



RATIONALE FOR INCLUSION IN PA PROGRAM

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-PDGFR α fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1- PDGFR α 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).

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



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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.
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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.