerability. The maximum dose administered in GI, RCC, and pNET was 125 mg daily.

Strong CYP3A4 inhibitors such as ketoconazole may increase sunitinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal enzyme induction potential is recommended for SUTENT to a maximum of 75 mg (GIST and RCC) or 62.5 mg (pNET) daily should be considered if SUTENT must be co-administered with a CYP3A4 inducer. If dose is increased, the patient should be monitored carefully for toxicity (see Drug Interactions [7.2] and Clinical Pharmacology [12.3]).

CYP3A4 inducers such as rifampin may decrease sunitinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal enzyme induction potential is recommended for SUTENT to a maximum of 75 mg (GIST and RCC) or 62.5 mg (pNET) daily should be considered if SUTENT must be co-administered with a CYP3A4 inducer. If dose is increased, the patient should be monitored carefully for toxicity (see Drug Interactions [7.2] and Clinical Pharmacology [12.3]).

3 DOSAGE FORMS AND STRENGTHS

12.5 mg capsules
Hard gelatin capsule with orange cap and orange body, printed with white ink “Pfizer” on the cap and “STN 12.5 mg” on the body.

25 mg capsules
Hard gelatin capsule with caramel cap and orange body, printed with white ink “Pfizer” on the cap and “STN 25 mg” on the body.

37.5 mg capsules
Hard gelatin capsule with yellow cap and yellow body, printed with black ink “Pfizer” on the cap and “STN 37.5 mg” on the body.

50 mg capsules
Hard gelatin capsule with caramel top and caramel body, printed with white ink “Pfizer” on the cap and “STN 50 mg” on the body.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Hepatotoxicity

Hepatotoxicity has been associated with hepatotoxicity, which may result in liver failure or death. Liver failure has been observed in clinical trials (7/2281 [0.3%]) and post-marketing experience. Liver failure signs include jaundice, elevated transaminases and/or hyperbilirubinemia.

5.2 Incomplete Remission

In the presence of clinical manifestations of congestive heart failure (CHF), discontinuation of SUTENT may be considered.

5.3 Cardiovascular Events

In the presence of cardiovascular events, treatment with SUTENT may be considered.

5.4 Post-Marketing Experience

Post-marketing experience in patients treated with SUTENT for MRCC, GIST and metastatic neuroendocrine tumors has been obtained.
Serious, sometimes fatal gastrointestinal complications including gastrointestinal perforation, have occurred rarely in patients with intra-abdominal malignancies treated with SUTENT.

5.7 Tumor Lysis Syndrome (TLS)
Cases of TLS, some fatal, have been observed in clinical trials and have been reported in post-marketing experience. Patients with RCC or GIST treated with SUTENT.

Patients generally at risk of TLS are those with high tumor burden prior to treatment. These patients should be monitored closely and treated as clinically indicated.

5.8 Thrombotic Microangiopathy
Thrombotic microangiopathy (TMA), including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome, sometimes leading to renal failure or a fatal outcome, has been reported in clinical trials and in post-marketing experience of SUTENT as monotherapy in combination with bevacizumab. Discontinue SUTENT in patients developing TMA. Reactivation of the clinical course of TMA has been observed after treatment was discontinued.

5.9 Proteinuria
Proteinuria and nephrotic syndrome have been reported. Some of these cases have resulted in renal failure and fatal outcomes. Monitor patients for the development or worsening of proteinuria, and periodic urinalyses during treatment, with follow up measurement of 24-hour urine protein as clinically indicated. Interrupt SUTENT and dose reduce for 24-hour urine protein ≥ 3 grams. Discontinue SUTENT for patients with nephrotic syndrome or repeat episodes of urine protein ≥ 3 grams despite dose reductions. The safety of continued SUTENT treatment in patients with moderate to severe proteinuria has not been systematically evaluated.

6.10 Dermatologic Toxicities
Severe cutaneous reactions have been reported, including cases of erythema multiforme (EM), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN). A number of fatalities were reported. Signs or symptoms suggestive of thyroid dysfunction should have laboratory monitoring of thyroid function performed and be treated as per standard medical practice.

Treatment-emergent acquired hypothyroidism was noted in eight GIST patients (4%) on SUTENT versus 11% (1% was reported as an adverse reaction in sixty-one patients (16%) on SUTENT in the treatment-naïve RCC study and in three patients (1%) in the IFN-α arm. Hypothyroidism was reported as an adverse reaction in 6/83 patients (7%) on SUTENT in the Phase 3 pNET study and in 1/82 patients (1%) in the placebo arm.

Cases of hyperthyroidism, some followed by hypothyroidism, have been reported in clinical trials and through post-marketing experience.

5.12 Hypoglycemia
SUTENT has been associated with symptomatic hypoglycemia, which may result in loss of consciousness, or require hospitalization. Hypoglycemia has occurred in clinical trials in 2% of the patients treated with SUTENT for RCC and GIST and in approximately 10% of the patients treated with SUTENT for pNET. For patients being treated with SUTENT for pNET, pre-existing abnormalities in glucose homeostasis were not present in all patients who experienced hypoglycemia, but blood glucose levels may be lowered in diabetic patients. Check blood glucose levels regularly during and after discontinuation of treatment with SUTENT. Assess if anti-diabetic drug dosage needs to be adjusted to minimize the risk of hypoglycemia.

6.13 Ocular Toxicity (ONJ)
ONJ has been observed in clinical trials and has been reported in post-marketing experience in patients treated with sunlight. Concomitant exposure to other risk factors, such as bisphosphonates or dental disease, may increase the risk of osteonecrosis of the jaw.

6.14 Wound Healing
Cases of impaired wound healing have been reported during SUTENT therapy. Temporary interruption of SUTENT therapy is recommended for precautionary reasons in patients undergoing major surgical procedures. There is limited clinical experience regarding the timing of reinitiation of therapy following major surgical intervention. Therefore, the decision to resume SUTENT therapy for a period of surgical intervention should be based upon clinical judgment of recovery from surgery.

