

SUTENT® (sunitinib malate) capsules
Fact Sheet

PRODUCT DESCRIPTION	SUTENT® (sunitinib malate) 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. ¹
INDICATIONS	SUTENT is an oral multi-kinase inhibitor approved for the treatment of advanced renal cell carcinoma (RCC), gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate and progressive, well-differentiated pancreatic neuroendocrine tumors (pNET) in patients with unresectable locally advanced or metastatic disease. The recommended dose for SUTENT in GIST and RCC is 50 mg taken once daily for 4 weeks followed by 2 weeks off treatment. The recommended dose for SUTENT in pNET is 37.5 mg taken once daily continuously without a scheduled off-treatment period. ¹
MECHANISM OF ACTION	SUTENT works by blocking multiple molecular targets implicated in the growth, proliferation and spread of cancer. Two important SUTENT targets, vascular endothelial growth factor receptor (VEGFR) and platelet-derived growth factor receptor (PDGFR), are expressed by many types of solid tumors and are thought to play a crucial role in angiogenesis, the process by which tumors acquire blood vessels, oxygen and nutrients needed for growth. SUTENT also inhibits other targets important to tumor growth, including KIT, FLT3 and RET. ^{1,2}
KIDNEY CANCER CLINICAL STUDIES	<p>In a Phase 3, randomized, multi-center trial comparing SUTENT with IFN-α as first-line therapy in 750 patients with treatment-naïve advanced kidney cancer:³</p> <ul style="list-style-type: none"> • SUTENT more than doubled median progression-free survival (PFS).³ <ul style="list-style-type: none"> ○ 11 months vs. 5 months with IFN-α (95 percent CI: 9.8, 11.7 and 3.8, 5.5, respectively [P<.000001]) ○ 58 percent reduced risk of progression or death (hazard ratio=0.42) (95 percent CI: 0.32 to 0.54 [P<.001]) • SUTENT demonstrated a 5-fold higher objective response rate (ORR) vs. IFN-α <ul style="list-style-type: none"> ○ 28 percent vs. 5 percent with IFN-α (95 percent CI: 23.0, 32.3 and 3.3, 8.1, respectively [P<.001]) in the first analysis (November 2005)² ○ 39 percent vs. 8 percent with IFN-α (95 percent CI: 34.0, 44.3 and 5.7, 11.8, respectively [P<.000001]) in the second analysis (June 2007)⁴ • Median overall survival (OS) for SUTENT was 114.6 weeks compared to 94.9 weeks for patients in the IFN-α arm (95 percent CI: 23.0, 32.9 and 17.9, 26.9, respectively [P=0.051] [log-rank])⁴ <p>SUTENT was also studied in two Phase 2 open-label, single-arm trials in 169 patients with advanced kidney cancer who had experienced failure of prior cytokine-based therapy.²</p> <ul style="list-style-type: none"> • An ORR of 34 percent (95% CI 25, 43.8) and 36.5 percent (95 percent CI 24.7, 49.6) was seen in studies 1 and 2 respectively.²
GIST CLINICAL STUDY	<p>SUTENT was studied in a large, Phase 3 clinical trial involving 312 patients with GIST who had disease progression during prior imatinib mesylate treatment or who were intolerant of imatinib.²</p> <ul style="list-style-type: none"> • Time to tumor progression (TTP) was significantly prolonged from 27.3 weeks in the SUTENT treatment group compared with 6.4 weeks in the placebo group (95 percent CI: 16.0, 32.1 and 4.4, 10.0 respectively [P<.0001]).² • SUTENT significantly improved PFS by delaying tumor progression for 24.1 weeks vs. 6.0 weeks in the placebo group (95 percent CI: 11.1, 28.3 and 4.4, 9.9 respectively [P<.0001]).² • The median OS was 72.7 weeks for the SUTENT arm and 64.9 weeks for the placebo arm (HR=0.876; 95 percent CI: 0.679, 1.129). • Ninety-nine of 118 patients initially randomized to placebo crossed over to receive SUTENT in the open-label treatment phase. <p>SUTENT is the only agent approved for the second-line treatment of GIST following treatment with imatinib mesylate.⁵</p>

