PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Imatinib Prior Authorization Policy
- Gleevec® (imatinib tablets– Novartis, generic)

REVIEW DATE: 05/04/2022; selected revision 06/22/2022

OVERVIEW

Imatinib, a tyrosine kinase inhibitor (TKI), is indicated for the treatment of:[1,2]

- **Acute lymphoblastic leukemia (ALL)**, Philadelphia chromosome positive (Ph+), in adults with relapsed or refractory disease.
- **ALL**, newly diagnosed and Ph+, in combination with chemotherapy in pediatric patients.
- **Aggressive systemic mastocytosis**, in adults, without the D816V c-Kit mutation or with unknown c-Kit mutational status.
- **Chronic myeloid leukemia (CML)**, newly diagnosed and Ph+, in adult and pediatric patients in chronic phase.
- **CML**, Ph+, in blast phase, accelerated phase, or in chronic phase after failure of interferon alfa therapy.
- **Dermatofibrosarcoma protuberans** in adults with unresectable, current, and/or metastatic disease.
- **Gastrointestinal stromal tumors (GIST)**, in patients with Kit (CD117) positive unresectable and/or metastatic malignant disease.
- **GIST**, Kit (CD117) positive, as adjuvant treatment of adults following resection.
- **Hypereosinophilic syndrome and/or chronic eosinophilic leukemia**, adults who have the *FIP1L1-PDGFR* alpha fusion kinase (mutation analysis or fluorescence in situ hybridization demonstration of CICH2 allele deletion) for patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia who are *FIP1l1-PDGFR* alpha fusion kinase negative or unknown.
- **Myelodysplastic/myeloproliferative diseases**, associated with *PDGFR* gene rearrangements in adults.

Guidelines

Imatinib is addressed in guidelines from National Comprehensive Cancer Network (NCCN):[3-15]

- **ALL:** The NCCN guidelines for ALL (version 1.2022 – April 4, 2022) [adults] recommend imatinib as an option for patients with relapsed or refractory ALL (category 2A) in many different clinical circumstances (e.g., induction therapy).[3] The NCCN guidelines for pediatric ALL (version 1.2022 – October 1, 2021)[4] feature imatinib prominently (category 2A) in a variety of clinical scenarios.
- **Bone Cancer:** The NCCN guidelines for bone cancer (version 2.2022 – October 8, 2021) state that imatinib, either as monotherapy (other recommended regimens) or in combination with cisplatin or Rapamune® (sirolimus tablets) [useful in certain circumstances], is recommended for treatment of chordoma (category 2A).[5]
- **CML:** NCCN guidelines for CML (version 3.2022 – January 27, 2022) state that for patients with chronic phase CML with a low-risk score, the primary treatment recommended includes a first-generation TKI (imatinib [brand or generic], or a second-generation TKI (Bosulif® [bosutinib tablets], Sprycel® [dasatinib tablets], or Tasigna® [nilotinib capsules] {all category 1}).[6] For patients with chronic phase CML with an intermediate- or high-risk score, a second-generation TKI is preferred (Bosulif [category 1], Sprycel [category 1], or Tasigna [category 1]). A first-generation TKI (imatinib [brand or generic]) is an alternative (category 2A). Iclusig® (ponatanib tablets) is an

option for patients with a T315I mutation and/or chronic phase CML with resistance or intolerance to at least two prior TKIs or for patients with accelerated-phase CML or blast-phase CML for whom no other TKI is indicated (category 2A). Scemblix® (asciminib tablets) is a treatment option for chronic phase CML in patients with the T315I mutation and/or chronic phase CML with resistance or intolerance to at least two prior TKIs (category 2A).

