09-J1000-46

Original Effective Date: 01/01/12

Reviewed: 01/09/19

Revised: 02/15/19

Subject: Imatinib Mesylate (Gleevec®) Tablets

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:

Imatinib mesylate (Gleevec) was the first tyrosine kinase inhibitor (TKI) to receive approval by the US Food and Drug Administration (FDA) for the treatment of persons with chronic myeloid leukemia (CML) in chronic phase in 2001. Following initial approval, imatinib was approved in 2002 for the treatment of metastatic and/or unresectable malignant gastrointestinal stromal tumors (GIST) and in 2006 for treatment of five rare diseases: dermatofibrosarcoma protuberans (DFSB), Philadelphia chromosome-positive (Ph+) acute lymphocytic leukemia (ALL), certain types of myelodysplastic/myeloproliferative disorders (MDS/MPD), hypereosinophilic syndrome/chronic eosinophilic leukemia (HES/CEL), and aggressive systemic mastocytosis (ASM). The FDA granted orphan designation to imatinib for the treatment of CML and GIST in 2001; and for the treatment of Ph+ ALL, DFSB, systemic mastocytosis without the D816V c-kit mutation, idiopathic hypereosinophilic syndrome including acute and chronic eosinophilic leukemia, and MDS/MPD associated with platelet-derived growth factor gene re-arrangements in 2005.

Imatinib exerts is mechanism of action through competitive inhibition at the ATP-binding site of the BCR-ABL protein, which results in inhibition of phosphorylation of proteins involved in cell signal transduction. In addition, imatinib blocks the platelet-derived growth factor receptor (PGDFR), as well as the c-KIT tyrosine kinase. Clinical practice guidelines from the National Comprehensive Cancer Network (NCCN) provide recommendations for the use of imatinib in a variety of settings, including FDA-approved indications. Additional off-label uses supported by NCCN include treatment of chordoma, a form of bone cancer, melanoma, certain soft tissue sarcomas, and lymphoblastic lymphoma, which is a type of non-Hodgkin's lymphoma (NHL).

Chronic myeloid leukemia (CML) is a hematopoietic stem cell disease characterized by a reciprocal translocation between chromosomes 9 and 22, resulting in the formation of the Philadelphia (Ph)

chromosome. CML occurs in three different phases (chronic, accelerated, and blast phase) and is usually diagnosed in the chronic phase. Untreated chronic phase CML will eventually progress to advanced phase disease in 3 to 5 years. The National Comprehensive Cancer Network (NCCN) guidelines provide treatment recommendations for all three phases. The NCCN guidelines for CML (Version 1.2019) list imatinib, bosutinib, nilotinib, and dasatinib as category 1 options for the initial first-line treatment of chronic-phase CML in patients with a low-risk Sokal or Hasford score. For CP-CML patients with an intermediate- or high-risk score, imatinib is listed as category 2A option, while bosutinib, nilotinib, and dasatinib (second-generation TKIs) are listed as category 1 options. In addition, bosutinib, dasatinib and nilotinib have a footnote stating "Based on long-term follow-up data from the DASISION and ENESTnd trials and preliminary data from the BFORE trial, second generation TKIs (dasatinib, nilotinib, or bosutinib) are preferred for patients with an intermediate- or high-risk Sokal or Hasford score, especially for young women whose goal is to achieve a deep and rapid molecular response and eventual drug discontinuation of TKI therapy for fertility purposes." The imatinib listing for intermediate- or high-risk scores includes a footnote stating, "Imatinib may be preferred for older patients with comorbidities such as cardiovascular disease." Age, toxicity profile of the TKI, tolerance of adverse effects, and comorbid conditions also may affect initial choice of treatment. Allogenic hematopoietic cell transplantation (HCT) is no longer recommended as first-line treatment option for patient with CP-CML. If the 3-month response milestone (i.e., early molecular response) is not achieved after first-line TKI therapy, patients are considered to be a high risk for disease progression and alternative treatment options should be considered. Evaluation for allogenic HCT is recommended if the response milestones are not achieved at 3, 6, and 12 months. For patients who do not achieve response milestone or those with a loss of response, BCR-ABL1 mutational analysis is recommended, as it is helpful in the selection of subsequent TKI therapy.

