09-J1000-51

Original Effective Date: 01/01/12

Reviewed: 01/08/20

Revised: 02/15/20

Subject: Sunitinib Malate (Sutent®) Capsules

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Sunitinib (Sutent®) is an oral multikinase inhibitor that acts by inhibiting tumor growth and disrupting tumor microvasculature through antiproliferative, anti-angiogenic and proapoptotic effects. It exerts these effects via inhibition of multiple targets including vascular endothelial growth factor receptor (VEGFR) tyrosine kinases; VEGFR-1, VEGRF-2, VEGRF-3 and platelet-derived growth factor receptor beta. In 2006, the Food and Drug Administration (FDA) approved sunitinib for the treatment of advanced renal cell carcinoma and treatment of gastrointestinal stromal tumor after disease progression on or intolerance to imatinib (Gleevec). In May 2011, sunitinib was FDA-approved for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in adults with unresectable locally advanced or metastatic disease. Sunitinib was most recently FDA-approved for adjuvant treatment of renal cell carcinoma following nephrectomy in patients at high risk of disease recurrence. In addition to FDA approved indications, the National Comprehensive Cancer Network (NCCN) Guidelines recommend use of sunitinib for the treatment of thyroid cancer, thymic cancer and various types of bone cancers and soft tissue sarcomas.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

I. Initiation of sunitinib (Sutent) **meets the definition of medical necessity** when the dose does not exceed 50 mg once daily* using the fewest number of capsules, it is administered for an indication in Table 1, and all of the indication specific criteria are met:

TABLE 1

Indication	Specific Criteria
Chordoma	Sunitinib will be used as a single agent for the treatment of recurrent chordoma
Kidney cancer*	When used as a single agent for **ONE** of the following: 1. Relapsed or stage IV disease meeting **ONE** of the following: a. Sunitinib is used as first line or subsequent therapy for disease with predominant clear cell histology b. Sunitinib is used for treatment of disease with non-clear cell histology 2. Adjuvant use following nephrectomy for member's meeting **ALL** of the following: a. Member has disease with predominant clear cell histology b. Member is at high risk of disease recurrence as indicated by at least **ONE** or more of the following: i. Tumor stage 3 or 4 ii. Regional lymph node metastasis
Pancreatic neuroendocrine tumor (pNET)*	When used as a single agent in member's with unresectable locoregional or distant metastatic disease and **ONE** of the following: 1. Progressive disease 2. Symptomatic disease 3. Significant tumor burden
Soft tissue sarcoma: Angiosarcoma Gastrointestinal stromal tumor (GIST)* Solitary Fibrous Tumor/Hemangiopericytoma	Sunitinib will be used to treat **ONE** of the following: 1. Angiosarcoma when used as a single agent 2. Gastrointestinal stromal tumor (GIST) when used as a single agent in member's who had disease progression on or intolerable side effects to imatinib (Gleevec) 3. Gastrointestinal stromal tumor (GIST) when used in combination with everolimus (Afinitor) in member's who had disease progression on single agent

	therapy with imatinib (Gleevec), sunitinib, and regorafenib (Stivarga) 4. Solitary Fibrous Tumor/Hemangiopericytoma when used as a single agent
Thymic carcinoma	Sunitinib is used as a single agent as second-line therapy
Thyroid cancer: Follicular carcinoma Hurthle cell carcinoma Papillary carcinoma Medullary carcinoma	When the member meets all criteria for treatment of **ONE** of the following: 1. Follicular carcinoma, Hurthle cell carcinoma, or Papillary carcinoma of the thyroid when used as a single agent for iodine-refractory symptomatic or progressive disease classified as **ONE** of the following: a. Unresectable locoregional disease that is recurrent or persistent b. Distant metastatic disease 2. Medullary carcinoma of the thyroid when used as a single agent for progressive or symptomatic distant metastatic disease and member meets **ONE** of the following: a. Member's disease progressed on vandetanib (Caprelsa) or cabozantinib (Cometriq) b. Member is unable to tolerate or has a contraindication to vandetanib (Caprelsa) or cabozantinib (Cometriq)
Other FDA-approved or NCCN supported diagnosis (not previously listed above)	**ONE** of the following is met: 1. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert) 2. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation

Approval Duration: 180 days (all indications)

II. Continuation of sunitinib (Sutent®) me**ets the definition of medical necessity** for the indications in Table 1 when the following criteria are met:

