PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Imatinib (Gleevec) [imatinib mesylate tablets for oral use – Novartis, generic]

DATE REVIEWED: 04/01/2020

OVERVIEW

Imatinib, a tyrosine kinase inhibitor (TKI), is indicated for the treatment of: newly-diagnosed adult and pediatric patients with Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP); Ph+ CML in blast crisis (BC), accelerated phase (AP) or in CP after failure of interferon-alpha therapy; adult patients with relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL); pediatric patients with newly-diagnosed Ph+ positive ALL in combination with chemotherapy, adults with myelodysplastic/myeloproliferative disease (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene rearrangements; adults with aggressive systemic mastocytosis (ASM); adults with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL); adults with unresectable, recurrent, and/or metastatic dermatofibrosarcoma protuberans (DFSP); patients with Kit (CD 117) positive unresectable and/or metastatic gastrointestinal stromal tumors (GIST); and as adjuvant treatment of adults following resection of Kit (CD117) positive GIST.[1] Imatinib is also available as a generic but it does not have any indications regarding GIST, now the indication for use in pediatric patients with ALL.[2] Currently, there are four other tyrosine kinase inhibitors (TKIs) approved for the treatment of Ph+ CML: Tasigna® (nilotinib capsules), Sprycel® (dasatinib tablets), Bosulif® (bosutinib tablets), and Iclusig® (ponatinib tablets).[3-6] These agents are indicated for the treatment of Ph+ CML in various phases. Iclusig is approved for patients with T315I-positive CML and in adult patients with CML for whom no other TKI therapy is indicated.[6] Sprycel also has FDA-approved indications regarding ALL.[3]

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for CML (version 3.2020 – January 30, 2020) state that for patients with CP CML with a low-risk score, the primary treatment recommended includes a first-generation TKI (Gleevec or generic imatinib 400 mg QD [Category 1]), or a second-generation TKI (Bosulif 400 mg QD [Category 1], Sprycel 100 mg QD [Category 1], or Tasigna 300 mg BID [Category 1]).[7] For patients with CP CML with an intermediate- or high-risk score, a second-generation TKI is preferred (Bosulif 400 mg QD [Category 1], Sprycel 100 mg QD [Category 1], or Tasigna 300 mg BID [Category 1]). A first-generation TKI (Gleevec or generic imatinib 400 mg QD) is an alternative [Category 2A]. Iclusig is an option for patients with a T315I mutation and for with disease that has not responded to multiple TKIs or in whom another TKI is not indicated.

The NCCN guidelines for ALL (adults and adolescent young adults) [version 1.2020 – January 15, 2020][8] and Pediatric ALL (pediatric and adolescent young adults) [version 2.2020 – November 25, 2019][9] recommend imatinib in a variety of clinical scenarios including induction therapy, maintenance, relapsed or refractory ALL and for use in specific mutations.

The NCCN guidelines on dermatofibrosarcoma protuberans (version 1.2020 – October 2, 2019)[10] recommend to consider imatinib in certain cases such as where disease is unresectable, or unacceptable functional or adverse cosmetic outcomes may occur with resection. Of note, the guidelines state that because tumors lacking the t(17;22) translocation may not respond to imatinib, molecular analysis of a tumor using cytogenetics may be useful before initiating imatinib therapy.

The NCCN guidelines on soft tissue sarcoma (version 6.2019 – February 10, 2020) address GIST.[11] GISTs can occur anywhere along the gastrointestinal (GI) tract, but most commonly occur in the

stomach and small intestine due to activating mutations in KIT (CD117). Surgery is the primary treatment for patients with resectable GIST; however, this is not always curative or cannot be done. Imatinib is recommended in various clinical settings, including preoperatively, postoperatively, as a primary therapy, as well as for patients with locally advanced or previously unresectable tumors. Imatinib is considered a primary therapy for metastatic GIST.

