PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 05/31/2023

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Imatinib, a tyrosine kinase inhibitor (TKI), is indicated for the following uses:[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**, without the D816V c-Kit mutation or with unknown c-Kit mutational status, in adults.
- **Chronic myeloid leukemia (CML)**, newly diagnosed and Ph+, chronic phase in adult and pediatric patients.
- **CML**, Ph+, in blast phase, accelerated phase, or in chronic phase in patients 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**, in adults who have the *FIP1L1-PDGFR* alpha fusion kinase (mutation analysis or fluorescence in situ hybridization demonstration of CICH2 allele deletion) and

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):

- **ALL:** NCCN guidelines for adults and adolescents (version 1.2022 – April 4, 2022) recommend imatinib for Ph+ disease in many different clinical circumstances (e.g., induction, consolidation therapy, maintenance, or relapsed or refractory disease) [category 2A].[3] NCCN guidelines for pediatric ALL (version 2.2023 – March 10, 2023) feature imatinib prominently (category 2A) in a variety of clinical scenarios.[4]
- **Bone Cancer:** NCCN guidelines (version 3.2023 – April 4, 2023) recommend imatinib either as monotherapy or as "other recommended regimens" or in combination with cisplatin or Rapamune® (sirolimus tablets) for chordoma as "useful in certain circumstances" (both category 2A).[5]
- **CML:** NCCN guidelines (version 2.2023 – April 13, 2023) state that for patients with chronic phase CML with a low-risk score, the primary treatment recommendations includes a first-generation TKI (imatinib) 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, Sprycel, or Tasigna [all category 1]); imatinib is an alternative (category 2A); imatinib is also recommended for other clinical scenarios (category 2A).
- **Dermatofibrosarcoma Protuberans:** NCCN guidelines (version 1.2023 – December 8, 2022) recommend to consider neoadjuvant imatinib for unresectable/borderline disease (category 2A) and for recurrent or metastatic disease in cases where the disease is unresectable, or unacceptable functional or adverse cosmetic outcomes may occur with resection (category 2A).[7]
- **GIST:** NCCN guidelines (version 1.2023 – March 13, 2023) recommend imatinib as 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 recommended in other clinical scenarios (e.g., neoadjuvant and adjuvant therapy)[category 2A].[8]
- **Graft-Versus-Host Disease (GVHD):** NCCN guidelines for hematopoietic cell transplantation (version 1.2023 – March 31, 2023) address GVHD.[9] Imatinib is cited as one of many therapies recommended for steroid-refractory, chronic GVHD (category 2A).
- **Kaposi Sarcoma:** NCCN guidelines (version 1.2023 – December 20, 2022) recommend imatinib for subsequent systemic therapy for relapsed/refractory therapy as "useful in certain circumstances".[10] First-line systemic therapy options are liposomal doxorubicin as "preferred regimen" and paclitaxel.
- **Melanoma: Cutaneous:** NCCN guidelines (version 2.2023 – March 10, 2023) recommend imatinib as second-line or subsequent therapy for

metastatic or unresectable disease for tumors with activating mutations of *KIT* as "useful in certain circumstances" (category 2A).[11]

- **Myelodysplastic Syndromes:** NCCN guidelines (version 1.2023 – September 12, 2022) note that data have demonstrated that patients with chronic myelomonocytic leukemia who have *PDGFRβ* gene rearrangement at 5q32 may respond well to imatinib.[12]
- **Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions:** NCCN guidelines (version 1.2023 – May 19, 2023) recommend imatinib for patients with *ABL1* rearrangements in the chronic phase or blast phase (category 2A).[13] Imatinib is also recommended for certain situations where the tumor has an FIP1L1-PDGFRA or PDGFRB rearrangement (category 2A). Imatinib is also recommended for treatment in combination with ALL- or acute myeloid leukemia-type induction chemotherapy followed by allogeneic hematopoietic stem cell transplantation (if eligible) for lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and ABL1 rearrangement in blast phase (category 2A).
- **Soft Tissue Sarcomas:** NCCN guidelines (version 2.2023 – April 25, 2023) recommend imatinib for desmoid tumors (aggressive fibromatosis) as a "preferred regimen" (category 2A). For dermatofibrosarcoma protuberans with fibrosarcomatous transformation, imatinib is recommended as a "preferred regimen" (category 2A). For pigmented villonodular synovitis/tenosynovial giant cell tumor, imatinib is recommended as "useful in certain circumstances" (category 2A).[14]
- **Systemic Mastocytosis:** NCCN guidelines (version 1.2023 – May 24, 2023,) recommend imatinib (for *KIT* D816V mutation negative or unknown; well differentiated systemic mastocytosis; eosinophilia is present with *FIP1L1-PDGFRA* fusion gene) for aggressive systemic mastocytosis as "useful in certain circumstances" (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.

- **Gleevec® (imatinib tablets - Novartis, generic)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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 criteria (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) The condition is associated with platelet-derived growth factor receptor (*PDGFR*) gene rearrangements.

Other Uses with Supportive Evidence

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

9. **Desmoid Tumors (Aggressive Fibromatosis.** Approve for 1 year

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, tablets, and oral suspension); low-dose methotrexate; sirolimus; Rezurock (belumosudil tablets); and Jakafi (ruxolitinib tablets).

