Sunitinib (Sutent®)

**What it does and how it is used**

- **Sunitinib** is a tyrosine kinase inhibitor indicated for the treatment of advanced (metastatic) renal cell carcinoma (RCC), gastrointestinal stromal tumors (GIST) where there is evidence of disease progression or intolerance with imatinib mesylate, and for advanced pancreatic neuroendocrine tumors. Sunitinib is also effective for the treatment of metastatic thyroid carcinomas.

- Receptor tyrosine kinases are a group of enzymes that promote proliferation, metastasis, and angiogenesis (the formation of new blood vessels) in cancer cells and tissues. By inhibiting these actions, Sutent prevents the growth of tumor cells.

- **Renal cell carcinoma (RCC)** is the most common form of kidney cancer representing approximately 90% of cases. Approximately 30% of patients present with metastatic disease, 25% with locally advanced disease and 45% with localized disease.

- Treatment of RCC is dependent on tumor type and disease stage. Surgical resection is currently the only effective treatment for localized RCC. Primary treatment involves removal of the entire kidney, adrenal gland and some surrounding fatty tissue and nearby lymph nodes. Smaller renal cell tumors are treated by performing a partial nephrectomy. Radiation therapy may be used to treat RCC either prior to or following surgical procedures. It may be used as the main form of treatment for those patients too fragile to undergo surgery, although it is not routinely recommended due to poor response rates. Adjuvant chemotherapy after removal of the tumor does not reduce the likelihood of relapse. Treatment of metastatic RCC involves the use of immunotherapy with interleukin-2 and interferon-alpha, alone or in combination with chemotherapy. Targeted therapy using tyrosine kinase inhibitors are used widely in first and second line treatments. There are currently five agents in addition to the sunitinib that are FDA approved to treat advanced metastatic RCC: sorafenib (nexavar), pazopanib (Votrient) and bevacizumab (Avastin), everolimus (Torisel) and temsirolimus (Afinitor).

- **Gastrointestinal stromal tumor (GIST)** is a soft tissue sarcoma of the GI tract. GIST occurs in only 1%-3% of all GI cancers, and affects approximately 5,000 patients per year in the US. Approximately 60%-70% occur in the stomach, 20%-30% in the small intestine, and the rest found in the large intestine, esophagus, rectum and anus.

- Treatment of choice for localized GIST is surgical resection. Surgery is also indicated for patients with recurrent or metastatic GIST. Radiation therapy is not very effective in the treatment of GIST; however, it may be used as palliative therapy for patients suffering from symptoms of pain. Standard chemotherapy is not effective in the treatment of GIST. The treatment of choice for GIST is imatinib mesylate (Gleevec®) which is a tyrosine kinase inhibitor.

- **Neuroendocrine tumors** are rare tumors arising from cells throughout the nervous and endocrine systems. Common sites include the pancreas; parathyroid, adrenal, and pituitary glands; calcitonin-producing cells of the thyroid (causing medullary thyroid carcinoma); and cells in the gut (causing carcinoid tumors).

- Neuroendocrine tumors can be benign (nonfunctional) or malignant (functional). Most neuroendocrine tumors are functionally active tumors that result in clinical symptoms due to the excessive production and release of hormones from the tumor cells.

- First line of therapy is complete resection of the tumor and all neoplastic tissue (for example, lymph nodes and any metastases to liver and other organs). In unresectable or metastatic disease, various systemic chemotherapy regimens are recommended. Other options include radiotherapy, embolization, ablative therapy, and cryotherapy. Patients taking sunitinib at a dose of 37.5 mg daily for advanced pancreatic neuroendocrine tumors who had progressed on prior therapies experienced a progression-free survival period of 11.4 months compared to patients taking placebo who progressed after 5.5 months.

