Gleevec

Description

Gleevec (imatinib)

Background
Gleevec is an anticancer medicine that works as an inhibitor of BCR-ABL tyrosine kinase enzyme. This enzyme is the abnormal tyrosine kinase created by the Philadelphia chromosome abnormality in chronic myeloid leukemia. Inhibition of this enzyme by Gleevec inhibits proliferation and induces apoptosis in BCR-ABL positive cell lines and fresh leukemic cells from Philadelphia chromosome positive chronic myeloid leukemia. Gleevec also acts to inhibit tyrosine kinase for platelet-derived growth factor, stem-cell factor, c-Kit, and cellular events mediated by platelet-derived growth factor and stem-cell factor (1).

Regulatory Status
FDA-approved indication: Gleevec is a tyrosine kinase inhibitor indicated for: (1)

1. Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase
2. Patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in blast crisis (BC), accelerated phase (AP), or in chronic phase (CP) after failure of interferon-alpha therapy
3. Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
4. Pediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) in combination with chemotherapy
5. Adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements
6. Adult patients with aggressive systemic mastocytosis (ASM) without the D816V c-Kit mutation or with c-Kit mutational status unknown
7. Adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) 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
8. Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP)
9. Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)
10. Adjuvant treatment of adult patients following resection of Kit (CD117) positive GIST

**Off-Label Uses:** (2-4)
1. Treatment of patients with advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Ph+ ALL/ Lymphoblastic lymphoma
4. Gastrointestinal Stromal tumor (GIST) (primary, preoperative, postoperative and continued treatment)
5. Dermatofibrosarcoma protuberans (DFSP)
6. Desmoid tumors
7. Pigmented villonodular synovitis / tenosynovial giant cell tumor (PVNS/TGCT)
8. Chordoma
9. C-Kit mutated melanoma

Gleevec should be used with caution in patients at increased risk for cardiac failure, patients with high eosinophil levels (e.g., HES, MDS/MPD and ASM), thyroidectomy patients, pregnant women, and children. Reports of edema, severe fluid retention, cytopenias, severe congestive heart failure, cardiogenic shock, left ventricular dysfunction, severe hepatotoxicity (including fatalities), hypothyroidism, fetal harm, growth retardation, and motor vehicle accidents have occurred in patients on Gleevec (1).

Patients should be weighed regularly and unexpected rapid weight gain should be managed by drug interruption and diuretics. CBC testing should also be performed weekly the first month, biweekly the second month, and periodically thereafter. Liver function should be assessed before initiation and monthly thereafter or as clinically indicated. TSH levels in thyroidectomy
patients and growth rates in children should be closely monitored. Patients should also be
cautioned about driving a car or operating machinery while on Gleevec (1).

The safety and effectiveness of Gleevec have not been established in children less than 1 year
of age (1).

Related policies
Bosulif, Blincyto, Erwinaze, Iclusig, Marqibo, Sprycel, Stivarga, Synribo

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval,
Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Gleevec may be considered medically necessary in patients that are 1 years of age or older
with one of the following diagnoses: patient has chronic myeloid leukemia (CML), chronic
myeloid leukemia (CML) post hematopoietic stem cell transplant (HSCT), Ph+ acute
lymphoblastic leukemia (ALL), myelodysplastic/myeloproliferative diseases (MDS/MPD),
aggressive systemic mastocytosis (ASM), gastrointestinal stromal tumors (GIST), pigmented
villonodular synovitis/tenosynovial giant cell tumor (PVNS/TGCT), dermatofibrosarcoma
protuberans (DFSP), hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia
(CEL), or melanoma; and when the conditions indicated below are met.

Gleevec is considered investigational in patients less than 1 year of age and for all other
indications.