A. The member's disease has not progressed while receiving treatment with sunitinib**

B. The member has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met all indication-specific criteria for coverage

C. The dose does not exceed 50 mg once daily* and will be provided using the fewest number of capsules

Approval duration: 1 year

***NOTE:** Avoid use with strong CYP3A4 inhibitors or inducers. Selection of an alternate concomitant medication with no or minimal enzyme interference potential is recommended. If coadministration of a strong CYP3A4 inducer (e.g., carbamazepine, dexamethasone, phenobarbital, phenytoin, rifabutin, rifampin, rifapentin) cannot be avoided, a dose greater than 50 mg daily will be permitted for FDA-approved indications. Per FDA- labeling, the dose maximum of 87.5 mg (GIST and RCC) or 62.5 mg (pNET) daily with coadministration of a strong CYP3A4 inducer may be considered. If the dose is increased, the patient should be monitored carefully for toxicity. A dose reduction should be considered if coadministration with strong CYP3A4 inhibitors cannot be avoided.

**Exception if use is in combination with everolimus (Afinitor) for Gastrointestinal Stromal Tumor for disease progression after single-agent therapy with sunitinib.

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved: sunitinib is indicated for the treatment of gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib (Gleevec), advanced renal cell carcinoma (RCC), adjuvant treatment of RCC following nephrectomy in patients at high risk of disease recurrence, and progressive, well-differentiated pancreatic neuroendocrine (pNET) in members with unresectable locally advanced or metastatic disease. The recommended dose for the treatment of GIST and advanced RCC is 50 mg orally once daily for 4 weeks followed by 2 weeks off. The recommended dose for the adjuvant treatment of RCC following nephrectomy is 50 mg orally once daily for 4 weeks followed by 2 weeks off for a total of nine 6 week cycles. The recommended dose for treatment of pNET is 37.5 mg orally once daily continuously without a scheduled off-treatment period. Sunitinib can be taken with or without food.

Dosage Adjustments

- **Hepatic Impairment:** Initiation dose adjustments are not required for members with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. Sunitinib was not evaluated in subjects with severe (Child-Pugh Class C) hepatic impairment.
- **Renal Impairment:** Initiation dose adjustments are not required for members with mild, moderate, severe renal impairment. In subjects with end-stage renal disease (ESRD) on dialysis, subsequent doses may be increased gradually up to 2 fold based on safety and tolerability.
- **Adverse reactions:** dose interruption and/or dose modification in 12.5 mg increments or decrements is recommended based on individual safety and tolerability.

Drug Interactions

- Strong CYP3A4 inhibitors (e.g., ketoconazole): If coadministration cannot be avoided, consider reducing dose to 37.5 mg (GIST and RCC) and 25 mg (pNET) daily.
- Strong CYP3A4 inducers (e.g., rifampin): If coadministration cannot be avoided, consider increasing dose to a maximum of 87.5 mg (GIST and RCC) or 62.5 mg (pNET) daily.

Drug Availability: sunitinib is available as 12.5-, 25-, 37.5-, and 50 mg hard gelatin capsules.

PRECAUTIONS:

Boxed Warning: hepatotoxicity has been observed in clinical trials and post-marketing experience. Hepatotoxicity may be severe and deaths have been reported.

Hepatotoxicity: Liver failure has been observed. Monitor liver function tests (ALT, AST, and bilirubin) before initiation of treatment, during each treatment cycle, and as clinically indicated. Sunitinib therapy should be interrupted for Grade 3 or 4 drug-related hepatic related events and discontinued if there is no resolution.

Cardiac Toxicity: cardiac toxicity, 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 members for signs and symptoms of congestive heart failure.

Prolonged QT and Torsade de Pointes: use with caution in members at higher risk for developing QT interval prolongation. Monitoring with on-treatment electrocardiograms and electrolytes should be considered.

Hypertension: monitor blood pressure and treat as needed.

Hemorrhagic events: Monitor complete blood counts (CBC) and assess for signs and symptoms.

Osteonecrosis of the Jaw: consider preventative dentistry prior to treatment with sunitinib. If possible, avoid invasive dental procedures, particularly in members receiving intravenous bisphosphonate therapy.

Tumor lysis syndrome (TLS): primarily reported in individuals with RCC and GIST with a high tumor burden; monitor these members closely and treat as clinically indicated.

Thrombotic microangiopathy: thrombotic thrombocytopenic purpura and hemolytic uremic syndrome sometimes leading to renal failure or a fatal outcome has been reported.

Thyroid dysfunction: Monitor thyroid function members with signs/symptoms suggestive of hypo- or hyperthyroidism; manage per standard medical practice.

Hypoglycemia: Check blood glucose levels regularly and adjust anti-diabetic medications as necessary.

