Clinical Policy: Imatinib (Gleevec)

Reference Number: AZ.CP.PHAR.65
Effective Date: 04.01.21
Last Review Date: 04.21 Revision Log
Line of Business: Arizona Medicaid (AzCH-CCP and Care1st)

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Imatinib mesylate (Gleevec®) is a kinase inhibitor.

FDA Approved Indication(s)

Gleevec is indicated for the treatment of:

- Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase
- Patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy
- Adult patients with relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL)
- Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy
- Adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene rearrangements
- Adult patients with aggressive systemic mastocytosis (ASM) without the D816V c-Kit mutation or with c-Kit mutational status unknown
- 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
- Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP)
- Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)
- Adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positive GIST

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Arizona Complete Health-Complete Care Plan and Care1st that Gleevec is **medically necessary** when the following criteria are met:

CLINICAL POLICY
Imatinib

I. Initial Approval Criteria

A. FDA Labeled Indications (must meet all)**:**

1. Diagnosis of one of the following:
   a. Ph+ (BCR-ABL1-positive) CML or Ph+ (BCR-ABL-positive) ALL;
   b. MDS/MPD and member meets one of the following (i or ii):
      i. Disease is positive for a PDGFR mutation;
      ii. If the member has a diagnosis of chronic myelomonocytic leukemia (an MDS/MPD subtype), disease is positive for either a 5q31-33 or a PDGFR mutation;
   c. ASM and member meets one of the following (i or ii):
      i. Disease is negative for the D816V c-KIT mutation;
      ii. c-Kit mutational status is unknown;
   d. HES/CEL, DFSP, or GIST (a soft tissue sarcoma);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. For generic imatinib, member must use brand Gleevec, unless contraindicated or clinically significant adverse effects are experienced;
4. Age ≥ 18 years if the diagnosis is MDS/MPD, ASM, DFSP, or GIST;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed any of the following (i, ii, or iii):
      i. 800 mg per day: CML, DFSP, GIST;
      ii. 600 mg per day: ALL;
      iii. 400 mg per day: MDS/MPD, ASM, HES/CEL;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Off-Label Indications (must meet all)**:**

1. Diagnosis of one of the following:
   a. AIDS-related Kaposi sarcoma (KS), and both of the following (i and ii):
      i. Imatinib is prescribed in combination with antiretroviral therapy;
      ii. Failure of liposomal doxorubicin and paclitaxel, unless clinically significant adverse effects are experienced or both are contraindicated;
   b. Recurrent conventional or chondroid chordoma (a bone cancer);
   c. KIT-positive melanoma as second-line or subsequent therapy;
   d. Desmoid tumor (also known as aggressive fibromatosis, a soft tissue sarcoma);
   e. Myeloid/lymphoid neoplasm with eosinophilia and tyrosine kinase fusion genes;
   f. Pigmented villonodular synovitis/tenosynovial giant cell tumor (a soft tissue sarcoma) that is associated with severe morbidity or functional limitations and not amenable to improvement with surgery;
   g. Chronic graft-versus-host disease - as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options;

2. Prescribed by or in consultation with one of the following specialists (a or b):
   a. AIDS-related KS: an oncologist or immunologist;
   b. All other diagnoses: an oncologist;
3. Age ≥ 18 years;
4. For generic imatinib, member must use brand Gleevec, unless contraindicated or clinically significant adverse effects are experienced ;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): AZ.CP.PMN.53 for Arizona Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Gleevec for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For generic imatinib, member must use brand Gleevec, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed any of the following (i, ii, or iii):
      i. 800 mg per day: CML, DFSP, GIST;
      ii. 600 mg per day: ALL;
      iii. 400 mg per day: MDS/MPD, ASM, HES/CEL;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
      **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): AZ.CP.PMN.53 for Arizona Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – AZ.CP.PMN.53 for Arizona Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
ASM: aggressive systemic mastocytosis
CEL: chronic eosinophilic leukemia
CML: chronic myeloid leukemia
DFSP: dermatofibrosarcoma protuberans
FDA: Food and Drug Administration
GIST: gastrointestinal stromal tumor
HES: hypereosinophilic syndrome
KS: Kaposi sarcoma
MDS: myelodysplastic syndromes
MPD: myeloproliferative diseases
PDGFR: platelet-derived growth factor receptor
Ph+: Philadelphia chromosome positive
PVNS/TGCT: pigmented villonodular synovitis/tenosynovial giant cell tumor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
liposomal doxorubicin (Doxil®, Lipodox® 50)	**AIDS-related KS** 20 mg/m^2 IV every 2-3 weeks with a cumulative lifetime dose of 400-450 mg/m^2 due to cardiotoxicity	See regimen
paclitaxel	**AIDS-related KS** 135 mg/m^2 IV every 3 weeks **or** 100 mg/m^2 every 2 weeks	See regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CML	Adult: 400-600 mg/day PO for chronic phase 600-800 mg/day PO for accelerated phase or blast crisis (800 mg given as 400 BID) Pediatric: 340 mg/m2/day PO for chronic phase	Adult: 800 mg/day Pediatric: 600 mg/day

Indication	Dosing Regimen	Maximum Dose
ALL	Adult: 600 mg/day PO for relapsed / refractory Ph+ ALL Pediatric: 340 mg/m^2/day PO in combination with chemotherapy for newly diagnosed Ph+ ALL	Adult: 600 mg/day Pediatric: 600 mg/day
MDS/MPD	Adult: 400 mg/day PO	Adult: 400 mg/day
ASM	Adult: 100-400 mg/day PO	Adult: 400 mg/day
HES/CEL	Adult: 100-400 mg/day PO	Adult: 400 mg/day
DESP	Adult: 800 mg/day PO	Adult: 800 mg/day
GIST	Adult: 400-800 mg/day PO for metastatic or unresectable GIST (800 mg given as 400 BID) and 400 mg/day PO or adjuvant GIST	Adult: 800 mg/day; 400 mg/day for adjuvant GIST

**Co-administration with strong CYP3A4 inducers may require an increased dose beyond that listed in the table. Examples of strong CYP3A4 inducers include dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifampacin, phenobarbital.*

VI. Product Availability

Tablets: 100 mg, 400 mg

VII. References

1. Gleevec Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2020. Available at https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/gleevec_tabs.pdf. Accessed February 21, 2021.
2. Imatinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 21, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created from CP.PHAR.65 Imatinib (Gleevec) Q2 2021 annual review version for Arizona Medicaid LOB due to AHCCCS preferred Oral Oncology – Oral – Hematologic update effective 4/1/21: brand name Gleevec is moved from non-preferred to preferred, generic is moved from preferred to non-preferred.	03.19.21	04.21
Added Care1st logo. Added verbiage to specify that criteria also applies to Care1st.	5.10.21	04.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.