Acute lymphoblastic leukemia (ALL) is a heterogeneous hematologic disease characterized by the proliferation of immature lymphoid cells in the bone marrow, peripheral blood and other organs. The long-term prognosis for adults with ALL remains poor, with cure rates of only 30% to 40%. The treatment approach to ALL represents one of the most complex and intensive programs in cancer therapy. In general, treatment phases can be largely grouped into induction, consolidation, and maintenance. The advent of novel agents targeted to specific genetic abnormalities, such as those associated with Ph+ ALL, or to specific cell antigens, has contributed to improvements in outcomes in some subtypes of ALL. These agents include BCR-ABL selective TKIs for Ph+ ALL. The NCCN guidelines for ALL (Version 1.2018) list imatinib as a category 2A treatment option in various induction protocol for AYA (adolescent and young adult) and adult patients, as a TKI option in post-induction maintenance regimens, and for relapsed or refractory Ph+ ALL in patients without certain mutations.

POSITION STATEMENT:

Comparative Effectiveness

The FDA 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.

Initiation of imatinib meets the definition of **medical necessity** when **ALL** of the following criteria are met ("1", "2", "3", and "4"):

1. Imatinib is used to treat **ANY** of the indications listed in Table 1, and **ALL** indication-specific criteria are met.

2. For **brand** Gleevec only: member has a contraindication or intolerance to generic imatinib (the specific intolerance or contraindication must be provided).
3. The member is **NOT** taking another tyrosine kinase inhibitor (TKIs) (i.e., dasatinib, nilotinib, bosutinib, or ponatinib) or omacetaxine mepesuccinate (Synribo) concurrently with imatinib.
4. The dosage does not exceed 800 mg daily and will be achieved using the fewest number of tablets per day.

Table 1

Indications and Specific Criteria	
Indication	**Criteria**
Acute lymphoblastic leukemia (ALL)	When **BOTH** of the following are met ("1" and "2"): 1. Member's ALL is Philadelphia chromosome-positive (Ph+) or BCR-ABL1-positive 2. Imatinib is used as a single-agent or in combination with chemotherapy for induction, consolidation, or maintenance therapy
Aggressive systemic mastocytosis (ASM)	When **ALL** of the following are met ("1", "2", and "3"): 1. Diagnosis is specific for the aggressive systemic form of mastocytosis (i.e., NOT cutaneous or indolent systemic mastocytosis) 2. **EITHER** of the following ("a" or "b"): a. Member is KIT D816V mutation negative or status unknown b. Eosinophilia is present with FIP1L1-PDGFRA fusion gene 3. Imatinib is used as singe-agent therapy
AIDS-related Kaposi sarcoma	When **ALL** of the following are met ("1", "2", and "3"): 1. The member has relapsed or refractory advanced disease 2. The member is receiving appropriate antiretroviral therapy (ART) for their HIV **3.** Member has been previously treated with or has contraindications to at least two separate lines of therapy with liposomal doxorubin monotherapy **AND** paclitaxel monotherapy (the specific contraindications must be provided)
Chronic myeloid leukemia (CML)	Member's CML is Philadelphia chromosome-positive (Ph+) or BCR-ABL1-positive
Chronic myelomonocytic leukemia (CMML) [a subtype of myelodysplastic syndromes]	When **EITHER** of the following are met ("1" or "2"): 1. Member has platelet-derived growth factor receptor (*PDGFR*) beta gene rearrangements (confirmatory laboratory documentation of mutation must be submitted) 2. Member has 5q31-33 translocations (confirmatory

	laboratory documentation of mutation must be submitted)
Chordoma (a type of bone cancer)	When **BOTH** of the following are met ("1" and "2"): 1. Member has recurrent disease 2. Imatinib is used in **ANY** of the following regimens ("a", "b", or "c"): a. Singe-agent therapy b. In combination with cisplatin c. In combination with sirolimus
Dermatofibrosarcoma protuberans (DFSP)	When **BOTH** of the following are met ("1" and "2"): 1. Tumor is positive for the t(17;22) translocation (confirmatory laboratory documentation of mutation must be submitted) 2. **EITHER** of the following ("a" or "b"): a. Use is for neoadjuvant treatment in a member with unresectable disease b. Member has recurrent disease following initial excision **AND** the disease recurrence is unresectable, or additional resection would lead to unacceptable functional or cosmetic outcomes
Desmoid tumors (aggressive fibromatosis)	Diagnosis only
Gastrointestinal stromal tumors (GIST)	When **ANY** of the following are met ("1", "2", or "3"): 1. Disease is resectable, and imatinib is being used as pre-operative treatment to decrease surgical morbidity 2. Disease is resectable, and imatinib is being used as post-operative treatment to reduce the risk of recurrence 3. Disease is unresectable, recurrent, or metastatic
Hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL)	Diagnosis only
Lymphoblastic lymphoma	See criteria for acute lymphoblastic leukemia (ALL)
Melanoma	When **ALL** of the following are met ("1", "2", "3", and "4"): 1. Imatinib is used as single-agent treatment 2. Tumor expresses activating mutations of c-KIT 3. Member has metastatic or unresectable disease 4. Imatinib is being used as second-line or subsequent therapy following prior treatment with immunotherapy and/or BRAF targeted therapy
Pigmented villonodular synovitis/ tenosynovial giant cell tumor (PVNS/TGCT)	Imatinib is used as single-agent treatment
Other FDA-approved or NCCN supported diagnosis (not previously	When **ONE** of the following is met ("1" or "2"): 1. Member is diagnosed with a condition that is consistent