Major surgical procedures: temporary interruption of sunitinib therapy is recommended due to impaired wound healing.

Proteinuria: Monitor urine protein and interrupt therapy for 24 hour urine protein $\geq$ 3 grams. Discontinue for repeat episodes of protein $\geq$ 3 grams despite dose reductions or nephrotic syndrome

Severe skin reaction: discontinue if necrotizing fasciitis, erythema multiforme, Stevens-Johnson syndrome or toxic epidermal necrolysis occur.

Pregnancy and Lactation:

- Sunitinib can cause fetal harm when administered to pregnant women.
- Although it is unknown whether sunitinib is excreted into human milk, sunitinib and its metabolites are excreted in rat milk.

BILLING/CODING INFORMATION:

HCPCS Coding

C9399	Unclassified drugs or biologicals
J8999	Prescription drug, oral, chemotherapeutic, NOS

ICD-10 Diagnoses Codes That Support Medical Necessity

C25.4	Malignant neoplasm of endocrine pancreas
C37	Malignant neoplasm of thymus
C47.8	Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous system
C48.0 – C48.8	Malignant neoplasm of retroperitoneum and peritoneum
C49.0 – C49.9	Malignant neoplasm of connective and soft tissue
C49.A0 – C49.A9	Gastrointestinal stromal tumor
C64.1 – C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1 – C65.9	Malignant neoplasm of unspecified renal pelvis
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
C73	Malignant neoplasm of thyroid gland
C7B.00 – C7B.09	Secondary neuroendocrine carcinoid tumors
C7B.8	Other secondary neuroendocrine tumors
D15.0	Benign neoplasm of thymus
E16.1	Hypoglycemia, other
E16.3	Increased secretion of glucagon
E16.8	Other specified disorders of pancreatic internal secretion

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

Medicare Advantage: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline

DEFINITIONS:

None

RELATED GUIDELINES:

Cabozantinib (Cometriq™) Capsules, 09-J1000-88

Imatinib Mesylate (Gleevec®) Tablets, 09-J1000-46

Pazopanib (Votrient™) Tablets, 09-J1000-49

Regorafenib (Stivarga®) Tablets, 09-J1000-83

Sorafenib (Nexavar®) Tablets, 09-J1000-50

Vandetanib (Caprelsa®) Tablets, 09-J1000-38

OTHER:

TABLE 1: Stages of Renal Cell Cancer

Stage I	The tumor is 7 centimeters or smaller and is found only in the kidney.
Stage II	The tumor is larger than 7 centimeters and is found only in the kidney.
Stage III	The tumor is any size and cancer is found only in the kidney and in 1 or more nearby lymph nodes; or cancer is found in the main blood vessels of the kidney or in the layer of fatty tissue around the kidney. Cancer may be found in 1 or more nearby lymph nodes.
Stage IV	Cancer has spread beyond the layer of fatty tissue around the kidney and may be found in the adrenal gland above the kidney with cancer, or in nearby lymph nodes; or to other organs, such as the lungs, liver, bones, or brain, and may have spread to lymph nodes.

TABLE 2: Child-Pugh Score and Classification

	1 point	2 points	3 points
Total bilirubin	< 2	2-3	> 3
Serum albumin	> 3.5	2.8-3.5	< 2.8
INR	> 1.7	1.71-2.20	< 2.20
Ascites	None	Mild	Severe
Hepatic encephalopathy	None	Grade I-II	Grade III-IV
Classification of Result: Class A: 5-6 points Class B: 7-9 points Class C: 10-15 points			

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/08/20

GUIDELINE UPDATE INFORMATION:

01/01/12	New Medical Coverage Guideline.
12/15/12	Review and revision to guideline; consisting of revising and reformatting position statement; revising description section, dosage/administration, and precaution section; updating references and coding.
12/15/13	Review and revision to guideline; consisting of updating position statement, related guidelines, references, coding, and program exceptions.
12/15/14	Review and revision to guideline; consisting of reformatting position statement and updating references.
12/15/15	Review and revision to guideline; consisting of revising position statement, updating dosage, warnings, coding and references.

12/15/16	Review and revision to guideline; consisting of updating position statement, precautions and references.
11/15/17	Review and revision to guideline; consisting of updating position statement, coding and references.
01/15/18	Review and revision to guideline; consisting of updating position statement, description, coding, dosing and references.
01/15/19	Review and revision to guideline; consisting of updating position statement, description, coding, and references.
02/15/20	Review and revision to guideline; consisting of updating position statement and references.