Prior-Approval Requirements

Age 1 year of age and older

Diagnoses

Patient must have ONE of the following:

1. Chronic myeloid leukemia (CML) -
2. Chronic myeloid leukemia (CML) post hematopoietic stem cell transplant (HSCT)
3. Ph+ Acute lymphoblastic leukemia (ALL)
AND ALL of the following for 1 thru 3:
   a. Confirmed by molecular testing by the detection of the Ph chromosome or
      BCR-ABL gene prior to initiation of therapy
   b. If the patient has had prior therapy with a TKI then ONE of the following
      requirements must be met:
      i. Member experienced resistance to prior therapy with TKI
         1) Results from mutational testing are negative for the T315I
         mutation
      ii. Member experienced toxicity or intolerance to prior therapy with a
          TKI

4. Myelodysplastic/myeloproliferative diseases (MDS/MPD)
   a. Confirmed with PDGFR (platelet-derived growth factor receptor) gene re-
      arrangement

5. Aggressive systemic mastocytosis (ASM) with ONE of the following mutations:
   a. Confirmed without the D816V c-Kit mutation by genetic test
   b. Confirmed with c-Kit mutational status unknown

6. Gastrointestinal stromal tumors (GIST)
7. Pigmented villonodular synovitis/tenosynovial giant cell tumor (PVNS/TGCT)
8. Dermatofibrosarcoma protuberans (DFSP)
9. Hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL)
10. Melanoma
    a. Confirmed c-Kit mutation-positive

AND the following for ALL diagnoses:
   a. **Brand Gleevec only:** Patient MUST have tried the preferred product (generic
      Gleevec: imatinib) unless the patient has a valid medical exception (e.g.
      inadequate treatment response, intolerance, contraindication)

**Prior – Approval Renewal Requirements**

**Age**
1 year of age and older

**Diagnoses**

Patient must have ONE of the following:

1. Chronic myeloid leukemia (CML)
2. Chronic myeloid leukemia (CML) post hematopoietic stem cell transplant (HSCT)
3. Ph+ Acute lymphoblastic leukemia (ALL)
4. Myelodysplastic / myeloproliferative diseases (MDS/MPD)
5. Aggressive systemic mastocytosis (ASM)
6. Gastrointestinal stromal tumors (GIST)
7. Pigmented villonodular synovitis/tenosynovial giant cell tumor (PVNS/TGCT)
8. Dermatofibrosarcoma protuberans (DFSP)
9. Hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL)
10. Melanoma

### Policy Guidelines

**Pre - PA Allowance**

None

**Prior - Approval Limits**

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<tr>
<th>Quantity</th>
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<tr>
<td>100 mg</td>
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**Duration**

12 months

**Prior – Approval Renewal Limits**

Same as above

### Rationale

Gleevec is a tyrosine kinase inhibitor that targets BCR-ABL, platelet-derived growth factor, stem-cell factor, c-Kit, and cellular events mediated by platelet-derived growth factor (PDGFR) and stem-cell factor. Gleevec inhibits proliferation and induces apoptosis in these cell lines and can be used to treat diseases characterized by these particular cell lines growing out of control. The safety and effectiveness of Gleevec have not been established in children less than 1 year of age (1).
Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Gleevec while maintaining optimal therapeutic outcomes.

References

Policy History

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<thead>
<tr>
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<tbody>
<tr>
<td>July 2016</td>
<td>Addition to PA</td>
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<tr>
<td>December 2016</td>
<td>Annual review Removal of first line treatment from CML and removal of confirmation the D816V c-Kit mutation from the renewal section Addition of the “genetic test” to confirmed without the D816V c-Kit mutation</td>
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<tr>
<td>March 2017</td>
<td>Annual editorial review Addition of no dual therapy with another tyrosine kinase inhibitor</td>
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<tr>
<td>November 2017</td>
<td>Addition of quantity limits</td>
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<td>March 2018</td>
<td>Annual editorial review Addition of “If the patient has had prior therapy with a TKI then ONE of the following requirements must be met: member experienced resistance to prior therapy with TKI and results from mutational testing are negative for the T315I mutation or member experienced toxicity or intolerance to prior therapy with a TKI to these indications CML, CML post HSCT and Ph+ ALL</td>
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<tr>
<td>June 2019</td>
<td>Annual review and reference update</td>
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<tr>
<td>December 2019</td>
<td>Annual review. Addition of requirement to trial preferred product for initiation of therapy and removed no dual therapy with another TKI requirement</td>
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective January 1, 2020.