6.15 Adrenal Function
Physicians prescribing SUTENT are advised to monitor for adrenal insufficiency in patients who experience stress such as surgery, trauma or severe infection. Adrenal toxicity was noted in non-clinical repeat dose studies of 14 days to 9 months in rats and monkeys at plasma exposures as low as 0.7 times the AUC observed in clinical studies. Histological changes of the adrenal gland were characterized as hemorrhage, necrosis, congestion, or apoptosis and atrophy. In clinical studies, CORT obtained in 336 patients after exposure to one or more cycles of SUTENT demonstrated no evidence of adrenal hemorrhage or necrosis. ACTH stimulation testing was performed in approximately 400 patients across multiple clinical trials of SUTENT. Among patients with normal baseline ACTH, 12% (2/16) of patients had abnormal ACTH stimulated ACTH suppression results during treatment that were unexplained and may be related to treatment with SUTENT. Eleven additional patients with normal baseline testing had abnormalities in the final test performed, with peak cortisol levels of 12-16 mcg/dL (normal >18 mcg/dL) following stimulation. None of these patients were reported to have clinical evidence of adrenal insufficiency.

6.16 Laboratory Tests
CBCs with platelet count and serum chemistries including phosphate should be performed at the beginning of each treatment cycle for patients receiving treatment with SUTENT.

6. ADVERSE REACTIONS
The data described below reflect exposure to SUTENT in 660 patients who participated in the double-blind treatment phase of a placebo-controlled trial (n=202) for the treatment of GIST [see Clinical Studies (14.1)], an active-controlled trial (n=375) for the treatment of RCC [see Clinical Studies (14.2)] or a placebo-controlled trial (n=83) for the treatment of pNET [see Clinical Studies (14.3)]. The GIST and RCC patients received a starting oral dose of 50 mg daily on Schedule 4/2 in repeated cycles, and the pNET patients received a starting oral dose of 37.5 mg daily without scheduled off-treatment periods.

The most common adverse reactions (≥20%) in patients with GIST, RCC or pNET were fatigue, nausea, diarrhea, vomiting, anorexia, abdominal pain, constipation, hypertension, peripheral edema, rash, hand-foot syndrome, skin discoloration, dry skin, hair color changes, altered taste, headache, back pain, arthralgia, extremity pain, cough, dyspnea, anorexia, and bleeding. The potentially serious adverse reactions of hepatotoxicity, left ventricular dysfunction, QT interval prolongation, hemorrhage, hypertension, thyroid dysfunction, and adrenal功能 disorder are discussed in Warnings and Precautions (5) Other adverse reactions occurring in GIST, RCC and pNET studies are described below.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

6.1 Adverse Reactions in GIST Study A

Median duration of blinded study treatment was two cycles for patients on SUTENT (mean 3.0, range 1.8-4.3), and one cycle (mean 1.8, range 1-6) for patients on placebo at the time of the interim analysis. Dose reductions occurred in 23 patients (11%) on SUTENT and none on placebo. Dose interruptions occurred in 59 patients (29%) on SUTENT and 31 patients (30%) on placebo. The rates of treatment-emergent, non-fatal adverse reactions resulting in permanent discontinuation were 7% and 6% in the SUTENT and placebo groups, respectively.

Most treatment-emergent adverse reactions in both study arms were Grade 1 or 2 in severity. Grade 3 or 4 treatment-emergent adverse reactions were reported in 56% versus 51% of patients on SUTENT versus placebo, respectively, in the double-blind treatment phase of the trial. Table 1 compares the incidence of common (≥10%) treatment-emergent adverse reactions for patients receiving SUTENT and reported more commonly in patients receiving SUTENT than in patients receiving placebo.

### Table 1. Adverse Reactions Reported in Study A in at Least 10% of GIST Patients Who Received SUTENT in the Double-Blind Treatment Phase and More Commonly Than in Patients Given Placebo

<table>
<thead>
<tr>
<th>Adverse Reaction, n (%)</th>
<th>SUTENT (n=202)</th>
<th>Placebo (n=102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.16 Laboratory Tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBCs with platelet count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum chemistries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>and dose reduce for 24-hour urine protein ≥ 3 grams</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Laboratory Abnormalities Reported in Study A in at Least 10% of GIST Patients Who Received SUTENT or Placebo in the Double-Blind Treatment Phase

<table>
<thead>
<tr>
<th>Laboratory Parameter, n (%)</th>
<th>SUTENT (n=202)</th>
<th>Placebo (n=102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.16 Laboratory Tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBCs with platelet count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum chemistries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>and dose reduce for 24-hour urine protein ≥ 3 grams</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6.2 Adverse Reactions in the Phase 3 RCC Study

The as-treated patient population for the treatment-naive RCC study included 735 patients, 375 randomized to SUTENT and 360 randomized to IFN-α. The median duration of treatment was 11.1 months (range: 0.4 - 46.1) for SUTENT treatment and 4.1 months (range: 0.1 - 45.6) for IFN-α treatment. Dose interruptions occurred in 202 patients (54%) on SUTENT and 141 patients (39%) on IFN-α. Dose reductions occurred in 194 patients (52%) on SUTENT and 98 patients (27%) on IFN-α. Discontinuation rates due to adverse reactions were 20% for SUTENT and 24% for IFN-α. Most treatment-emergent adverse reactions in both study arms were Grade 1 or 2 in severity. Grade 3 or 4 treatment-emergent adverse reactions were reported in 77% versus 55% of patients on SUTENT versus IFN-α, respectively.

Table 3 compares the incidence of common (>10%) treatment-emergent adverse reactions for patients receiving SUTENT versus IFN-α.

