Sunitinib malate capsules — Worldwide 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 AND DOSING	Therapy with sunitinib should be initiated by a physician experienced in the administration of anti-cancer agents.[1] **Metastatic Renal Cell Carcinoma (mRCC)**[1] Sunitinib is indicated for the treatment of advanced/metastatic renal cell carcinoma (mRCC). **Gastrointestinal Stromal Tumor (GIST)**[1] Sunitinib is indicated for the treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumor (GIST) after failure of imatinib mesilate treatment due to resistance or intolerance. For mRCC and GIST, the recommended dose of sunitinib is 50 mg once daily, taken orally for 4 consecutive weeks, followed by a 2-week rest period (schedule 4/2) to comprise a complete cycle of 6 weeks.[1] Dose modifications in 12.5-mg steps may be applied based on individual safety and tolerability. Daily dose should not exceed 75 mg nor be decreased below 25 mg.[1] **Pancreatic neuroendocrine tumours (pNET)**[1] Sunitinib is indicated for the treatment of unresectable or metastatic, well-differentiated pancreatic neuroendocrine tumors with disease progression in adults. Experience with sunitinib as first-line treatment is limited. For pNET, the recommended dose of sunitinib is 37.5 mg taken orally once daily without a scheduled rest period.[1] Dose modification in 12.5 mg steps may be applied based on individual safety and tolerability. The maximum dose administered in the Phase 3 pNET study was 50 mg daily.[1]
MECHANISM OF ACTION	Sunitinib works by blocking multiple molecular targets implicated in the growth, proliferation and spread of cancer. Two important sunitinib 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. Sunitinib also inhibits other targets important to tumor growth, including KIT, FLT3 and RET.[1,2]

KIDNEY CANCER CLINICAL STUDIES	In a Phase 3, randomized, multi-center trial comparing sunitinib with IFN-α as first-line therapy in 750 patients with treatment-naïve advanced kidney cancer:[3]
	
	• Suntinib more than doubled median progression-free survival (PFS).[3]
	  o 11 months vs. 5 months with IFN-α (95 percent CI: 9.8, 11.7 and 3.8, 5.5, respectively [P<.000001])
	  o 58 percent reduced risk of progression or death (hazard ratio=0.42) (95 percent CI: 0.32 to 0.54 [P<.001])
	• Suntinib demonstrated a 5-fold higher objective response rate (ORR) vs. IFN-*α*
	  o 39 percent vs. 8 percent with IFN-*α* (95 percent CI: 34.0, 44.3 and 5.7, 11.8, respectively [P<.000001]) (June 2007)[4]
	• Median overall survival (OS) for sunitinib 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])[1]
	
	Suntinib 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.[1]
	• An ORR of 35.8 percent (95% CI: 26.8, 47.5) and 36.5 percent (95 percent CI:

	24.7, 49.6) was seen in studies 1 and 2 respectively.[1] The most common treatment-related adverse events include: fatigue/asthenia, diarrhea, nausea, taste disturbance, decreased appetite, stomatitis/aphthous stomatitis, dyspepsia, vomiting, hypertension and yellow discoloration/skin discoloration/pigment disorder.[1] The most common treatment-related serious adverse events include: fatigue/asthenia, hypertension, neutropenia, palmar-plantar erythrodysaesthesia syndrome, thrombocytopenia, diarrhea, anemia, leucopenia, nausea, and vomiting.[1]
GIST CLINICAL STUDY	Suntinib was studied in a large, Phase 3 clinical trial involving 312 patients with GIST who had disease progression during prior imatinib mesilate treatment or who were intolerant of imatinib.[1] • Time to tumor progression (TTP) was significantly prolonged from 27.3 weeks in the sunitinib 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]). • Suntinib 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]). • The median OS was 72.7 weeks for the sunitinib arm and 64.9 weeks for the placebo arm (HR=0.876; 95 percent CI: 0.679, 1.129). • A total of 255 patients received sunitinib in the open-label treatment phase of the study, including 99 patients who were initially treated with placebo. Suntinib is the only agent approved for the second-line treatment of GIST following treatment with imatinib mesilate.[5] The most common treatment-related adverse events include: fatigue/asthenia, diarrhea, nausea, yellow skin/skin discoloration, decreased appetite, palmar-plantar erythrodysaesthesia syndrome, taste disturbance, hypertension, vomiting and stomatitis.[1] The most common treatment-related serious adverse events include: fatigue/asthenia, neutropenia, hypertension, palmar-plantar erythrodysaesthesia syndrome, anemia, thrombocytopenia, diarrhea, white blood cell count decreased, abdominal pain/distension and nausea.[1]
PANCREATIC NET CLINICAL STUDY	In a Phase 3, multicenter, international, randomized, double-blind, placebo-controlled trial of 171 patients with unresectable pNET: • Suntinib provided a clinically significant improvement in PFS, the primary endpoint, compared to placebo.[1] o Investigator-assessed data from the trial showed sunitinib more than doubled median PFS compared with placebo (11.4 vs. 5.5 months, P<0.0001),[1, 6] 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).[7] • Treatment with sunitinib 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 suntinib 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. The most common treatment-related adverse events include: fatigue/asthenia, diarrhea, nausea, neutropenia, hair color changes, vomiting, hypertension, palmar-plantar erythrodysaesthesia syndrome, stomatitis, and anorexia.[1]

	The most common treatment-related serious adverse events include: hypertension, neutropenia, palmar-plantar erythrodysaesthesia syndrome, fatigue/asthenia, leucopenia, diarrhea, and stomatitis.[1]
PATIENT ACCESS TO SUTENT	For patients in the U.S., Pfizer's First Resource program offers patient assistance to eligible patients and reimbursement support services, including appeals process and alternate funding information, for Pfizer Oncology medicines, including Sutent.
IMPORTANT SAFETY INFORMATION ABOUT SUTENT[1]	**Important SUTENT® (sunitinib malate) Safety Information[1]** Serious adverse reactions associated with sunitinib are renal failure, heart failure, pulmonary embolism, intestinal perforation, and haemorrhages (e.g. respiratory, gastrointestinal, tumour haemorrhages). The most common (≥20%) adverse events (AEs) in patients receiving SUTENT were decreased appetite, taste disturbance, hypertension, fatigue, gastrointestinal disorders, skin discoloration, and hand-foot syndrome. Fatal events, other than those listed, included multi-system organ failure, disseminated intravascular coagulation, peritoneal hemorrhage, rhabdomyolysis, cerebrovascular accident, dehydration, adrenal insufficiency, renal failure, respiratory failure, pleural effusion, pneumothorax, shock, and sudden death. For more information on SUTENT (sunitinib malate), including full prescribing information, please visit www.pfizer.com
CONTACT & ADDITIONAL INFORMATION	If you are interested in speaking with a Pfizer Oncology representative, please contact Chris Loder at Christoper.Loder@pfizer.com or (347) 453-8199. For information about sunitinib clinical trials currently enrolling in their area, patients and their physicians are encouraged to call the sunitinib clinical trial information line at 1-877-416-6248 (in the U.S.) or 001-646-277-4066 (outside the U.S.) or visit www.pfizercancertrials.com.

[1] SUTENT Summary of Product Characteristics: Sutent Pfizer Limited, Kent UK, February 2012. Available: http://emc.medicines.org.uk/medicine/18531/SPC/SUTENT+12.5mg%2c+25mg%2c+37.5mg+and+50mg+Hard+Capsules/ Accessed Aug. 18, 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-alpha (IFN-α) as first-line treatment of metastatic renal cell carcinoma (mRCC). Oral Presentation. May 31, 2008: 4:00-4:15 pm. 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.