Clinical Policy: Imatinib (Gleevec)

Reference Number: CP.PHAR.65
Effective Date: 06/11
Last Review Date: 07/17 Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for imatinib (Gleevec®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that imatinib (Gleevec) is **medically necessary** when one of the following criteria is met:

I. Initial Approval Criteria

A. Chronic Myeloid Leukemia (must meet all):

1. Diagnosis of chronic myeloid leukemia (CML);
2. CML is Philadelphia chromosome positive (Ph+) or BCR-ABL1 positive;
3. Member meets a or b:
   a. FDA approved use (i or ii):
      i. Newly diagnosed CML in chronic phase;
      ii. Blast, accelerated or chronic phase CML after failure of interferon-alpha therapy;
   b. Off-label NCCN recommended use (any of the following):
      i. As a single agent for accelerated or myeloid blast phase CML;
      ii. In combination with steroids as primary treatment for lymphoid blast phase CML;
      iii. In combination with induction chemotherapy followed by stem cell transplant for blast phase CML;
      iv. Post stem cell transplant.
4. Prescribed dose of Gleevec does not exceed 800 mg/day (co-administration with strong CYP3A4 inducers may require an increased dose - e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifampacin, phenobarbital).

Approval duration: 6 months

B. Acute Lymphoblastic Leukemia (must meet all):

1. Diagnosis of acute lymphoblastic leukemia (ALL);
2. ALL is Philadelphia chromosome positive (Ph+);
3. Member meets a or b:
   a. FDA approved use (i or ii):
      i. Relapsed or refractory ALL;
      ii. Newly diagnosed ALL in combination with chemotherapy;
   b. Off-label NCCN recommended use (i or ii):
      i. Induction or consolidation therapy;

ii. Maintenance therapy (a or b):
   a) In combination with vincristine and prednisone with or without methotrexate and mercaptopurine;
   b) Post stem cell transplant.

4. Prescribed dose of Gleevec does not exceed 600 mg/day (co-administration with strong CYP3A4 inducers may require an increased dose - e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifampacin, phenobarbital).

Approval duration: 6 months

C. Myelodysplastic/Myeloproliferative Disease (must meet all):
1. Diagnosis of myelodysplastic/myeloproliferative disease (MDS/MPD);
2. Disease is associated with a PDGFR (platelet-derived growth factor receptor) gene re-arrangement;
3. Prescribed dose of Gleevec does not exceed 400 mg/day (co-administration with strong CYP3A4 inducers may require an increased dose - e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifampacin, phenobarbital).

Approval duration: 6 months

D. Aggressive Systemic Mastocytosis (must meet all):
1. Diagnosis of aggressive systemic mastocytosis (ASM);
2. Negative for the D816V c-Kit mutation or c-Kit mutational status is unknown;
3. Prescribed dose of Gleevec does not exceed 400 mg/day (co-administration with strong CYP3A4 inducers may require an increased dose - e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifampacin, phenobarbital).

Approval duration: 6 months

E. Hypereosinophilic Syndrome or Chronic Eosinophilic Leukemia (must meet all):
1. Diagnosis of hypereosinophilic syndrome (HES) or chronic eosinophilic leukemia (CEL);
2. Prescribed dose of Gleevec does not exceed 400 mg/day (co-administration with strong CYP3A4 inducers may require an increased dose - e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifampacin, phenobarbital).

Approval duration: 6 months

F. Dermatofibrosarcoma Protuberans (must meet all):
1. Diagnosis of dermatofibrosarcoma protuberans (DFSP);
2. Member meets a or b:
   a. FDA approved use: disease is unresectable, recurrent or metastatic;
   b. Off-label NCCN recommended use: as adjuvant therapy for positive surgical margins following excision;

3. Prescribed dose of Gleevec does not exceed 800 mg/day (co-administration with strong CYP3A4 inducers may require an increased dose - e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifampacin, phenobarbital).

Approval duration: 6 months

G. Gastrointestinal Stromal Tumor (must meet all):
1. Diagnosis gastrointestinal stromal tumor (GIST);
2. Member meets a or b:
   a. FDA approved use (i or ii):
      i. Kit (CD117) positive disease that is unresectable or metastatic;
      ii. Adjuvant treatment for Kit (CD117) positive disease following resection;
   b. Off-label NCCN recommended use (any of the following):
      i. Primary or preoperative treatment for unresectable, recurrent or metastatic disease;
      ii. Postoperative treatment following complete resection or for persistent residual disease;
      iii. Ongoing treatment for progressive disease;
4. Prescribed dose of Gleevec does not exceed 800 mg/day (co-administration with strong CYP3A4 inducers may require an increased dose - e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifampacin, phenobarbital).

Approval duration: 6 months

H. Other diagnoses/indications:
1. Additional NCCN recommended uses meeting NCCN categories 1, 2a or 2b are covered for the following indications per the CP.PHAR.57 Global Biopharm Policy:
   a. Chordoma (a type of bone cancer);
   a. Melanoma;
   b. Lymphoblastic lymphoma (a type of non-Hodgkin's lymphoma);
   c. Soft tissue sarcoma (i or ii):
      i. Desmoid tumor (aggressive fibromatosis);
      ii. Pigmented villonodular synovitis/tenosynovial giant cell tumor (PVNS/TGCT).