### Table 3. Adverse Reactions Reported in at Least 10% of Patients with RCC Who Received SUTENT or IFN-α

<table>
<thead>
<tr>
<th>Adverse Reaction, n (%)</th>
<th>SUTENT (n=375)</th>
<th>IFN-α (n=360)</th>
<th>SUTENT (n=375)</th>
<th>IFN-α (n=360)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constitutional Fatigue</td>
<td>233 (63)</td>
<td>55 (15)</td>
<td>202 (56)</td>
<td>54 (15)</td>
</tr>
<tr>
<td>Anemia</td>
<td>96 (26)</td>
<td>42 (11)</td>
<td>81 (22)</td>
<td>21 (6)</td>
</tr>
<tr>
<td>Fever</td>
<td>84 (22)</td>
<td>3 (1)</td>
<td>13 (37)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Weight decreased</td>
<td>60 (16)</td>
<td>1 (&lt;1)</td>
<td>60 (17)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Chills</td>
<td>53 (14)</td>
<td>3 (1)</td>
<td>111 (31)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>50 (13)</td>
<td>7 (2)</td>
<td>24 (7)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Influence like illness</td>
<td>10 (3)</td>
<td>0 (0)</td>
<td>54 (15)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>246 (66)</td>
<td>37 (10)</td>
<td>76 (21)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Nausea</td>
<td>216 (58)</td>
<td>21 (6)</td>
<td>147 (41)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Mucositis/stomatitis</td>
<td>178 (47)</td>
<td>13 (3)</td>
<td>19 (5)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>148 (39)</td>
<td>19 (5)</td>
<td>62 (17)</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>128 (34)</td>
<td>8 (2)</td>
<td>16 (4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>113 (30)</td>
<td>20 (5)</td>
<td>42 (12)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Constipation</td>
<td>85 (23)</td>
<td>4 (1)</td>
<td>49 (14)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>50 (13)</td>
<td>0 (0)</td>
<td>27 (7)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>GERD/reflux esophagitis</td>
<td>47 (12)</td>
<td>1 (&lt;1)</td>
<td>3 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Flatulence</td>
<td>52 (14)</td>
<td>0 (0)</td>
<td>8 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Oral pain</td>
<td>54 (14)</td>
<td>2 (&lt;1)</td>
<td>2 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Glossodynia</td>
<td>40 (11)</td>
<td>0 (0)</td>
<td>2 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>38 (10)</td>
<td>0 (0)</td>
<td>6 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cardiac</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>127 (34)</td>
<td>50 (13)</td>
<td>13 (4)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Edema, peripheral pain</td>
<td>91 (24)</td>
<td>7 (2)</td>
<td>17 (5)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>61 (16)</td>
<td>10 (3)</td>
<td>19 (5)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Dermatologic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>109 (29)</td>
<td>6 (2)</td>
<td>39 (11)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Hand-foot syndrome</td>
<td>108 (29)</td>
<td>32 (9)</td>
<td>3 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Skin discoloration/</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yellow skin</td>
<td>94 (25)</td>
<td>1 (&lt;1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Dry skin</td>
<td>85 (23)</td>
<td>1 (&lt;1)</td>
<td>26 (7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hair color changes</td>
<td>73 (20)</td>
<td>0 (0)</td>
<td>1 (&lt;1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>51 (14)</td>
<td>0 (0)</td>
<td>34 (10)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Erythema</td>
<td>46 (12)</td>
<td>2 (&lt;1)</td>
<td>5 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>44 (12)</td>
<td>1 (&lt;1)</td>
<td>24 (7)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Neurologic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altered taste</td>
<td>178 (47)</td>
<td>1 (&lt;1)</td>
<td>54 (15)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Headache</td>
<td>86 (23)</td>
<td>4 (1)</td>
<td>69 (19)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>43 (11)</td>
<td>2 (&lt;1)</td>
<td>50 (14)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>105 (28)</td>
<td>19 (5)</td>
<td>52 (14)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>111 (30)</td>
<td>10 (3)</td>
<td>69 (19)</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Pain in extremity/</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>limb discomfort</td>
<td>150 (40)</td>
<td>19 (5)</td>
<td>107 (30)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Endocrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>61 (16)</td>
<td>6 (2)</td>
<td>3 (1)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

6.3 Adverse Reactions in the Phase 3 pNET Study

The median number of days on treatment was 139 days (range 13-532 days) for patients on SUTENT and 113 days (range 1-614 days) for patients on placebo. Nineteen patients (23%) on SUTENT and 4 patients (5%) on placebo were on study for >1 year. Dose interruptions occurred in 25 patients (30%) on SUTENT and 10 patients (12%) on placebo. Dose reductions occurred in 26 patients (31%) on SUTENT and 9 patients (11%) on placebo. Discontinuation rates due to adverse reactions were 22% for SUTENT and 17% for placebo.

Most treatment-emergent adverse reactions in both study arms were Grade 1 or 2 in severity. Grade 3 or 4 treatment-emergent adverse reactions were reported in 54% versus 50% of patients on SUTENT versus placebo, respectively. Table 5 compares the incidence of common (>10%) treatment-emergent adverse reactions for patients receiving SUTENT and reported more commonly in patients receiving SUTENT than in patients receiving placebo.
Grade 3. One patient was permanently withdrawn from SUTENT due to pulmonary embolism; dose interruption occurred in two patients with pulmonary embolism and one with DVT. In treatment-naïve RCC patients receiving IFN-α, six (2%) venous thromboembolic events occurred; one patient (<1%) experienced a Grade 3 DVT and five patients (1%) had pulmonary embolism, all Grade 4. One patient (1%) receiving SUTENT for pNET had a venous thromboembolic event reported compared to 5 patients (6%) receiving placebo. The SUTENT patient had Grade 2 thrombosis. Two placebo patients had DVT, one was Grade 3, two placebo patients had pulmonary embolism, one was Grade 3 and one was Grade 4, and one placebo patient had Grade 3 jugular thrombosis.

6.5 Reversible Posterior Leukoencephalopathy Syndrome

There have been reports (<1%), some fatal, of subjects presenting with seizures and radiological evidence of reversible posterior leukoencephalopathy syndrome (RPLS). Patients with seizures and signs/symptoms consistent with RPLS, such as hypertension, headache, decreased alertness, altered mental function, and visual loss, including cortical blindness should be controlled with medical management including control of hypertension. Treatment of such patients with SUTENT is recommended; following resolution, treatment may be resumed at the discretion of the treating physician.

6.6 Pancreatic and Hepatic Function

If symptoms of pancreatitis or hepatic failure are present, patients should have SUTENT discontinued. Pancreatitis was observed in 5 (1%) patients receiving SUTENT for treatment-naïve RCC compared to 1 (<1%) patient receiving IFN-α. Pancreatitis was observed in 1 (1%) patient receiving SUTENT for pNET and 1 (1%) patient receiving placebo. Hepatotoxicity was observed in patients receiving SUTENT [see Boxed Warning and Warnings and Precautions (5.1)].

6.7 Post-marketing Experience

The following adverse reactions have been identified during post-approval use of SUTENT. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Blood and lymphatic system disorders: hemorrhage associated with thrombocytopenia*. Suspension of SUTENT is recommended; following resolution, treatment may be resumed at the discretion of the treating physician. Gastrointestinal disorders: esophagitis. Hepatobiliary disorders: cholecystitis, particularly acalculous cholecystitis. Immune system disorders: hypersensitivity reactions, including angioedema. Infections and infestations: serious infection (with or without neutropenia)*. The infections most commonly observed with sunitinib treatment include respiratory, urinary, skin infections, sepsis/septic shock.

