Custom Criteria for
BlueCross Blue Shield of Rhode Island Commercial

GLEEVEC® (imatinib)

GPI CODING:

GLEEVEC 100mg 21534035100320
GLEEVEC 400mg 21534035100340

DESCRIPTION:

Imatinib mesylate is a protein tyrosine kinase inhibitor belonging to the signal transduction inhibitor class of anti-cancer agents. Tyrosine kinases function as mediators of cell growth, differentiation, and death. The enzymes catalyze transfer of phosphate from adenosine triphosphate (ATP) to the hydroxyl group of a tyrosine residue on the protein substrate, which in turn initiates a cascade of events causing uncontrolled cell growth and inhibition of apoptosis. Imatinib competitively inhibits the ATP binding site on a number of tyrosine kinase-producing oncogenes, but primarily the breakpoint cluster region-Abelson murine leukemia (BCR-ABL) fusion gene seen in chronic myelogenous leukemia (CML). Blockade of tyrosine kinase blocks further disease progression. Imatinib is also an inhibitor of receptor tyrosine kinases for the platelet-derived growth factor (PDGF) and stem cell factor (SCF), c-KIT, and inhibits PDGF- and SCF-mediated cellular events. *In vitro*, imatinib inhibits proliferation and induces apoptosis in gastrointestinal stromal tumor (GIST) cells, which express an activating c-KIT mutation. Imatinib is used primarily in malignancies caused by an overexpression of tyrosine kinase.

APPROVAL DURATION:

Quantity Limits
100-mg tablets: 6 tablets/day
400-mg tablets: 2 tablets/day

Initial approvals and renewals: 12 months

CRITERIA FOR GLEEVEC

<u>Adult indications (≥18 years of age)</u>

I. Philadelphia chromosome positive chronic myelogenous leukemia
   A. Patient has documented Ph+ CML that is newly diagnosed in the chronic phase (CP), **OR**
   B. Patient has documented Ph+ CML that is in accelerated phase (AP) or blast crisis (BC), **OR**
   C. Patient has documented Ph+ CML that is in chronic phase after failure of interferon alpha therapy

OR

II. Philadelphia chromosome positive acute lymphoblastic leukemia
   A. Patient has documented Ph+ ALL that is relapsed or refractory

OR

III. Gastrointestinal stromal tumor
   A. Patient has documented c-KIT (CD117) positive unresectable or metastatic malignant GIST, **OR**
   B. Patient had resection of c-KIT (CD117) positive GIST and imatinib will be used as an adjuvant therapy

OR

IV. Dermatofibrosarcoma protuberans that is unresectable, recurrent, or metastatic
OR
V. Hypereosinophilic syndrome or chronic eosinophilic leukemia
   A. Patient has HES or CEL with documentation of FIP1L1-PDGFR-α fusion kinase [mutational analysis or FISH demonstration of CHIC2 allele deletion], **OR**
   B. Patient has HES or CEL and is FIP1L1-PDGFR-α fusion kinase negative or unknown
OR
VI. Myelodysplastic syndrome or myeloproliferative disease associated with PDGFR gene rearrangements
OR
VII. Systemic mastocytosis without the D816V c-KIT mutation or with c-KIT mutational status unknown
OR
VIII. Off label uses for oncology drugs are approvable if considered medically acceptable in one or more of the following compendia (i.e., Micromedex DrugDex, AHFS, Clinical Pharmacology, and NCCN.)) A use is identified by a compendium as medically accepted if the:
   A. Indication is a Category 1 or 2A in NCCN,
   B. Indication is a Class I, Class IIa or Class IIb in DrugDex,
   C. Narrative text in AHFS or Clinical Pharmacology is supportive; or
   D. The use is supported by clinical research in 2 or more peer-reviewed medical journals

<u>Pediatric indications (patient must be at least 2 years of age)</u>
I. Documented Ph+ CML that is newly diagnosed in the chronic phase
II. Newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)

Authorization for continued use shall be reviewed at least every 12 months to confirm the following: patient has experienced a measurable response to therapy