<p>PANCREATIC NET CLINICAL STUDY</p>	<p>In a Phase 3, multicenter, international, randomized, double-blind, placebo-controlled trial of 171 patients with unresectable pNET:</p> <ul style="list-style-type: none"> • SUTENT provided a clinically significant improvement in PFS, the primary endpoint, compared to placebo (FDA assessment of 10.2 versus 5.4 months, P=0.000146).¹ <ul style="list-style-type: none"> ○ Investigator-assessed data from the trial showed SUTENT more than doubled median PFS compared with placebo (11.4 vs. 5.5 months, P<0.0001), which was found to be consistent in a blinded, independent central review of scans from the study (12.6 vs. 5.8 months, P=0.000015).^{6,7} • Treatment with SUTENT yielded a statistically significant improvement in tumor response, with an ORR of 9.3 percent (95% CI: 3.2, 15.4, P=0.0066). No objective responses were observed with placebo.⁶ • In addition, while OS was not mature at the time of final analysis, nine deaths were observed in patients enrolled in the SUTENT arm versus 21 deaths in patients enrolled in the placebo arm.⁶ • In February 2009, the independent Data Monitoring Committee for the Phase 3 trial recommended that randomization to the study be halted early in the interest of patient safety and based on the very strong likelihood that the study would meet its primary endpoint if continued to completion. This may have led to an overestimate of the magnitude of PFS effect.
<p>SAFETY PROFILE</p>	<p>Important safety information:</p> <ul style="list-style-type: none"> • Hepatotoxicity has been observed in clinical trials and post-marketing experience. This hepatotoxicity may be severe, and deaths have been reported. 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. • Women of childbearing potential should be advised of the potential hazard to the fetus and to avoid becoming pregnant. • Given the potential for serious adverse reactions (ARs) in nursing infants, a decision should be made whether to discontinue nursing or SUTENT. • Cardiovascular events, including heart failure, myocardial disorders, and cardiomyopathy, some of which were fatal, have been reported. Monitor patients for signs and symptoms of congestive heart failure (CHF) and, in the presence of clinical manifestations, discontinuation is recommended. Patients who presented with cardiac events, pulmonary embolism, or cerebrovascular events within the previous 12 months were excluded from clinical studies. • SUTENT has been shown to prolong QT interval in a dose-dependent manner, which may lead to an increased risk for ventricular arrhythmias including torsades de pointes, which has been seen in <0.1% of patients. Monitoring with on-treatment electrocardiograms and electrolytes should be considered. • Hypertension may occur. Monitor blood pressure and treat as needed with standard antihypertensive therapy. In cases of severe hypertension, temporary suspension of SUTENT is recommended until hypertension is controlled. • There have been rare (<1%) nonfatal reports of subjects presenting with seizures and radiological evidence of reversible posterior leukoencephalopathy syndrome (RPLS). • Hemorrhagic events, including tumor-related hemorrhage such as pulmonary hemorrhage, have occurred. Some of these events were fatal. Perform serial complete blood counts (CBCs) and physical examinations. • Osteonecrosis of the jaw (ONJ) has been reported. Consider preventive dentistry prior to treatment with SUTENT. If possible, avoid invasive dental procedures, particularly in patients receiving bisphosphonates. • Cases of tumor lysis syndrome (TLS) have been reported primarily in patients with high tumor burden. Monitor these patients closely and treat as clinically indicated.