Vascular disorders: arterial thromboembolic events*. The most frequent events included cerebrovascular accident, transient ischemic attack and cerebral infarction.

* including some fatalities

7 DRUG INTERACTIONS

7.1 CYP3A4 Inhibitors

Strong CYP3A4 inhibitors such as ketoconazole may increase sunitinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal enzyme inducer is recommended. If concomitant use of SUTENT with the strong CYP3A4 inhibitor, ketoconazole, resulted in 49% and 51% increases in the combined (sunitinib + primary active metabolite) C_{0-∞} and AUC_{0-∞} values, respectively, after a single dose of SUTENT in healthy volunteers. Co-administration of SUTENT with strong inhibitors of the CYP3A4 family (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nelfinavir, ribavirin, nevirapine, ritonavir, telithromycin, voriconazole), should be avoided due to increase sunitinib concentrations. Grapefruit may also increase plasma concentrations of sunitinib. A dose reduction for SUTENT should be considered when it must be co-administered with strong CYP3A4 inhibitors [see Dosage and Administration (2.2)].

7.2 CYP3A4 Inducers

CYP3A4 inducers such as rifampin may decrease sunitinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal enzyme induction potential is recommended. Concurrent administration of SUTENT with the strong CYP3A4 inducer, rifampin, resulted in a 33% and 46% reduction in the combined (sunitinib + primary active metabolite) C_{0-∞} and AUC_{0-∞} values, respectively, after a single dose of SUTENT in healthy volunteers. Co-administration of SUTENT with inducers of the CYP3A4 family (e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifapentin, phenobarbital, St. John’s Wort) may decrease sunitinib concentrations. St. John’s Wort may decrease sunitinib plasma concentrations unpredictably. Patients receiving SUTENT should not take St. John’s Wort concomitantly. A dose increase for SUTENT should be considered when it must be co-administered with CYP3A4 inducers [see Dosage and Administration (2.2)].

7.3 In Vivo Studies of CYP Inhibition and Induction

In vitro studies indicated that sunitinib does not inhibit or inhibit major CYP enzymes. The in vitro data suggested that sunitinib does not inhibit major CYP enzymes.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category D [see Warnings and Precautions (5.2)]. SUTENT can cause fatal harm when administered to a pregnant woman. As angiosarcoma is a critical component of embryonic and fetal development, inhibition of angiosarcoma following administration of SUTENT should be expected to result in adverse effects on pregnancy. In animal reproductive studies in rats and rabbits, sunitinib was teratogenic,
Sunitinib is a small molecule that inhibits multiple receptor tyrosine kinases (RTKs), some of which are implicated in tumor growth, pathologic angiogenesis, and metastatic progression of cancer. Sunitinib was evaluated for its inhibitory activity against a variety of kinases (-80 kinases) and was identified as an inhibitor of platelet-derived growth factor receptors (PDGFRs) and VEGFR family members. VEGFR2-dependent tumor angiogenesis and VEGFR2- and VEGFR3), stem cell factor receptor (KIT), Fms-like tyrosine kinase-3 (FLT3), colony stimulating factor receptor Type 1 (CSF-1R), and the glial cell-line derived neurotrophic factor receptor (RET). Sunitinib inhibition of the activity of these RTKs has been demonstrated in biochemical and cellular assays, and inhibition of function has been observed in animal tumor xenograft models. The primary metabolite exhibits similar potency compared to sunitinib in biochemical and cellular assays.

Sunitinib inhibited the phosphorylation of multiple RTKs (PDGFRα, VEGFR2, KIT) in tumor xenografts expressing RTK targets in vivo and demonstrated inhibition of tumor growth in orthotopic tumor models. Sunitinib inhibited metastases in some experimental models of cancer. Sunitinib demonstrated the ability to inhibit growth of tumor cells expressing dysregulated target RTKs (PDGFR, RET, or KIT) in vitro and to inhibit PDGFR- and VEGFR2-dependent tumor angiogenesis in vivo.

12.3 Pharmacokinetics

The pharmacokinetics of sunitinib and sunitinib malate have been evaluated in 135 healthy volunteers and in 266 patients with solid tumors. Maximum plasma concentrations (Cmax) of sunitinib are generally observed between 6 and 12 hours (Tmax) following oral administration. Food has no effect on the bioavailability of sunitinib. Sunitinib is not removed by hemodialysis or peritoneal dialysis.

Binding of sunitinib and its primary active metabolite to human plasma proteins in vitro was 95% and 90%, respectively, with no concentration dependence in the range of 100 - 4000 ng/mL. The apparent volume of distribution (Vd/F) for sunitinib was 2230 L. In the dosing range of 25 - 100 mg, the area under the plasma concentration-time curve (AUC) was directly proportional to dose.

Sunitinib is metabolized primarily by the cytochrome P450 enzyme, CYP3A4, to produce its primary active metabolite, which is further metabolized by CYP3A4. The primary active metabolite comprises 23% to 37% of the total exposure. Elimination is primarily via feces. In a human mass balance study of [14C]sunitinib, 61% of the dose was recovered in urine and 35% in feces. Sunitinib and its primary active metabolite were the major drug-related compounds identified in plasma, urine, and feces, representing 91.5%, 86.4% and 73.8% of radioactivity in pooled samples, respectively. Minor metabolites were identified in urine and feces but generally not found in plasma. Total oral clearance (CL/F) ranged from 34 to 62 L/hr with an oral bioavailability of 27%.

Following administration of a single oral dose in healthy volunteers, the terminal half-lives of sunitinib and its primary active metabolite are approximately 40 to 60 hours and 80 to 110 hours, respectively. With repeated daily administration, sunitinib accumulates to 3- to 4-fold while the primary metabolite accumulates 7- to 10-fold. Steady-state concentrations of sunitinib and its primary active metabolite are achieved within 10 to 14 days. By Day 14, combined plasma concentrations of sunitinib and its active metabolite ranged from 62.9 – 101 ng/mL. No significant changes in the pharmacokinetics of sunitinib or the primary active metabolite were observed with repeated daily administration or with repeated cycles in the dosing regimens tested.

The pharmacokinetics were similar in healthy volunteers and in the solid tumor patient populations tested, including patients with GIST and RCC.

Pharmacokinetics in Special Populations

Population pharmacokinetic analyses of demographic data indicate that there are no clinically relevant effects of age, weight, creatinine clearance, race, gender, or ECOG score on the pharmacokinetics of SUTEN or the primary active metabolite.