listed above)	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: 6 months

The continuation of imatinib **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1", "2", "3". "4" and "5"):

1. The member has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of a condition listed in Table 1 or other FDA-approved or NCCN-supported diagnosis, **OR** the member has previously met all indication-specific criteria.
2. **ANY** of the following ("a", "b", or "c"):
    a. Member's disease has not progressed during treatment with imatinib
    b. Member has GIST with progressive disease, and alternative treatment options are not suitable
    c. Member's disease has progressed but the dosage is being increased up to a maximum dosage of 800 mg per day.
3. For brand Gleevec only: member has had a contraindication or intolerance to generic imatinib (the specific intolerance or contraindication must be provided).
4. Member is **NOT** taking another TKI (i.e., dasatinib, nilotinib, bosutinib, or ponatinib) or omacetaxine concurrently with imatinib.
5. Dosage of imatinib does not exceed 800 mg daily and will be achieved using the fewest number of capsules per day.

Approval duration: 1 year

NOTE: Quest Diagnostics® can perform the BCR-ABL kinase domain mutation test, PDGFR-beta gene arrangement test, and c-KIT mutation tests. Current guidelines recommend checking mutational analysis in the following situations: if there is inadequate initial response, any sign of loss of response, and in disease progression to accelerate-phase or blast-phase CML (CML-AP and CML-BP, respectively).

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: Imatinib is indicated for the treatment of several indications which are listed in Table 2. The recommended dosing is specific to the indication. All doses of imatinib should be administered with a

meal and a large class of water. Doses of 400 or 600 mg should be administered once daily, whereas doses of 800 mg should administered as 400 mg twice a day. For daily dosing of 800 mg and above, dosing should be accomplished using the 400 mg tablet to reduce exposure to iron (i.e., do **NOT** use eight 100-mg tablets). Imatinib can be dispersed in water or apple juice for members having difficulty swallowing.

Table 2

FDA-approved Indications and Recommended Dosing	
Indication	**Recommended Dose**
Adults	
Ph+ CML-CP	400 mg/day (may increase to 600 mg/day)
Ph+ CML-AP or CML-BC	600 mg/day (may increase to 800 mg/day)
Ph+ ALL	600 mg/day
Myelodysplastic/Myeloproliferative Disease (MDS/MPD)	400 mg/day
Aggressive Systemic Mastocytosis (ASM)	100 or 400 mg/day (100 mg/day if ASM associated with eosinophilia; may increase to 400 mg/day)
Hypereosinophilic Syndrome and/or Chronic Eosinophilic Leukemia (HES/CEL)	100 or 400 mg/day (100 mg/day if presence of FIP1L1-PDGFRα fusion kinase; may increase to 400 mg/day)
Dermatofibrosarcoma Protuberans (DFSP)	800 mg/day
Gastrointestinal Stromal Tumor (GIST)	400 mg/day (may increase up to 800 mg/day if for metastatic or unresectable disease)
Pediatrics	
Ph+ CML CP	340 mg/m^2/day (not to exceed 600 mg)
Ph+ ALL	340 mg/m^2/day (not to exceed 600 mg)