- **Thyroid carcinoma** is uncommon. The lifetime risk of being diagnosed with thyroid carcinoma in the United States is less than 1%. Approximately 56,460 new cases of thyroid carcinoma will occur in 2012 in the United States. Thyroid cancer is commonly diagnosed at a younger age than most other adult cancers:80% of newly diagnosed thyroid cancer patients are under 65 years of age. The chance of being diagnosed with thyroid cancer has risen in recent years and is now more than twice what it was in 1990. Some of this is the result of the increased use of thyroid ultrasound, which can detect small thyroid nodules that might not otherwise have been found in the past. Still, at least part of the increase is from finding more large tumors as well.

- The treatment of choice for thyroid carcinoma is surgery when possible followed by radiiodine and thyroxine therapy in most patients. Traditional systemic cytotoxic chemotherapy (doxorubicin) has minimal efficacy in patients with metastatic disease. Although sunitinib is not FDA approved for metastatic thyroid carcinoma, metastatic thyroid carcinomas may be treated with small molecule kinase inhibitors (e.g., tyrosine kinase inhibitors). Patients taking sunitinib at a dose of 37.5 mg once daily for metastatic thyroid cancer refractory to iodine had an objective response rate of 31% (includes partial responses and complete response). In addition, 46% of patients had stable disease.

- The recommended dose of sunitinib for RCC and GIST is 50 mg once daily, on a schedule of 4 weeks on treatment followed by 2 weeks off. Dose increase or reduction of 12.5 mg is recommended based on individual safety and tolerability. A dose reduction of sunitinib to 37.5 mg daily should be considered if sunitinib is co-administered with a CYP3A4 inhibitor (drugs known to decrease the clearance of sunitinib). A dose increase to 87.5 mg daily should be considered if sunitinib is co-administered with a CYP3A4 inducer (drugs known to increase the clearance of sunitinib).
The recommended dose of sunitinib for neuroendocrine tumors is 37.5 mg taken orally once daily continuously without a scheduled off-treatment period. SUTENT may be taken with or without food.

- Sunitinib should not be used in combination with other kinase inhibitors such as sorafenib (nexavar), pazopanib (Votrient) and bevacizumab (Avastin).
- Sunitinib is currently being investigated in the treatment of various other forms of cancer including colorectal, breast and lung cancer.

### What it costs

<table>
<thead>
<tr>
<th>Dosing</th>
<th>AWP per capsule/dose</th>
<th>AWP per month</th>
<th>AWP per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 mg once daily</td>
<td>$410</td>
<td>$12,300</td>
<td>$106,600 (4 weeks on, 2 weeks off)</td>
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<tr>
<td>25 mg once daily</td>
<td>$218</td>
<td>$6,540</td>
<td></td>
</tr>
<tr>
<td>12.5 mg once daily</td>
<td>$109</td>
<td>$3,270</td>
<td></td>
</tr>
<tr>
<td>37.5 mg once daily (25 mg + 12.5 mg capsule)</td>
<td>$327</td>
<td>$9,810</td>
<td>$117,720</td>
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</tbody>
</table>

### Rationale for prior authorization

To reduce exposure to cost associated with the treatment of conditions and other cancers for which the effectiveness of sunitinib is not known.

### Benefit design

- Coverage is determined through prior authorization for every claim.
- To provide coverage for a quantity sufficient for treating the majority of patients with up to 50 mg per day.

### Prior authorization criteria

Coverage for Sutent is provided in accord with the following:

1. For the treatment of advanced renal cell carcinoma.
2. For the treatment of gastrointestinal stromal tumor where there is evidence of disease progression or intolerance with imatinib mesylate.
3. For the treatment of advanced neuroendocrine tumor in situations where patients have had inadequate response to octreotide and systemic chemotherapy, if indicated.
4. For the treatment of metastatic thyroid cancer

AND

5. Coverage is not provided for combination use of Sutent with other kinase inhibitors [e.g., sorafenib (Nexavar®), pazopanib (Votrient), or bevacizumab (Avastin)].

Coverage duration: Coverage is provided for 6 months and is renewable for additional 6 month intervals in the absence of disease progression.

Quantity duration limit:

Coverage is provided at a dose of up to 50 mg per day

Coverage for doses greater than 50 mg per day is provided for patients taking potent CYP 3A4 Inducers, e.g., rifampicin.

### References