Clinical Policy: Nilotinib (Tasigna)

Reference Number: CP.PHAR.76
Effective Date: 09.01.11
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Nilotinib (Tasigna®) is a kinase inhibitor.

FDA Approved Indication(s)

Tasigna is indicated for the treatment of:

- Adult and pediatric patients greater than or equal to 1 year of age with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP).*
- Adult patients with Ph+ CML-CP and accelerated phase (Ph+ CML-AP) CML resistant or intolerant to prior therapy that included imatinib.
- Pediatric patients greater than or equal to 1 year of age with Ph+ CML-CP and CML-AP resistant or intolerant to prior tyrosine-kinase inhibitor (TKI) therapy.

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 health plans affiliated with Centene Corporation® that Tasigna is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Myeloid Leukemia (must meet all):

1. Diagnosis of Ph+ (BCR-ABL1-positive) CML;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member does not have the following mutations: T315I, Y253H, E255K/V, F359V/C/I;
4. One of the following (a or b):
   a. Member has contraindication, intolerance, or disease progression on imatinib;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix D)*;
5. For brand Tasigna requests, member must use generic nilotinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 800 mg per day;
   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:
Medicaid/HIM - 6 months
Commercial - 12 months or duration of request, whichever is less

B. Acute Lymphoblastic Leukemia (off-label) (must meet all)**:**
1. Diagnosis of Ph+ (BCR-ABL1-positive) acute lymphoblastic leukemia (ALL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member does not have the following mutations: T315I, Y253H, E255K/V, F359V/C/I , G250E;
4. One of the following (a or b):
   a. Member has contraindication, intolerance, or disease progression on imatinib;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix D)*;
5. For brand Tasigna requests, member must use generic nilotinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. 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:
Medicaid/HIM - 6 months
Commercial - 12 months or duration of request, whichever is less

C. Gastrointestinal Stromal Tumor (off-label) (must meet all)**:**
1. Diagnosis of gastrointestinal stromal tumor (GIST, a soft tissue sarcoma);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Failure of imatinib, Quinlock™, Sutent®, Sprycel ®, or Stivarga® unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required.*
5. For brand Tasigna requests, member must use generic nilotinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. 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:
Medicaid/HIM - 6 months
Commercial - 12 months or duration of request, whichever is less

D. Myeloid/Lymphoid Neoplasms (off-label) (must meet all)**:**
1. Diagnosis of lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and ABL1 rearrangement in blast or chronic phase;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. Member has contraindication, intolerance, or disease progression on imatinib;

b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix D)*;

5. For brand Tasigna requests, member must use generic nilotinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. 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:
Medicaid/HIM - 6 months
Commercial - 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for 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 Tasigna for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Tasigna requests, member must use generic nilotinib, if available, 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 800 mg per day;
   b. New 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:
Medicaid/HIM - 6 months
Commercial - 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for 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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
CML: chronic myeloid leukemia
FDA: Food and Drug Administration
GIST: gastrointestinal stromal tumor
Ph+: positive Philadelphia chromosome

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
imatinib (Gleevec)	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 CML: Adult: 400-600 mg/day PO for chronic phase	800 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	600-800 mg/day PO for accelerated phase or blast crisis (800 mg given as 400 BID) Pediatric: 340 mg/m^2/day PO for chronic phase GIST: 400 mg PO QD to 800 PO BID MLNE: 100-400 mg PO QD [NCCN]	
Sutent (sunitinib)	GIST: 50 mg PO QD	50 mg/day
Stivarga (regorafenib)	GIST: 160 mg PO QD for the first 21 days of each 28-day cycle	160 mg/day
Quinlock (ripretinib)	GIST: 150 mg PO QD	150 mg/day
Sprycel (dasatinib)	GIST: 70 mg PO BID	140 mg/day

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

- Contraindication(s): hypokalemia, hypomagnesemia, long QT syndrome
- Boxed warning(s): QT prolongation, sudden death

Appendix D: States with Regulations against Redirections in Certain Oncology Settings

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to HIM requests only** For stage 4 metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Newly diagnosed Ph+ CML-CP	Adults: 300 mg PO BID	Adults: 600 mg/day Pediatrics: 800 mg/day

Indication	Dosing Regimen	Maximum Dose
	Pediatrics: 230 mg/m^2 PO BID, rounded to the nearest 50 mg dose (to a maximum single dose of 400 mg)	
Resistant/intolerant Ph+ CML-CP or Ph+ CML-AP	Adults: 400 mg PO BID Pediatrics: 230 mg/m^2 PO BID, rounded to the nearest 50 mg dose (to a maximum single dose of 400 mg)	Adults and pediatrics: 800 mg/day

VI. Product Availability

Capsules: 50 mg, 150 mg, 200 mg

VII. References

1. Tasigna Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2021. Available at: https://www.novartis.us/sites/www.novartis.us/files/tasigna.pdf. Accessed January 27, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed January 27, 2022.
3. National Comprehensive Cancer Network Guidelines. Chronic Myeloid Leukemia Version 2.2022. Available at https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Accessed January 27, 2022.
4. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia Version 4.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed January 27, 2022.
5. National Comprehensive Cancer Network Guidelines. Gastrointestinal Stromal Tumors (GISTs) Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf. Accessed January 27, 2022.
6. National Comprehensive Cancer Network Guidelines. Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf. Accessed January 27, 2022.
7. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 27, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
CML NCCN: 1) added "myeloid" to "As a single agent for accelerated or myeloid blast phase CML"; 2) "In combination with steroids as primary treatment for CML in lymphoid blast phase" is added; 3) "for relapse" is deleted from "post stem cell transplant therapy;" 4) CML positive for a F317L/V/I/C, T315A, or V299L mutation is added. Maximum dose added. Reasons to discontinue removed. Approval periods are lengthened from 3/6 to 6/12 months.	06.17	07.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: no significant changes; policies combined for Medicaid and Commercial; HIM line of business added; added age (not ALL) ; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; added continuity of care statement; references reviewed and updated.	02.13.18	05.18
No significant changes: new 50 mg capsule formulation added; pediatric labeled indications added for CML; CML age limit removed; package insert updated.	06.29.18	
2Q 2019 annual review: hematologist added to CML/ALL; references reviewed and updated.	02.19.19	05.19
2Q 2020 annual review: no significant changes; HIM nonformulary language removed; references reviewed and updated.	02.11.20	05.20
2Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	02.12.21	05.21
RT4: converted coverage of pediatric CML-AP from off-label to FDA-approved status.	10.07.21	
2Q 2022 annual review: modified commercial approval duration from length of benefit to "12 months or duration of request, whichever is less"; WCG.CP.PHAR.76 to be retired and approval durations consolidated to 6 months; per NCCN for CML and ALL added exclusions for mutations that are contraindicated, for GIST added Quinlock and Sprycel as additional prior therapy options, added criteria set for off-label use in myeloid/lymphoid neoplasms; for CML, AML, and myeloid/lymphoid neoplasms added that member has contraindication, intolerance, or disease progression on imatinib or allowed by-passing of redirection if state regulations do not allow step therapy in certain oncology settings; added generic redirection language per template for oral oncology products; references reviewed and updated.	01.27.22	05.22
Template changes applied to other diagnoses/indications.	10.12.22	

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.