Pediatric Use: The pharmacokinetics of SUTEN have not been evaluated in pediatric patients.

Renal Insufficiency: Sunitinib systemic exposure after a single dose of SUTEN was similar in subjects with severe renal impairment (Clcr<30 mL/min) compared to subjects with normal renal function (Clcr>80 mL/min). Although sunitinib was not eliminated through hemodialysis, the sunitinib systemic exposure was 47% lower in subjects with ESRD on hemodialysis compared to subjects with normal renal function.

Hepatic Insufficiency: Systemic exposures after a single dose of SUTEN were similar in subjects with mild cirrhosis (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment compared to subjects with normal hepatic function.

The pharmaceutics of SUTEN capsules are supplied as printed hard shell capsules containing sunitinib malate and inactive ingredients.

The chemical structure of sunitinib malate is:
13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of sunitinib has been evaluated in two species; rhesus transgenic mice and Sprague-Dawley rats. There were similar positive findings in both species. In rhesus transgenic mice gastroduodenal carcinomas and/or gastric mucosal hyperplasia, as well as an increased incidence of background hemangiosarcomas were observed at doses of ≥25 mg/kg/day following daily dose administration of sunitinib in studies of 1 to 6 months duration. No proliferative changes were observed in rhesus transgenic mice at 8 mg/kg/day. Similarly, in a 2-year rat carcinogenicity study, administration of sunitinib in 28-day cycles followed by 7-day dose-free periods resulted in findings of duodenal carcinomas at dose as low as 1 mg/kg/day (approximately 0.9 times the AUC in patients given the RDD of 50 mg/day). At the high dose of 3 mg/kg/day (approximately 7.8 times the AUC in patients at the RDD of 50 mg/day) the incidence of duodenal tumors was increased and was accompanied by findings of gastric mucous cell hyperplasia and by an increased incidence of pheochromocytoma and hyperplasia of the adrenal. Sunitinib did not cause genetic damage when tested in in vitro assays (bacterial mutation [AMES Assay], human lymphocyte chromosome aberration) and an in vivo rat bone marrow micronucleus test.

The female reproductive system were identified in a 3-month repeat dose monkey study (2, 6, 12 mg/kg/day). When ovarian changes (decreased follicular development) were noted at 12 mg/kg/day (>5.1 times the AUC in patients administered the RDD), while uterine changes (endometrial atrophy) were noted at ≥2 mg/kg/day (>3.4 times the AUC in patients administered the RDD). With the addition of vaginal atrophy, the uterine and ovarian effects were introduced at 6 mg/kg/day in the 9-month monkey study (0.3, 1.5, and 6 mg/kg/day administered daily for 28 days followed by a 14 day rest period; the 6 mg/kg/day produced a mean AUC that was >0.8 times the AUC in patients administered the RDD). No adverse effect level was not identified in the 3-month study; 1.5 mg/kg/day represents a no effect level in monkeys administered sunitinib for 9 months.

Although fertility was not affected in rats, SUTENT may impair fertility in humans. In female rats, no fertility effects were observed at doses of ≥50 mg/kg/day ([0.5, 1.5, 5.0 mg/kg/day) administered for 21 days up to gestational day 7; the 5.0 mg/kg dose produced an AUC that >5 times the AUC in patients administered the RDD), however significant embryotoxicity was observed at ≥5 mg/kg/day. No reproductive effects were observed for up to 28 days prior to breeding with untreated females. Fertility, copulation, conception indices, and sperm evaluation (morphology, concentration, and motility) were unaffected by sunitinib at doses <10 mg/kg/day (the 10 mg/kg/day dose produced a mean AUC that was ≥25.8 times the AUC in patients administered the RDD).

14 CLINICAL STUDIES

14.1 Gastrinomas Tumor Stromal Tumor

**GIST Study A**

A study was a two-arm, international, randomized, double-blind, placebo-controlled trial of SUTENT in patients with GIST who had disease progression during prior imatinib (imatinib) treatment or who were intolerant of imatinib. The objective was to compare progression-free survival (PFS) in patients receiving SUTENT plus best supportive care versus patients receiving placebo plus best supportive care. Other objectives included Progression-Free Survival (PFS), Objective Response Rate (ORR), and Overall Survival (OS).

Patients were randomized (2:1) to receive either 50 mg SUTENT or placebo orally, once daily, on Schedule 4/2 until disease progression or withdrawal from the study for another reason. Treatment was unblinded at the time of disease progression. Patients randomized to placebo were then offered crossover to open-label SUTENT, and patients randomized to SUTENT were permitted to continue treatment per investigator judgment.

At the time of a pre-specified interim analysis, the intent-to-treat (ITT) population included 312 patients. Two-hundred-seven (207) patients were randomized to the SUTENT arm, and 105 patients were randomized to the placebo arm. Demographics were comparable between the SUTENT and placebo groups with regard to age (69% vs. 72% <65 years for SUTENT vs. placebo, respectively), gender (Male: 64% vs. 61%), race (White: 88% both arms, Asian: 5% both arms, Black: 4% both arms, remainder not reported), and Performance Status (ECOG 0: 44% vs. 46%, ECOG 1: 55% vs. 52%, and ECOG 2: 1% vs. 2%). Prior treatment included surgery (94% vs. 93%) and radiotherapy (8% vs. 15%). Outcome of prior imatinib treatment was also comparable between arms with intolerance (4% vs. 4%), progression between 6 months of starting treatment (17% vs. 16%), or progression beyond 6 months (78% vs. 80%) balanced.

The planned interim efficacy and safety analysis was performed after 149 TTP events had occurred. There was a statistically significant advantage for SUTENT over placebo in TTP, meeting the primary endpoint. Efficacy results are summarized in Table 7 and the Kaplan-Meier Curve for TTP in ITT, as shown in Figure 1. The final ITT population enrolled in the double-blind treatment phase of the study included 243 patients randomized to the SUTENT arm and 118 patients randomized to the placebo arm. Although the primary endpoint was met at the interim analysis, the study was unblinded, and patients on the placebo arm were offered open-label SUTENT treatment.

**Study B**

Study B was an open-label, multi-center, single-arm, dose-escalation study conducted in patients with GIST following progression on or intolerance to imatinib. Following identification of the recommended Phase 2 regimen (once daily on Schedule 4/2), 55 patients in this study received the 50 mg dose of SUTENT on treatment Schedule 4/2. Partial responses were observed in 5 of 55 patients [91% PR rate, 95% CI (3.0, 20.0)].