Dose Modifications

- **Hepatic Impairment:** Members with severe hepatic impairment (Child-Pugh Class C) should receive a 25% reduction in the recommended dose.
- **Renal Impairment**
    - **Mild Renal Impairment:** Doses should not exceed 600 mg/day in members with mild renal impairment (creatinine clearance [CrCl] 40-59 ml/min).
    - **Moderate Renal Impairment:** members with moderate renal impairment (CrCl 20-39 ml/min) should receive a 50% decrease in the recommended starting dose; future doses can be increased as tolerated.
    - **Severe Renal Impairment:** Use with caution in members with severe renal impairment. A dose of 100 mg may be reasonable based on limited data.
- **Concomitant Strong CYP3A4 Inducers:** Avoid concomitant use with strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, dexamethasone, rifampin, rifabutin, rifampacin, phenobarbital). If concomitant use cannot be avoided, the dosage of imatinib should be reduced by at least 50% and clinical response should be carefully monitored.
- **Dose Adjustments for Adverse Reactions**

- **Hepatotoxicity:** If elevations in bilirubin greater than 3-times upper limit of normal (ULN) (for laboratory performing the test) or in liver transaminases greater than 5-times the ULN occur, imatinib should be withheld until bilirubin levels are less than 1.5-times ULN and transaminase levels are less than 2.5-times ULN.
    - **Adults:** Reinitiate at a reduced daily dose (i.e., 400 mg to 300 mg, 600 mg to 400 mg, or 800 mg to 600 mg).
    - **Children:** Reinitiate at a reduced dose (i.e., 340 mg/m^2/day to 260 mg/m^2/day).

- **Severe Non-Hematologic Adverse Reactions:** Withhold imatinib until the event has resolved; thereafter, treatment can be resumed as appropriate depending on the initial severity of the event.
- **Hematologic Adverse Reactions:** Dose reductions or treatment interruptions for severe neutropenia and thrombocytopenia are recommended as indicated in Table 3.

Table 3

Dose Adjustments for Neutropenia and Thrombocytopenia		
Indication	**Laboratory Value**	**Dosing Recommendation**
ASL Associated with Eosinophilia, or HES/CEL with FIP1L1-PDGFR-alpha fusion kinase (starting dose of 100 mg)	ANC <1,000/mcL *and/or* platelets <50,000/mcL	1. Stop imatinib until ANC ≥1,500/mcL and platelets ≥75,000/mcL 2. Resume treatment with imatinib at previous dose (i.e., dose before severe adverse reaction)
Chronic-phase CML, or MDS/MPD, or ASM, or HES/CEL, or GIST (starting dose 400 mg)	ANC <1,000/mcL and/or platelets <50,000/mcL	1. Stop imatinib until ANC ≥1,500/mcL and platelets ≥75,000 2. Resume at 400 mg dose (original starting dose) 3. if recurrence of ANC <1,000/mcL and/or platelets <50,000/mcL, repeat step 1 and resume at reduced dose of 300 mg
Accelerated-phase and Blast-crisis Ph+ CML, or Ph+ ALL (starting dose of 600 mg)	ANC <500/mcL *and/or* platelets <10,000/mcL	1. Check if cytopenia is related to leukemia (marrow aspirate or biopsy) 2. If cytopenia is unrelated to leukemia, reduce dose of imatinib to 400 mg 3. If cytopenia persists 2 weeks, reduce further to 300 mg 4. If cytopenia persists 4 weeks and is still unrelated to leukemia, stop imatinib until ANC ≥1,000/mcL and platelets ≥20,000/mcL and then resume treatment at 300 mg
Dermatofibrosarcoma Protuberans (starting dose 800 mg)	ANC <1,000/mcL and/or	1. Stop imatinib until ANC ≥1,500 and platelets ≥75,000 2. Resume at 600 mg dose 3. If recurrence of ANC <1,000/mcL and/or platelets <50,000/mcL, repeat step 1 and resume at reduced dose of 400

	platelets <50,000/mcL	mg
Pediatric patient with newly diagnosed CML-CP (starting dose 340 mg/m^2)	ANC <1,000/mcL and/or platelets <50,000/mcL	1. Stop imatinib until ANC ≥1,500/mcL and platelets ≥75,000/mcL 2. Resume at previous dose (i.e., dose before severe adverse reaction) 3. If recurrence of ANC <1,000/mcL and/or platelets <50,000/mcL, repeat step 1 and resume at reduced dose of 260 mg/m^2/day
ANC, absolute neutrophil count; CML-CP, chronic myelogenous leukemia chronic phase; GIST, gastrointestinal stromal tumor; Ph+, Philadelphia chromosome positive; CML-AP, CML accelerated phase; ALL, acute lymphoblastic lymphoma.		

