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Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	July 1, 2016
Subject:	Gleevec	**Page:**	1 of 7

Last Review Date: December 13, 2024

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 indications: 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, Scemblix, Sprycel, Stivarga, Synribo, Tasigna

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** if the conditions indicated below are met.

Gleevec may be considered **investigational** 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** indications:

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

Quantity 800 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

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

1. Gleevec [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation; March 2024.
2. NCCN Drugs & Biologics Compendium® Imatinib 2024. National Comprehensive Cancer Network, Inc. Accessed on October 3, 2024.
3. NCCN Clinical Practice Guidelines in Oncology® Chronic Myeloid Leukemia (Version 1.2025). National Comprehensive Cancer Network, Inc. August 2024. Accessed on October 3, 2024.

4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 2. 2024). National Comprehensive Cancer Network, Inc. July 2024. Accessed on October 3, 2024.

Policy History

Date	Action
July 2016	Addition to PA
December 2016	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
March 2017	Annual editorial review Addition of no dual therapy with another tyrosine kinase inhibitor
November 2017	Addition of quantity limits
March 2018	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
June 2019	Annual review and reference update
December 2019	Annual review. Addition of requirement to trial preferred product for initiation of therapy and removed no dual therapy with another TKI requirement
March 2020	Updated requirement of trial preferred product for CML
June 2020	Annual review and reference update
June 2021	Annual review and reference update
March 2022	Annual review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.21.074
June 2023	Annual review and reference update
December 2023	Annual review and reference update
June 2024	Annual editorial review and reference update. Changed quantity limit to 800 mg per day
December 2024	Annual review and reference update. Changed Medex requirement to t/f imatinib only for all indications

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.