14.2 Renal Cell Carcinoma

**Treatment-Naive RCC**

A multicenter, international randomized study comparing single-agent SUTENT with IFN-α was conducted in patients with treatment-naive RCC. The objective was to compare Progression-Free Survival (PFS) in patients receiving SUTENT versus patients receiving IFN-α. Other endpoints included Objective Response Rate (ORR), Overall Survival (OS) and safety. Seven hundred fifty (750) patients were randomized (1:1) to receive either 50 mg SUTENT, once daily on Schedule 4/2 or to receive IFN-α administered subcutaneously at 9 MIU three times a week. Patients were treated until disease progression or withdrawal from the study.

The ITT population included 750 patients, 375 randomized to SUTENT and 375 randomized to IFN-α. Demographics were comparable between the SUTENT and IFN-α groups with regard to age (59% vs. 67% <65 years for SUTENT vs. IFN-α, respectively), gender (Male: 71% vs. 72%), race (White: 94% vs. 91%, Asian: 2% vs. 3%, Black: 1% vs. 2%, remainder not reported), and Performance Status (ECOG 0: 62% vs. 61%, ECOG 1: 38% each arm, ECOG 2: 0 vs. 1%). Prior treatment included nephrectomy (91% vs. 89%) and radiotherapy (14% each arm). The most common site of metastases present at screening was the lung (78% vs. 80%, respectively), followed by the lymph nodes (58% vs. 53%, respectively) and bone (30% each arm); the majority of the patients had multiple (2 or more) metastatic sites at baseline (80% vs. 77%, respectively).

There was a statistically significant advantage for SUTENT over IFN-α in the endpoint of PFS (see Table 8 and Figure 2). In the pre-specified stratification factors of LDH (>1.5 ULN vs. ≤1.5 ULN), ECOG performance status (0 vs. 1), and prior nephrectomy (yes vs. no), the hazard ratio favored SUTENT over IFN-α. The ORR was higher in the SUTENT arm (see Table 8).

**Table 7. Treatment-Naive RCC Efficacy Results (interim analysis)**

<table>
<thead>
<tr>
<th>Efficacy Parameter</th>
<th>SUTENT (n=375)</th>
<th>IFN-α (n=375)</th>
<th>P-value (log-rank test)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression-Free</td>
<td>24.1 (23.0, 32.3)</td>
<td>22.5 (16.4, 24.0)</td>
<td>&lt;0.00001⁵</td>
<td>0.320, 0.539</td>
</tr>
<tr>
<td>Survivability (%)</td>
<td>8.5 (3.7, 11.1)</td>
<td>8.0 (0.006)</td>
<td>0.230, 0.47</td>
<td></td>
</tr>
</tbody>
</table>

**Table 8. Treatment-Naive RCC Efficacy Results (interim analysis)**

<table>
<thead>
<tr>
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<td></td>
</tr>
</tbody>
</table>

**Figure 1. Kaplan-Meier Curve of TTP in GIST Study A (Intent-to-Treat Population)**

The Kaplan-Meier Curve of PFS in Treatment-Naive RCC Study (Intent-to-Treat Population)
The use of single-agent SUTENT in the treatment of cytokine-refractory RCC was investigated in two single-arm, multi-center studies. All patients enrolled into these studies experienced failure of prior cytokine-based therapy. In Study 1, failure of prior cytokine therapy was based on radiographic evidence of disease progression defined by RECIST or World Health Organization (WHO) criteria during or within 9 months of completion of a cytokine therapy treatment (IFN-α, interleukin-2, or IFN-α plus interleukin-2; patients who were treated with IFN-α alone must have received treatment for at least 28 days). In Study 2, failure of prior cytokine therapy was defined as disease progression or unacceptably treatment-related toxicity. The endpoint for both studies was ORR. Duration of Response (DR) was also evaluated.

One hundred six patients (106) were enrolled into Study 1, and 63 patients were enrolled into Study 2. Patients received 50 mg SUTENT on Schedule 4/2. Therapy was continued until the patients met withdrawal criteria or had progressive disease. The baseline age, gender, race and ECOG performance statuses of the patients were comparable between Studies 1 and 2. Approximately 86-94% of patients in the two studies were White. Men comprised 65% of the pooled population. The median age was 57 years and ranged from 24 to 87 years in the studies. All patients had an ECOG performance status <2 at the screening visit.

The baseline malignancy and prior treatment history of the patients were comparable between Studies 1 and 2. Across the two studies, 85% of the pooled population of patients had at least some component of clear-cell histology. All patients in Study 1 were required to have a histological clear-cell component. Most patients enrolled in the studies (97% of the pooled population) had undergone nephrectomy; prior nephrectomy was required for patients enrolled in Study 1. All patients had received one previous cytokine regimen.

Metastatic disease had been documented at the time of study entry included metastases in 81% of patients. Liver metastases were more common in Study 1 (27% vs. 16% in Study 2) and bone metastases were more common in Study 2 (51% vs. 25% in Study 1); 52% of patients in the pooled population had at least 3 metastatic sites. Patients with known brain metastases or cases of brain disease progression from both studies were excluded from this analysis.

The ORR and DR data from Studies 1 and 2 are provided in Table 9. There were 36 PRs in Study 1 as assessed by a core radiology laboratory for an ORR of 34.0% (95% CI 25.0, 43.8). There were 23 PRs in Study 2 as assessed by the investigators for an ORR of 36.5% (95% CI 24.8, 49.6). The majority (>80%) of objective disease responses were observed during the first four cycles; the latest reported response was observed in Cycle 10. DR data from Study 1 is premature as only 9 of 36 patients (25%) responding to treatment had experienced disease progression or died at the time of the data cutoff.