Drug Availability: imatinib is available as 100- and 400 mg scored tablets.

PRECAUTIONS:

CONTRAINDICATIONS

- None

WARNINGS

- **Fluid Retention:** Edema and severe fluid retention have occurred. Weigh members regularly and manage unexpected rapid weight gain by drug interruption and diuretics.
- **Myelosuppression:** Cytopenias, particularly anemia, neutropenia, and thrombocytopenia, have occurred. Manage with dose reduction or dose interruption and in rare cases discontinuation of treatment. Perform complete blood counts weekly for the first month, biweekly for the second month, and periodically thereafter (e.g., every 2 to 3 months).
- **Cardiovascular:** Severe congestive heart failure and left ventricular dysfunction have been reported, particularly in persons with comorbidities and risk factors. Members with cardiac disease or risk factors for cardiac failure should be monitored and treated.
- **Hepatotoxicity:** Severe hepatotoxicity including fatalities may occur. Assess liver function before initiation of treatment and monthly thereafter or as clinically indicated. Monitor liver function when combined with chemotherapy known to be associated with liver dysfunction.
- **Hemorrhage:** Grade 3/4 hemorrhage has been reported in clinical studies in persons with newly diagnosed CML and with GIST. GI tumor sites may be the source of GI bleeds in GIST. Monitor for GI symptoms at the start of therapy.
- **Gastrointestinal Perforations:** Gastrointestinal perforations, some fatal, have been reported.
- **Cardiogenic Shock/Left Ventricular Dysfunction:** has been associated with the initiation of imatinib in persons with conditions associated with high eosinophil levels (e.g., HES, MDS/MPD and ASM).
- **Dermatologic Reactions:** Bullous dermatologic reactions (e.g., erythema multiforme and Stevens-Johnson syndrome) have been reported with the use of imatinib.
- **Endocrine:** Hypothyroidism has been reported in thyroidectomy patients undergoing levothyroxine replacement. Closely monitor TSH levels in such members.

- **Long-Term Use:** Consider potential toxicities, specifically, liver, kidney, and cardiac toxicity, and immunosuppression from long-term use
- **Tumor Lysis Syndrome:** Close monitoring is recommended.
- **Driving and Using Machinery:** Reports of motor vehicle accidents have been reported in persons administered imatinib. Caution members about driving a car or operating machinery.
- **Renal Toxicity:** A decline in renal function may occur in patients receiving imatinib. Evaluate renal function at baseline and during therapy, with attention to risk factors for renal dysfunction.
- **Special Populations**
    - Growth retardation occurring in children and pre-adolescents administered imatinib has been reported. Close monitoring of growth in children under imatinib treatment is recommended.
    - Imatinib is classified as pregnancy category D. Fetal harm can occur when administered to pregnant women. Advise female members of childbearing age of the potential harms to a fetus.

BILLING/CODING INFORMATION:

HCPCS Coding

S0088	Imatinib, 100 MG

ICD-10 Diagnosis Codes That Support Medical Necessity

C43.0	Malignant melanoma of lip
C43.10 – C43.12	Malignant melanoma of eyelid, including canthus
C43.20 – C43.22	Malignant melanoma of ear and external auricular canal
C43.30 – C43.39	Malignant melanoma of other and unspecified parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51 – C43.59	Malignant melanoma trunk
C43.60 – C43.62	Malignant melanoma of upper limb, including shoulder
C43.70 – C43.72	Malignant melanoma of lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C44.90	Unspecified malignant neoplasm of skin, unspecified
C46.0 - C46.9	Kaposi's sarcoma
C47.8	Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous system
D48.1	Neoplasm of uncertain behavior of connective and other soft tissue
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C49.A0 – C49.A9	Gastrointestinal stromal tumor
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
C79.31	Secondary malignant neoplasm of brain
C80.0	Disseminated malignant neoplasm, unspecified
C80.1	Malignant (primary) neoplasm, unspecified
C83.50	Lymphoblastic (diffuse) lymphoma, unspecified site