	<ul style="list-style-type: none"> • Thyroid dysfunction may occur. Monitor thyroid function in patients with signs and/or symptoms of hypothyroidism or hyperthyroidism and treat per standard medical practice. • Cases of impaired wound healing have been reported. Temporary interruption of therapy with SUTENT is recommended in patients undergoing major surgical procedures. • Adrenal hemorrhage was observed in animal studies. Monitor adrenal function in case of stress such as surgery, trauma, or severe infection. • 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. • Dose adjustments are recommended when administered with CYP3A4 inhibitors or inducers. • The most common ARs occurring in $\geq 20\%$ of patients receiving SUTENT for treatment-naïve metastatic RCC (all grades, vs IFN-α) were diarrhea (66% vs 21%), fatigue (62% vs 56%), nausea (58% vs 41%), anorexia (48% vs 42%), altered taste (47% vs 15%), mucositis/stomatitis (47% vs 5%), pain in extremity/limb discomfort (40% vs 30%), vomiting (39% vs 17%), bleeding, all sites (37% vs 10%), hypertension (34% vs 4%), dyspepsia (34% vs 4%), arthralgia (30% vs 19%), abdominal pain (30% vs 12%), rash (29% vs 11%), hand-foot syndrome (29% vs 1%), back pain (28% vs 14%), cough (27% vs 14%), asthenia (26% vs 22%), dyspnea (26% vs 20%), skin discoloration/yellow skin (25% vs 0%), peripheral edema (24% vs 5%), headache (23% vs 19%), constipation (23% vs 14%), dry skin (23% vs 7%), fever (22% vs 37%), and hair color changes (20% vs <1%). The most common grade 3/4 ARs (occurring in $\geq 5\%$ of patients with RCC receiving SUTENT vs IFN-α) were fatigue (15% vs 15%), hypertension (13% vs <1%), asthenia (11% vs 6%), diarrhea (10% vs <1%), hand-foot syndrome (8% vs 0%), dyspnea (6% vs 4%), nausea (6% vs 2%), back pain (5% vs 2%), pain in extremity/limb discomfort (5% vs 2%), vomiting (5% vs 1%), and abdominal pain (5% vs 1%). • The most common grade 3/4 lab abnormalities (occurring in $\geq 5\%$ of patients with RCC receiving SUTENT vs IFN-α) included lymphocytes (18% vs 26%), lipase (18% vs 8%), neutrophils (17% vs 9%), uric acid (14% vs 8%), platelets (9% vs 1%), hemoglobin (8% vs 5%), sodium decreased (8% vs 4%), leukocytes (8% vs 2%), glucose increased (6% vs 6%), phosphorus (6% vs 6%), and amylase (6% vs 3%). • The most common ARs occurring in $\geq 20\%$ of patients with GIST and more commonly with SUTENT than placebo (all grades, vs placebo) were diarrhea (40% vs 27%), anorexia (33% vs 29%), skin discoloration (30% vs 23%), mucositis/stomatitis (29% vs 18%), asthenia (22% vs 11%), altered taste (21% vs 12%), and constipation (20% vs 14%). The most common grade 3/4 ARs (occurring in $\geq 4\%$ of patients with GIST receiving SUTENT vs placebo) were asthenia (5% vs 3%), hand-foot syndrome (4% vs 3%), diarrhea (4% vs 0%), and hypertension (4% vs 0%). • The most common grade 3/4 lab abnormalities (occurring in $\geq 5\%$ of patients with GIST receiving SUTENT vs placebo) included lipase (10% vs 7%), neutrophils (10% vs 0%), amylase (5% vs 3%), and platelets (5% vs 0%). • The most common ARs occurring in $\geq 20\%$ of patients with advanced pNET and more commonly with SUTENT than placebo (all grades, vs placebo) were diarrhea (59% vs 39%), stomatitis/oral syndromes (48% vs 18%), nausea (45% vs 29%), abdominal pain (39% vs 34%), vomiting (34% vs 31%), asthenia (34% vs 27%), fatigue (33% vs 27%), hair color changes (29% vs 1%), hypertension (27% vs 5%), hand-foot syndrome (23% vs 2%), bleeding events (22% vs 10%), epistaxis (21% vs 5%), and dysgeusia (21% vs 5%). The most commonly reported grade 3/4 ARs (occurring in $\geq 5\%$ of patients with advanced pNET receiving SUTENT vs placebo) were hypertension (10% vs 1%), hand-foot syndrome (6% vs 0%), stomatitis/oral syndromes (6% vs 0%), abdominal pain (5% vs 10%), fatigue (5% vs 9%), asthenia (5% vs 4%), and diarrhea (5% vs 2%). • The most common grade 3/4 lab abnormalities (occurring in $\geq 5\%$ of patients with advanced pNET receiving SUTENT vs placebo) included decreased neutrophils (16% vs 0%), increased glucose (12% vs 18%), increased alkaline phosphatase
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	<p>(10% vs 11%), decreased phosphorus (7% vs 5%), decreased lymphocytes (7% vs 4%), increased creatinine (5% vs 5%), increased lipase (5% vs 4%), increased AST (5% vs 3%), and decreased platelets (5% vs 0%).</p> <p>Please see full prescribing information enclosed. It is also available at www.sutent.com.</p>
PATIENT ACCESS TO SUTENT	Through Pfizer's FirstRESOURCE™ patient assistance program, SUTENT is available for eligible, uninsured and underinsured patients in the US who meet program eligibility criteria.
PATIENT SUPPORT	Pfizer offers several programs to help patients throughout their treatment journey. SUTENT In Touch is a free, personalized program for US patients taking SUTENT and their caregivers. The program connects patients to relevant tips and tools to support them through their treatment with SUTENT. It also includes a partnership with an Oncology Certified Nurse. Patients can enroll by simply calling 1-877-5-SUTENT (1-877-578-8368) or visiting SUTENT.com.
CONTACT & ADDITIONAL INFORMATION	<p>If you are interested in speaking with a Pfizer Oncology representative, please contact Jenifer Antonacci at Jenifer.Antonacci@pfizer.com or (610) 427-0369.</p> <p>For information about SUTENT clinical trials currently enrolling in their area, patients and their physicians are encouraged to call the Pfizer Oncology clinical trial information line at 1-877-416-6248 or visit www.pfizerclinicaltrials.com.</p>