II. Continued Approval

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy (in cases of CML, Gleevec may be continued in cases of complete or partial response, or relapse).

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy;
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Imatinib mesylate is a small molecule protein-kinase inhibitor that inhibits the BCR-ABL tyrosine kinase, the constitutive abnormal tyrosine kinase created by the Philadelphia chromosome abnormality in CML. Imatinib inhibits proliferation and induces apoptosis in BCR-ABL positive cell lines as well as fresh leukemic cells from Philadelphia chromosome positive chronic myeloid leukemia. Imatinib inhibits colony formation in assays using ex vivo peripheral blood and bone marrow samples from CML patients. Imatinib is also an inhibitor of the receptor tyrosine kinases for platelet-derived growth factor (PDGF) and stem cell factor (SCF), c-kit, and inhibits PDGF- and SCF-mediated cellular events.

Formulations:

Tablet, oral administration

Gleevec: 100 mg, 400 mg

FDA Approved Indications:

Gleevec (imatinib) is a kinase inhibitor/oral tablet formulation indicated for the treatment of:

- Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase.
- Patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.
- Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL).
- Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy.
- Adult patients with myelodysplastic/myeloproliferative diseases associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements as determined with an FDA-approved test.
- Adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation as determined with an FDA-approved test or with c-Kit mutational status unknown.
- Adult patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown.
- Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans.
- Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors.
- Adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positive GIST.

Appendices

Appendix A: Abbreviation Key

ALL: acute lymphoblastic leukemia
ASM: aggressive systemic mastocytosis
CEL: chronic eosinophilic leukemia
CML: chronic myelogenous leukemia
DFSP: dermatofibrosarcoma protuberans
FISH: fluorescent in situ hybridization
GIST: gastrointestinal stromal tumor
HES: hypereosinophilic syndrome
MDS: myelodysplastic syndromes
MPD: myeloproliferative diseases
PDGFR: platelet-derived growth factor receptor
Ph+: positive Philadelphia chromosome
PVNS: pigmented villonodular synovitis
TGCT: tenosynovial giant cell tumor
TKI: tyrosine kinase inhibito

Reviews, Revisions, and Approvals	Date	Approval Date
Removed question related to dose increase Combined questions about disease progression and toxicity Added info about length of treatment to match drug labeling Added pertinent information for treatment of children	06/13	07/13
Updated cytogenetic and TKI question to Figure 1 algorithm Updated length of treatment question to Figure 2 algorithm Updated high risk question to Figure 3 algorithm Added background information	07/14	07/14
Reworked narrative for CML and ALL per NCCN guidelines. Removed requests for documentation from all algorithms; added age requirements to all algorithms. Figure 1 (CML): added diagnoses questions and questions about age; modified monitoring per NCCN guidelines – see also corresponding narrative and Appendix B. Figure 2 (ALL): changed question about less than or greater than 12 months to initial auth for 3 months and subsequent auths for 6 months – while there is monitoring per NCCN guidelines, Gleevec is always a potential option so specific monitoring questions were not added. Figure 4 (ASM): Added c-Kit mutational status unknown to the first question in the pathway per PI. Restructured safety section into list per the package insert.	05/15	07/15
Policy converted to new template. Added NCCN compendium disease indication and recommendations.	06/16	07/16
CML NCCN: 1) “myeloid” is inserted to describe blast phase in “As a single agent for accelerated or myeloid blast phase CML”; 2) “In combination with steroids as primary treatment for CML in lymphoid blast phase” is added; 3) continued use of Gleevec in cases where members are not candidates for other drugs or in cases of poor or partial response is deleted in initial criteria and added to continuation criteria; 4) “for relapse” is deleted from “post stem cell transplant therapy.” ALL NCCN: 1) Allowed regimens deleted; 2) “post stem cell transplant” is added under maintenance therapy.	06/17	07/17

Reviews, Revisions, and Approvals	Date	Approval Date
HES/CEL: "FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) or HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown" is removed. GIST NCCN: 1) "resectable disease with risk of significant morbidity" is removed from under primary/preoperative therapy; 2) "ongoing treatment for progressive disease" is added. Maximum dose added for CML, ALL and dose exception due to CYP inducers is added to all indications. Reasons to discontinue removed. Approval periods lengthened from 3/6 to 6/12 months.		

References

1. Gleevec Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2017. Available at https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/gleevec_tabs.pdf. Accessed June 15, 2017.
2. Imatinib mesylate. In: National Comprehensive Cancer network Drug and Biologics Compendium. Available at www. NCCN.org. Accessed June 15, 2017.
3. Chronic myelogenous leukemia (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed June 19, 2017.
4. Acute lymphoblastic leukemia (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed June 19, 2017.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and

regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs and LCDs should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.