**Table 9. Cytokine-Refractory RCC Efficacy Results**

<table>
<thead>
<tr>
<th>Efficacy Parameter</th>
<th>Study 1 (N=106)</th>
<th>Study 2 (N=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective Response Rate</td>
<td><strong>34.0</strong> a</td>
<td><strong>36.5</strong> b</td>
</tr>
<tr>
<td>Duration of Response</td>
<td>(25.0, 43.8)</td>
<td>(24.7, 49.6)</td>
</tr>
<tr>
<td>Median, weeks (95% CI)</td>
<td>42.0, <strong>45.6</strong></td>
<td>34.3, 70.1</td>
</tr>
</tbody>
</table>

14.3 Pancreatic Neuroendocrine Tumors

The Phase 3 study was a multi-center, international, randomized, double-blind placebo-controlled study to compare the efficacy and safety of SUTENT (50 mg) with placebo in patients with unresectable pNET patients who had received a prior treatment with a somatostatin analogue or an SSRI. Patients were randomized to receive 37.5 mg SUTENT or placebo (N=85) once daily without a scheduled off-treatment period. The primary objective was to compare the percentage of patients receiving SUTENT versus patients receiving placebo. Other endpoints included Overall Survival (OS), Objective Response Rate (ORR), and safety. Use of somatostatin analogs was allowed in the study.

Demographics were comparable between the SUTENT and placebo groups. Additionally, 49% of SUTENT patients had non-functioning tumors vs 52% of placebo patients, and 92% patients in both arms had liver metastases. A total of 66% of SUTENT patients received prior systemic therapy compared with 72% of placebo patients and 35% of SUTENT patients had received somatostatin analogs compared with 38% of placebo patients. Patients were treated until disease progression or withdrawal from the study. Upon disease progression, or study closure, patients were offered access to SUTENT in a separate extension study.

As recommended by the Independent Data Monitoring Committee, the study was terminated prematurely prior to the pre-specified interim analysis. This may have led to an overestimate of the magnitude of PFS effect. A clinically significant improvement for SUTENT over placebo in PFS was seen by both investigator and independent assessment. A hazard ratio favoring SUTENT was observed in all subgroups of baseline characteristics evaluated. OS data were not mature at the time of the analysis. There were 9 deaths in the SUTENT arm and 21 deaths in the placebo group. The statistical significance of the difference in ORR favoring SUTENT over placebo was observed. Efficacy results are summarized in Table 10 and the Kaplan-Meier curve for PFS is in Figure 3.

**Table 10. pNET Efficacy Results from the Phase 3 Study**

<table>
<thead>
<tr>
<th>Efficacy Parameter</th>
<th>SUTENT (n=86)</th>
<th>Placebo (n=85)</th>
<th>P-value</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression-Free Survival [median, months (95% CI)]</td>
<td><strong>10.2</strong> (7.4, 16.9)</td>
<td>3.4 (3.4, 6.0)</td>
<td>0.000146*</td>
<td>0.427 (0.271, 0.673)</td>
</tr>
<tr>
<td>Objective Response Rate [% (95% CI)]</td>
<td>9.3 (3.2, 15.4)</td>
<td>0</td>
<td>0.0066*</td>
<td>NA</td>
</tr>
</tbody>
</table>

**16 HOW SUPPLIED/STORAGE AND HANDLING**

12.5 mg Capsules

Hard gelatin capsule with orange cap and orange body, printed with white ink “Pfizer” on the cap, “STN 12.5 mg” on the body, available in:

- Bottles of 28: NDC 0608-0550-38
- 5 mg Capsules

Hard gelatin capsule with orange cap and orange body, printed with white ink “Pfizer” on the cap, “STN 5 mg” on the body, available in:

- Bottles of 28: NDC 0608-0770-38
- 2.5 mg Capsules

Hard gelatin capsule with yellow cap and yellow body, printed with black ink “Pfizer” on the cap, “STN 2.5 mg” on the body, available in:

- Bottles of 28: NDC 0608-0830-38

**17 PATIENT COUNSELING INFORMATION**

Advise the patient to read the FDA-Approved Patient Labeling (Medication Guide).

17.1 Gastrointestinal Disorders

Gastrointestinal disorders such as diarrhea, nausea, stomatitis, dyspnea, and vomiting were the most commonly reported gastrointestinal events occurring in patients who received SUTENT. Supportive care for gastrointestinal adverse events requiring treatment may include anti-emetic or anti-diarrheal medication.

17.2 Skin Effects

Skin discoloration possibly due to the drug color (yellow) occurred in approximately one third of patients. Patients should be advised that depigmentation of the hair or skin may occur during treatment with SUTENT. Other possible dermatologic effects may include dryness, thickness or cracking of skin, blister or rash on the palms of the hands and soles of the feet. Severe dermatologic toxicities including Stevens-Johnson Syndrome and Toxic Epiderm al N ecrolysis have been reported. Patients should be advised to immediately inform their healthcare provider if severe dermatologic reactions occur.

17.3 Other Common Events

Other commonly reported adverse reactions included fatigue, high blood pressure, bleeding, swelling, mouth pain/irritation and taste disturbance.

17.4 Osteonecrosis of the Jaw

Prior to treatment with SUTENT, a dental examination and appropriate preventive dentistry should be considered. In patients being treated with SUTENT who have previously received or are receiving bisphosphonates, invasive dental procedures should be avoided, if possible.

17.5 Hypoglycemia

Patients should be advised of the signs, symptoms, and risks associated with hypoglycemia that may occur during treatment with SUTENT. Hypoglycemia may be more severe in patients with diabetes taking anti-diabetic medications. Severe hypoglycemia, including loss of consciousness or requiring hospitalization has been reported. Patients should be advised to immediately inform their healthcare provider if severe signs or symptoms of hypoglycemia occur.

17.6 Thrombotic Microangiopathy

Thrombotic microangiopathy related to renal insufficiency and neurologic abnormalities was observed in patients who received SUTENT as monotherapy or in combination with bevacizumab. Patients should be advised that signs and symptoms of thrombotic microangiopathy may occur during treatment with SUTENT. Patients should be advised to immediately inform their healthcare provider if signs and symptoms of thrombotic microangiopathy occur.

17.7 Proteinuria

Proteinuria and nephrotic syndrome has been reported. Patients should be advised that urinalysis will be performed prior to starting as well as during treatment with SUTENT. In cases with impact to renal function, treatment with SUTENT may be interrupted or discontinued.

17.8 Concomitant Medications

Patients should be advised to inform their healthcare providers of all concomitant medications, including over-the-counter medications and dietary supplements [see Drug Interactions (7)].

This product’s label may have been updated. For full prescribing information, please visit www.pfizer.com.
SUTENT (su TENT)
(sunitinib malate)
capsules

Read the Medication Guide that comes with SUTENT before you start taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your healthcare provider about your medical condition or treatment. If you have any questions about SUTENT, ask your healthcare provider or pharmacist.