¹ SUTENT [Package Insert]. New York, NY: Pfizer, Inc. 2012.

² Potapova O, Laird AD, Nannin MA, et al. Contribution of individual targets to the antitumor efficacy of the multitargeted receptor tyrosine kinase inhibitor SU11248. *Mol Cancer Ther.* 2006;5:1280-1289.

³ Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl J Med.* 2007;356:115-124.

⁴ Figlin RA, Hutson TE, Tomczak P, et al. Overall survival with sunitinib versus interferon- α (IFN- α) as first-line treatment of metastatic renal cell carcinoma (mRCC). Slide deck presented at ASCO 2008. Oral Presentation. May 31, 2008: 4:00-4:15 p.m. 44th Annual American Society of Clinical Oncology Meeting. Chicago, IL. May 30-June 3, 2008.

⁵ National Comprehensive Cancer Network Task Force. NCCN Task Force Report: Optimal management of patients with gastrointestinal stromal tumor (GIST) – Update of the NCCN Clinical Practice Guidelines. *J NCCN* 2007; 5(Supp 2)

⁶ Raymond E, et al. Sunitinib Malate for the Treatment of Pancreatic Neuroendocrine Tumors. *N Engl J Med* 2011; 334: 501-13.

⁷ ASCO GI Abstract #249. Evaluation of Progression Free Survival by Blinded Independent Central Review in Patients With Progressive, Well-Differentiated Pancreatic Neuroendocrine Tumors Treated With Sunitinib or Placebo. E. Van Cutsem - Presenter. 8th Annual Gastrointestinal (GI) Cancers Symposium, San Francisco, CA, January 20-22, 2011.