C83.51	Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.53	Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
C83.54	Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
C83.55	Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb
C83.56	Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
C83.57	Lymphoblastic (diffuse) lymphoma, spleen
C83.58	Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
C83.59	Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse
C92.10	Chronic myeloid leukemia, bcr/abl-positive, not having achieved remission
C92.11	Chronic myeloid leukemia, bcr/abl-positive, in remission
C92.12	Chronic myeloid leukemia, bcr/abl-positive, in relapse
C93.10	Chronic myelomonocytic leukemia, not having achieved remission
C96.20	Malignant mast cell neoplasm, unspecified
C96.21	Aggressive systemic mastocytosis
C96.22	Mast cell sarcoma
C96.29	Other malignant mast cell neoplasm
D47.02	Systemic mastocytosis
D48.1	Neoplasm of uncertain behavior of connective and other soft tissue

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

DEFINITIONS:

Acute lymphoblastic leukemia: an aggressive (fast-growing) type of leukemia (blood cancer) in which too many immature white blood cells are found in the blood and bone marrow. Also called acute lymphocytic leukemia and ALL.

Aggressive systemic mastocytosis: A rare disease in which too many mast cells (a type of immune system cell) are found in the skin, bones, joints, lymph nodes, liver, spleen, and gastrointestinal tract. Mast cells give off chemicals such as histamine that can cause flushing (a hot, red face), itching, abdominal cramps, muscle pain, nausea, vomiting, diarrhea, low blood pressure, and shock

Chordoma: A type of bone cancer that usually starts in the lower spinal column or at the base of the skull

c-KIT: a type III receptor tyrosine kinase; the interaction between c-KIT and its ligand, stem cell factor (SCF), plays a key role in regulating mast cell proliferation, maturation, adhesion, chemotaxis, and survival.

Dermatofibrosarcoma Protuberans: A type of tumor that begins as a hard nodule and grows slowly. These tumors are usually found in the dermis (the inner layer of the two main layers of tissue that make up the skin) of the limbs or trunk of the body. They can grow into surrounding tissue but do not spread to other parts of the body. These tumors are related to giant cell fibroblastomas

Hypereosinophilic syndrome: a myeloproliferative disorder characterized by persistent eosinophilia that is associated with damage to multiple organs.

Melanoma: A form of cancer that begins in melanocytes (cells that make the pigment melanin). It may begin in a mole (skin melanoma), but can also begin in other pigmented tissues, such as in the eye or in the intestines

Myelodysplastic syndrome: A group of diseases in which the bone marrow does not make enough healthy blood cells.

Myeloproliferative disorder: a heterogenous group of disorders characterized by cellular proliferation of one or more hematologic cell lines in the peripheral blood, distinct from acute leukemia.

Philadelphia chromosome or Philadelphia translocation: is a specific chromosomal abnormality that is associated CML or ALL.

RELATED GUIDELINES:

Autologous Bone Marrow and Stem Cell Transplantation, 02-38241-01

Bosutinib (Bosulif) Tablets, 09-J1000-84

Cytogenetic Studies (Chromosomal Studies), 05-82000-18

Dasatinib (Sprycel) Tablets, 09-J1000-43

Nilotinib (Tasigna) Capsules, 09-J1000-48

Omacetaxine (Synribo) Injection, 09-J1000-87

Ponatinib (Iclusig) Tablet, 09-J1000-89

Regorafenib (Stivarga), 09-J1000-83

Sunitinib Malate (Sutent) Capsules, 09-J1000-51

OTHER:

None

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/09/19.

GUIDELINE UPDATE INFORMATION:

01/01/12	New Medical Coverage Guideline.
11/15/12	Review and revision to guideline; consisting of updating position statement, dosage and administration, added contraindications, update coding, exceptions, related guidelines and references.

03/15/13	Review and revision to guideline; consisting of revising and reformatting position statement; revising and reformatting description, dosage/administration, and precautions sections; updating references and coding; adding pertinent definitions and related guidelines.
03/15/14	Review and revision to guideline; consisting of reformatting position statement and adding approval duration, updating dosage/administration, references, coding, and program exceptions.
03/15/15	Review and revision to guideline; consisting of revising position statement and updating the description, dosage/administration, warnings, and references.
07/15/15	Revision to guideline; updated coding.
11/01/15	Revision: ICD-9 Codes deleted.
03/15/16	Review and revision to guideline consisting of description, position statement, definitions, and references.
10/01/16	Revision: ICD-10 code updates.
03/15/17	Review and revision to guideline consisting of updates to description, position statement, and references sections.
02/15/18	Review and revision to guideline consisting of updates to description, position statement, precautions, billing/coding, and references sections.
02/15/19	Review and revision to guideline consisting of updates to description, position statement, billing//coding, and references sections.