The NCCN guidelines on myelodysplastic syndromes (MDS) [version 2.2020 – February 28, 2020] note that data have demonstrated that patients with chronic myelomonocytic leukemia (CMML)/myeloproliferative disease (MPD) who have PDGFRβ fusion genes may respond well to imatinib.[12]

The NCCN guidelines for systemic mastocytosis (version 2.2019 – September 20, 2018) recommend imatinib (only if KITD816V mutation negative or unknown or if eosinophilia is present with FIP1L1-PDGFRA fusion gene).[13]

The NCCN guidelines for acquired immune deficiency syndrome (AIDS)-Related Kaposi Sarcoma (version 1.2020 – February 12, 2020) recommended imatinib for subsequent systemic therapy options for relapsed/refractory therapy.[14] First-line systemic therapy options include liposomal doxorubicin (preferred), and paclitaxel. Other subsequent systemic therapy options for relapsed/refractory therapy are also cited (e.g., Pomalyst® [pomalidomide capsules] {preferred], Revlimid® [lenalidomide capsules], Thalomid [thalidomide capsules]).

The NCCN guidelines on bone cancer (version 1.2020 – August 12, 2019) state that imatinib, either as monotherapy or in combination with cisplatin or Rapamune® (sirolimus tablets), is recommended for treatment of chordoma.[15]

The NCCN guidelines on soft tissue sarcoma (version 6.2019 – February 10, 2020) have included non-steroidal anti-inflammatory drugs (NSAIDs), hormonal or biologic agents (tamoxifen, Fareston® [toremifene tablets], or low-dose interferon), chemotherapy (methotrexate and vinorelbine, doxorubicin-based regimens), and TKIs (imatinib and Nexavar® [sorafenib tablets]) as options for systemic therapy for patients with advanced or unresectable desmoid tumors (aggressive fibromatosis).[11]

The NCCN has guidelines regarding hematopoietic cell transplantation (version 1.2020 – October 30, 2019) that address GVHD.[16] Imatinib is cited as one of many therapies recommended for steroid-refractory, chronic GVHD. Some other agents include Imbruvica® (ibrutinib tablets and capsules), low-dose methotrexate, sirolimus, mycophenoate mofetil, Jakafi® (ruxolitinib tablets).

The NCCN guidelines on cutaneous melanoma (version 1.2020 – December 19, 2019) cite imatinib as useful in certain scenarios as systemic therapy for metastatic or resectable disease such as for tumors with activating mutations of KIT.[17]

The NCCN guidelines on soft tissue sarcoma (version 6.2019 – February 10, 2020) cite Turalio (pexidartinib capsules) [category 1] and imatinib (category 2A) as systemic therapies with activity in PVNS/TGCT.[11]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Gleevec and generic imatinib mesylate tablets. If the patient does not meet the criteria regarding brand Gleevec, auto-approvals will

be given for generic imatinib mesylate tablets when patients meet conditions for coverage of imatinib as defined in this policy.

Automation: None.

Documentation: In the imatinib (Gleevec) PA, documentation is required for use of generic imatinib as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts and/or other information.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Gleevec and generic imatinib mesylate tablets are recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Acute Lymphoblastic Leukemia (ALL) That is Philadelphia Chromosome Positive (Ph+).** Approve for 3 years if the patient meets one of the following criteria (A or B):
   - **A)** Generic imatinib mesylate tablets are requested; OR
   - **B)** If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

2. **Chronic Myeloid Leukemia (CML) That is Philadelphia Chromosome Positive (Ph+).** Approve for 3 years if the patient meets one of the following criteria (A or B):
   - **A)** Generic imatinib mesylate tablets are requested; OR
   - **B)** If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

3. **Dermatofibrosarcoma Protuberans (DFSP).** Approve for 3 years if the patient meets one of the following criteria (A or B):
   - **A)** Generic imatinib mesylate tablets are requested; OR
   - **B)** If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

4. **Gastrointestinal Stromal Tumors (GIST).** Approve for 3 years if the patient meets one of the following criteria (A or B):
   - **A)** Generic imatinib mesylate tablets are requested; OR
   - **B)** If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the

bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

5. **Hypereosinophilic Syndrome (HES) and/or Chronic Eosinophilic Leukemia (CEL).** Approve for 3 years if the patient meets one of the following criteria (A or B):
   A) Generic imatinib mesylate tablets are requested; OR
   B) If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