- **Dermatofibrosarcoma Protuberans:** The NCCN guidelines on dermatofibrosarcoma protuberans (version 2.2022 – March 24, 2022)[7] recommend to consider imatinib in certain cases such as where disease is unresectable, or unacceptable functional or adverse cosmetic outcomes may occur with resection (category 2A).
- **GIST:** In the NCCN GIST guidelines (version 1.2022 – January 21, 2022), imatinib features prominently.[8] Imatinib is a preferred regimen for first-line therapy (category 1) in various scenarios (e.g., for sensitive mutations or for *PDGFRA* exon 18 mutations [excluding the D842V mutation) and is recommendation in other clinical scenarios as well in patients with GIST (category 2A) [e.g., resectable GISTs with intermediate to high risk as neoadjuvant and adjuvant therapy].
- **Graft-Versus-Host Disease (GVHD):** The NCCN has guidelines regarding hematopoietic cell transplantation (version 1.2022 – April 1, 2022) that address GVHD.[9] Imatinib is cited as one of many therapies recommended for steroid-refractory, chronic GVHD (category 2A). Jakafi® (ruxolitinib tablets) is the only agent with a category 1 recommendation. Some other agents (all category 2A) include Imbruvica® (ibrutinib tablets and capsules), low-dose methotrexate, sirolimus, mycophenoate mofetil, hydroxychloroquine, calcineurin inhibitors (e.g., tacrolimus cyclosporine), and Rezurock™ (belumosudil tablets).
- **Kaposi Sarcoma:** The NCCN guidelines for Kaposi sarcoma (version 1.2022 – February 3, 2022) recommended imatinib for subsequent systemic therapy for relapsed/refractory therapy (useful in certain circumstances).[10] First-line systemic therapy options are liposomal doxorubicin (preferred) and paclitaxel. Other subsequent systemic therapy options for relapsed/refractory are cited (e.g., Pomalyst® [pomalidomide capsules] {preferred}, lenalidomide capsules [other recommended regimen], and Thalomid® [thalidomide capsules] {other recommended regimen}).
- **Mastocytosis:** The NCCN guidelines for systemic mastocytosis (version 1.2022 – April 14, 2022) recommend imatinib (only if *KIT D816V* mutation negative or known; well differentiated systemic mastocytosis; eosinophilia is present with *FIP1L1-PDGFRA* fusion gene) as a single agent for aggressive systemic mastocytosis (useful in certain circumstances) [category 2A].[11]
- **Melanoma:** The NCCN guidelines on cutaneous melanoma (version 3.2022 – April 11, 2022) cite imatinib as useful in certain scenarios as systemic therapy (second-line or subsequent therapy) for metastatic or unresectable disease such as for tumors with activating mutations of KIT.[12]
- **Myelodysplastic Syndromes (MDS):** The NCCN guidelines on MDS (version 3.2022 – January 13, 2022) note that data have demonstrated that patients with chronic myelomonocytic leukemia/myeloproliferative disease who have *ETV6-PDGFRβ* fusion genes may respond well to imatinib.[13]
- **Myeloid/Lymphoid Neoplasms with Eosinophilia:** The NCCN guidelines for myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase fusion genes (version 1.2022 – April 14, 2022) note that imatinib is a TKI with activity against ABL1 rearrangements or in the situation where the tumor has an *FIP1L1-PDGFRA* or *PDGFRB* rearrangement (category 2A).[14]
- **Soft Tissue Sarcomas:** The NCCN guidelines on soft tissue sarcoma (version 1.2022 – March 29, 2022) state that for desmoid tumors (aggressive fibromatosis) imatinib is a preferred regimen (category 2A) if time to response is critical. Nexavar® (sorafenib tablets) is a category 1 recommended therapy. Other regimens cited as category 2A recommendations include liposomal doxorubicin, doxorubicin with or without dacarbazine, and Votrient® (pazopanib tablets). For dermatofibrosarcoma protuberans with fibrosarcomatous transformation, imatinib is the one preferred regimen listed (category 2A). Turalio® (pexidartinib capsules) is the preferred agent for pigmented villonodular synovitis/tenosynovial giant cell tumor (category 1) [preferred]. Systemic

therapies that are listed as useful in certain circumstances are imatinib (category 2A) and Tasigna (category 2A).[15]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of imatinib tablets. All approvals are provided for the duration noted below.

Documentation: None.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of imatinib is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Acute Lymphoblastic Leukemia.** Approve for 1 year if the patient has Philadelphia chromosome-positive acute lymphoblastic leukemia.

2. **Aggressive Systemic Mastocytosis.** Approve for 1 year if the patient is ≥ 18 years of age.

3. **Chronic Myeloid Leukemia.** Approve for 1 year if the patient has Philadelphia chromosome-positive chronic myeloid leukemia.

4. **Dermatofibrosarcoma Protuberans.** Approve for 1 year if the patient is ≥ 18 years of age.

5. **Gastrointestinal Stromal Tumors.** Approve for 1 year.

6. **Hypereosinophilic Syndrome and/or Chronic Eosinophilic Leukemia.** Approve for 1 year if the patient is ≥ 18 years of age.

7. **Myelodysplastic/Myeloproliferative Disease.** Approve for 1 year if the patient meets the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Condition is associated with platelet-derived growth factor receptor (*PDGFR*) gene rearrangements.

Other Uses with Supportive Evidence

8. **Chordoma.** Approve for 1 year.

9. **Fibromatosis (Desmoid Tumors).** Approve for 1 year if the patient has advanced, aggressive, or unresectable fibromatosis (desmoid tumors).

10. **Graft-Versus-Host Disease, Chronic.** Approve for 1 year if the patient has tried at least one conventional systemic treatment for graft-versus-host disease.

Note: Examples include corticosteroids (methylprednisolone, prednisone); cyclosporine; tacrolimus; mycophenolate mofetil; Imbruvica (ibrutinib capsules and tablets); low-dose methotrexate; sirolimus; Rezurock (belumosudil tablets); and Jakafi (ruxolitinib tablets).

11. Kaposi Sarcoma. Approve for 1 year if the patient meets the following (A and B):
- **A)** Patient has tried at least one medication; AND
  Note: Examples include liposomal doxorubicin, paclitaxel, Pomalyst (pomalidomide capsules), lenalidomide, etoposide, and Thalomid (thalidomide capsules).
- **B)** Patient has relapsed or refractory disease.

12. Metastatic Melanoma. Approve for 1 year if the patient has c-Kit-positive advanced/recurrent or metastatic melanoma.

13. Myeloid/Lymphoid Neoplasms with Eosinophilia. Approve for 1 year if the patient meets the following criteria (A and B):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets one of the following (i or ii)
  - **i.** The tumor has an *ABL1* rearrangement; OR
  - **ii.** The tumor has an *FIP1L1-PDGFRA* or *PDGFRB* rearrangement.

14. Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor. Approve for 1 year if the patient meets one of the following (A or B):
- **A)** Patient has tried Turalio (pexidartinib capsules); OR
- **B)** Patient cannot take Turalio, according to the prescriber.
  Note: Examples of reasons for not being able to take Turalio include patients with elevated liver enzymes or concomitant use of medications that are associated with hepatotoxicity.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of imatinib is not recommend in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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