What is the most important information I should know about SUTENT?

SUTENT can cause serious liver problems, including death.

• Tell your healthcare provider right away if you develop any of the following signs and symptoms of liver problems during treatment with SUTENT:
  • itching,
  • yellow eyes or skin,
  • dark urine, and
  • pain or discomfort in the right upper stomach area.

• Your healthcare provider should do blood tests to check your liver function before you start taking SUTENT and during treatment.

What is SUTENT?

SUTENT is a prescription medicine used to treat people with:

• a rare cancer of the stomach, bowel, or esophagus called GIST (gastrointestinal stromal tumor) and when:
  • the medicine Gleevec® (imatinib mesylate) did not stop the cancer from growing, or
  • you cannot take Gleevec®.

• advanced kidney cancer (advanced renal cell carcinoma or RCC).

• a type of pancreatic cancer known as pancreatic neuroendocrine tumors (pN ET), that has progressed and cannot be treated with surgery.

It is not known if SUTENT is safe and effective in children.

What should I tell my healthcare provider before taking SUTENT?

Before taking SUTENT tell your healthcare provider if you:

• have any heart problems
• 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
• 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
• have any other medical conditions
• are pregnant, could be pregnant or plan to become pregnant. SUTENT may harm an unborn baby. You should not become pregnant while taking SUTENT. Tell your healthcare provider right away if you become pregnant while taking SUTENT.
• are breastfeeding or plan to breastfeed. You and your healthcare provider should decide if you will take SUTENT or breastfeed. You should not do both. Tell all of your healthcare providers and dentists that you are taking SUTENT. They should talk to the healthcare provider who prescribed SUTENT for you, before you have any surgery, or medical or dental procedure.

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

You may have an increased risk of severe jaw bone problems (osteonecrosis) if you take SUTENT and a bisphosphonate medicine. Especially tell your healthcare provider if you are taking or have taken Actonel, Arebia, Boniva, Didronel, Fosamax, Reclast, Skelid or Zometa.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine. Talk with your healthcare provider before starting any new medicines.

How should I take SUTENT?

• Take SUTENT exactly the way your healthcare provider tells you.
• Take SUTENT 1 time each day with or without food.
• If you take SUTENT 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 SUTENT for pN ET, take it one time each day until your healthcare provider tells you to stop.
• Do not open the SUTENT capsules.
• Do not drink grapefruit juice or eat grapefruit during your treatment with SUTENT. They may cause you to have too much SUTENT in your body.
• Your healthcare provider may do blood tests before each cycle of treatment.
• If you miss a dose, take it as soon as you remember. Do not take it if it is close to your next dose. Just take the next dose at your regular time. Do not take more than 1 dose of SUTENT at a time. Tell your healthcare provider about any missed dose.
• Call your healthcare provider right away, if you take too much SUTENT.

What are possible side effects of SUTENT?

SUTENT may cause serious side effects including:

• See “What is the most important information I should know about SUTENT?”

• Heart problems. Heart problems may include heart failure, heart attack and heart muscle problems (cardiomyopathy) that can lead to death. Tell your healthcare provider if you feel very tired, are short of breath, or have swollen feet and ankles.

• Abnormal heart rhythm changes. Your healthcare provider may do electrocardiograms and blood tests to watch for these problems during your treatment with SUTENT. Tell your healthcare provider if you feel dizzy, faint, or have abnormal heartbeats while taking SUTENT.

• High blood pressure. Your healthcare provider may check your blood pressure during treatment with SUTENT. Your healthcare provider may prescribe medicine for you to treat high blood pressure, if needed.

• Bleeding sometimes leading to death. Tell your healthcare provider right away if you have any of these symptoms or a serious bleeding problem during treatment with SUTENT.
  • painful, swollen stomach (abdomen)
  • vomiting blood
  • black, sticky stools
  • bloody urine
  • headache or change in your mental status

Your healthcare provider can tell you other symptoms to watch for.

• Jaw-bone problems (osteonecrosis) Severe jaw bone problems may happen when you take SUTENT. Your healthcare provider should examine your mouth before you start SUTENT. Your healthcare provider may tell you to see your dentist before you start SUTENT.

• Tumor lysis syndrome (TLS). TLS is caused by the fast breakdown of cancer cells and may lead to death. TLS may cause you to have nausea, shortness of breath, irregular heartbeat, clouding of urine and tiredness associated with abnormal laboratory test results (high potassium, uric acid and phosphorous levels and low calcium levels in the blood) that can lead to changes in kidney function and acute kidney failure. Your healthcare provider may do blood tests to check you for TLS.

MEDICATION GUIDE
• Common side effects of SUTENT include:
  - rash or other skin changes, including drier, thicker, or cracking skin
  - The medicine in SUTENT is yellow, and it may make your skin look yellow.
  - Your skin and hair may get lighter in color.
  - tiredness
  - weakness
  - fever
  - gastrointestinal symptoms, including diarrhea, nausea, vomiting, mouth sores, upset stomach, abdominal pain, and constipation. Talk with your healthcare provider about ways to handle these problems.
  - rash or other skin changes, including drier, thicker, or cracking skin
  - loss of appetite
  - pain or swelling in your arms or legs
  - cough
  - shortness of breath
  - bleeding, such as nosebleeds or bleeding from cuts

Call your healthcare provider if you have any swelling or bleeding during treatment with SUTENT.

These are not all the possible side effects of SUTENT. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How do I store SUTENT?
• Store SUTENT at room temperature, between 59°F to 86°F (15°C to 30°C).

Keep SUTENT and all medicines out of the reach of children.

General information about SUTENT
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use SUTENT for a condition for which it was not prescribed. Do not give SUTENT to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide gives the most important information about SUTENT. For more information about SUTENT, talk with your healthcare provider or pharmacist. You can ask your healthcare provider or pharmacist for information about SUTENT that is written for health professionals.

For more information go to www.SUTENT.com or call 1-877-5-SUTENT.

What are the ingredients in SUTENT?
Active ingredient: sunitinib malate
Inactive ingredients: mannitol, croscarmellose sodium, povidone (K-25), magnesium stearate
Orange gelatin capsule shell: titanium dioxide, red iron oxide
Caramel gelatin capsule shell: titanium dioxide, red iron oxide, yellow iron oxide, black iron oxide
White printing ink: shellac, propylene glycol, sodium hydroxide, povidone, titanium dioxide

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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