6. **Aggressive Systemic Mastocytosis (ASM).** Approve for 3 years if the patient meets one of the following criteria (A or B):
   A) Generic imatinib mesylate tablets are requested; OR
   B) If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

7. **Myelodysplastic/Myeloproliferative Disease (MDS/MPD) [e.g., polycythemia vera, myelofibrosis].** Approve for 3 years if the patient meets the following criteria (A and B):
   A) The condition is associated with platelet-derived growth factor receptor (PDGFR) gene rearrangements; AND
   B) The patient meets one of the following criteria (i or ii):
      i. Generic imatinib mesylate tablets are requested; OR
      ii. If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

Other Uses with Supportive Evidence

8. **Acquired Immune Deficiency Syndrome (AIDS)-Related Kaposi's Sarcoma.** Approve for 3 years if the patient meets the following criteria (A, B and C):
   - **A)** The patient has tried at least one regimen or therapy; AND
     Note: Examples include liposomal doxorubicin, paclitaxel, Pomalyst® (pomalidomide capsules), Revlimid® (lenalidomide capsules), etoposide, and Thalomid® (thalidomide capsules).
   - **B)** The patient has relapsed or refractory disease; AND
   - **C)** The patient meets one of the following criteria (i or ii):
     - **i.** Generic imatinib mesylate tablets are requested; OR
     - **ii.** If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

9. **Chordoma.** Approve for 3 years if the patient meets one of the following criteria (A or B)
   - **A)** Generic imatinib mesylate tablets are requested; OR
   - **B)** If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

10. **Fibromatosis (Desmoid Tumors).** Approve for 3 years if the patient meets the following criteria (A and B).
    - **A)** The patient has advanced or unresectable fibromatosis (desmoid tumors); AND
    - **B)** The patient meets one of the following criteria (i or ii):
      - **i.** Generic imatinib mesylate tablets are requested; OR
      - **ii.** If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

11. **Graft Versus Host Disease (GVHD), Chronic.** Approve for 1 year if the patient meets the following criteria (A and B).
    - **A)** The patient has tried at least one conventional systemic treatment for graft versus host disease; AND
      Note: Examples include corticosteroids (methylprednisolone, prednisone); cyclosporine; tacrolimus; mycophenolate mofetil; Imbruvica® (ibrutinib capsules and tablets); low-dose methotrexate; sirolimus; and Jakafi® (ruxolitinib tablets).
    - **B)** The patient meets one of the following criteria (i or ii):
      - **i.** Generic imatinib mesylate tablets are requested; OR
      - **ii.** If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

12. **Metastatic Melanoma:** Approve for 3 years if the patient meets the following criteria (A and B).
    - **A)** The patient has c-Kit-positive advanced/recurrent or metastatic melanoma; AND
    - **B)** The patient meets one the following criteria (i or ii):
        - **i.** Generic imatinib mesylate tablets are requested; OR
        - **ii.** If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

13. **Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor (PVNS/TGCT).** Approve for 3 years if the patient meets both of the following criteria (A and B):
    - **A)** The patient meets one of the following (i or ii):
        - **i.** The patient has tried Turalio (pexidartinib capsules); OR
        - **ii.** According to the prescriber, the patient cannot take Turalio.

        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; AND
    - **B)** The patient meets one of the following (i or ii):
        - **i.** Generic imatinib mesylate tablet are requested; OR
        - **ii.** If brand Gleevec is prescribed, the patient has tried generic imatinib mesylate tablets AND cannot take generic imatinib mesylate tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction **[documentation required]**.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Imatinib has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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

1. Gleevec® tablets [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals, Inc.; July 2018.
2. Imatinib tablets [prescribing information]. Cranbury, NJ and Jacksonville, FL: Sun Pharmaceuticals and Ranbaxy Pharmaceuticals; October 2016.
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