11. **Kaposi Sarcoma.** Approve for 1 year if the patient meets the following criteria (A, B and C):
    A) Patient is ≥ 18 years of age; AND
    B) Patient has tried at least one medication; AND
    Note: Examples include liposomal doxorubicin, paclitaxel, Pomalyst (pomalidomide capsules), lenalidomide, etoposide, and Thalomid (thalidomide capsules).
    C) Patient has relapsed or refractory disease.

12. **Melanoma, Cutaneous.** Approve for 1 year if the patient meets the following criteria (A, B, C, and D):
    A) Patient is ≥ 18 years of age; AND
    B) Patient has metastatic or unresectable disease; AND
    C) Patient has an activating *KIT* mutation; AND
    D) Patient has tried at least one systemic regimen.

Note: Examples of a systemic regimen include: Opdivo (nivolumab intravenous infusion) + Yervoy (ipilimumab intravenous infusion), Opdivo + Opdualag (nivolumab/relatlimab-rmbw intravenous infusion), Keytruda (pembrolizumab intravenous infusion), Opdivo, Tafinlar (dabrafenib capsules) + Mekinist (trametinib tablets), Zelboraf (vemurafenib tablets) + Cotellic (cobimetinib tablets), Braftovi (encorafenib capsules) + Mektovi (binimetinib tablets).

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 criteria (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 criteria (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 COVERED

- **Gleevec® (imatinib tablets(Novartis, generic)**

is(are) considered experimental, investigational, or unproven for ANY other use(s) (criteria will be updated as new published data are available).

REFERENCES

1. Gleevec® tablets [prescribing information]. East Hanover, NJ: Novartis; March 2022.
2. Imatinib tablets [prescribing information]. Cranbury, NJ: Sun; April 2022.
3. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 1.2022 – April 4, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 25, 2023.
4. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 2.2023 – March 10, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 25, 2023.
5. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 3.2023 – April 4, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 25, 2023.
6. The NCCN Chronic Myeloid Leukemia Clinical Practice Guidelines in Oncology (version 2.2023 – April 13, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 25, 2023.
7. The NCCN Dermatofibrosarcoma Protuberans Clinical Practice Guidelines in Oncology (version 1.2023 – December 8, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 12, 2023.

8. The NCCN Gastrointestinal Stromal Tumors Clinical Practice Guidelines in Oncology (version 1.2023 – March 13, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 12, 2023.
9. The NCCN Hematopoietic Cell Transplantation (HCT) Clinical Practice Guidelines in Oncology (version 1.2023 – March 31, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 25, 2023.
10. The NCCN Kaposi Sarcoma Clinical Practice Guidelines in Oncology (version 1.2023 – December 20, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 25, 2023.
11. The NCCN Cutaneous Melanoma Clinical Practice Guidelines in Oncology (version 2.2023 – March 10, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 12, 2023.
12. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 1.2023 – September 12, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 25, 2023.
13. The NCCN Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions Clinical Practice Guidelines in Oncology (version 1.2023 – May 19, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 25, 2023.
14. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 2.2023 – April 25, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 25, 2023.
15. The NCCN Systemic Mastocytosis Clinical Practice Guidelines in Oncology (version 1.2023 – May 24, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 25, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	The name of the policy was changed to reflect generic availability. **Graft-Versus-Host Disease, Chronic:** Rezurock (belumosudil tablets) was added to the Note as an example of one of the agents listed that meets the requirement that the patient has tried one conventional system treatment for the condition.	05/04/2022
Selected Revision	**Acute Lymphoblastic Leukemia:** Approval duration changed from 3 years to 1 year. **Aggressive Systemic Mastocytosis:** Approval duration changed from 3 years to 1 year. **Chronic Myeloid Leukemia:** Approval duration changed from 3 years to 1 year. **Dermatofibrosarcoma Protuberans:** Approval duration changed from 3 years to 1 year. **Gastrointestinal Stromal Tumors:** Approval duration changed from 3 years to 1 year. **Hypereosinophilic Syndrome and/or Chronic Eosinophilic Leukemia:** Approval duration changed from 3 years to 1 year. **Myelodysplastic/Myeloproliferative Disease:** Approval duration changed from 3 years to 1 year. **Chordoma:** Approval duration changed from 3 years to 1 year. **Fibromatosis (Desmoid Tumors):** Approval duration changed from 3 years to 1 year. **Kaposi Sarcoma:** Approval duration changed from 3 years to 1 year. **Metastatic Melanoma:** Approval duration changed from 3 years to 1 year. **Myeloid/Lymphoid Neoplasms with Eosinophilia:** Approval duration changed from 3 years to 1 year.	06/22/2022

	Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor: Approval duration changed from 3 years to 1 year.	
Annual Revision	**Desmoid tumors (aggressive fibromatosis):** The "fibromatosis (desmoid tumors) indication was reworded to "Desmoid tumors (aggressive fibromatosis)." The requirement that the patient has advanced or unresectable disease was removed. **Kaposi Sarcoma:** The requirement that the patient is ≥ 18 years of age was added. **Melanoma, Cutaneous:** The "metastatic melanoma" indication was reworded to "melanoma, cutaneous." The criterion that the patient has "advanced/recurrent" disease was changed to "unresectable." The criterion that the patient has "c-kit-positive melanoma" was reworded to patient has an "activating *KIT* mutation." The following criteria were added: Patient is ≥ 18 years of age; and patient has tried at least one systemic regimen with a note with examples of a systemic regimen.	05/31/2023