Tasigna® (nilotinib)
(Oral)

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I. Length of Authorization [1]

Coverage will be provided for 6 months and may be renewed.

Patients with Ph+ CML-CP who have achieved a sustained molecular response should be evaluated for discontinuation after taking nilotinib for a minimum of 3 years. §

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Tasigna 50 mg capsules: 4 capsules per day
- Tasigna 150 mg capsules: 4 capsules per day
- Tasigna 200 mg capsules: 4 capsules per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- 800 mg per day

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **AND**
- Patient has a baseline QTc interval of ≤ 480 ms AND does not have a history of long QT-syndrome; **AND**

Universal Criteria [1]

- Patient does not have hypokalemia or hypomagnesemia; **AND**
- Patient will avoid concomitant use of all of the following:
    - Coadministration with strong CYP3A inhibitors (e.g., itraconazole, ketoconazole, clarithromycin, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

- Coadministration with strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
- Coadministration with proton pump inhibitors (PPIs), or if acid-reduction therapy is required, use of H2-receptor antagonists or antacids may be used at staggered administration times; **AND**
- Coadministration with drugs that prolong QT/QTc interval (e.g., amiodarone, sotalol, levofloxacin, venlafaxine, quetiapine, sumatriptan, etc.); **AND**

Chronic Myelogenous Leukemia (CML) † Φ [1,2,4,9-14]

- Patient has Philadelphia chromosome-positive (Ph+) or *BCR-ABL1* positive disease; **AND**
- Patient does not have any of the following *BCR-ABL1* mutations: T315I, Y253H, E255K/V, or F359V/C/I (****NOTE:** This does not apply to newly diagnosed chronic phase disease or continued therapy); **AND**
  - Patient is resistant, intolerant, or had an inadequate response to prior therapy consisting of a 3 month trial or longer with a tyrosine kinase inhibitor (e.g., imatinib, bosutinib, dasatinib, etc.) †; **AND**
    - Patient is at least 1 year of age; **AND**
    - Used as a single agent for chronic phase or accelerated phase disease; **OR**
  - Used as primary treatment †; **AND**
    - Used as single agent for newly diagnosed chronic phase disease in patients at least 1 year of age †; **OR**
    - Used as a single agent for accelerated or myeloid blast phase disease; **OR**
    - Used in combination with steroids for lymphoid blast phase disease; **OR**
    - Used in combination with induction chemotherapy for disease in lymphoid blast phase or myeloid blast phase; **OR**
  - Used as switch therapy ‡; **AND**
    - Patient received primary therapy with one of the following: imatinib, bosutinib, or dasatinib; **AND**
    - Patient has *BCR-ABL1* transcript levels:
      - >0.1% to 1% at 12 months (if treatment goal is treatment-free remission); **OR**
      - >1% to 10% at 12 months; **OR**
      - >10% at any response milestone; **OR**
  - Used as continued therapy ‡; **AND**
    - Patient has *BCR-ABL1* transcript levels:
      - ≤10% at any response milestone; **OR**
      - >10% at 3 months; **OR**
  - Used post-allogeneic hematopoietic stem cell transplant (HCT) ‡; **AND**

- Used for at least one year in patients with prior complete cytogenetic response (CCyR) for accelerated or blast phase disease; **OR**
- Used as follow-up therapy in patients with molecular relapse (BCR-ABL1 transcript positive) following CCyR; **OR**
- Used as follow-up therapy in patients with relapse or less than CCyR; **OR**

o Re-initiation of treatment †; **AND**

- Patient lost molecular response (MMR or MR4.0) after discontinuation of therapy with nilotinib

Acute Lymphoblastic Leukemia (ALL) ‡ [2,3,5]

- Patient has Philadelphia chromosome-positive (Ph+) B-ALL; **AND**
- Patient does not have any of the following BCR-ABL1 mutations: T315I, Y253H, E255K/V, F359V/C/I or G250E; **AND**
  - o Used for relapsed or refractory disease; **AND**
    - Used as a single agent; **OR**
    - Used in combination with an induction therapy not previously used; **OR**
    - Used in combination with inotuzumab ozogamicin; **OR**
    - Used in combination with blinatumomab; **OR**
  - o Used as maintenance therapy; **AND**
    - Used in combination with vincristine and prednisone with or without methotrexate and mercaptopurine for patients with negative minimal residual disease after complete response to induction therapy; **OR**
    - Used as a single agent post-hematopoietic stem cell transplant; **OR**
    - Used as a single agent for patients who are unfit for additional therapies; **OR**
  - o Used as consolidation therapy; **AND**
    - Patient has persistent/rising minimal residual disease following a complete response to induction therapy; **AND**
      - Used in combination with blinatumomab; **OR**
      - Used as a single agent for patients who are unfit for additional therapies; **OR**
    - Patient has negative minimal residual disease following a complete response to induction therapy; **AND**
      - Used in combination with blinatumomab for patients who are not candidates for multi-agent chemotherapy; **OR**
      - Used as a single agent for patients who are unfit for additional therapies; **OR**
  - o Patient is at least 15 years of age OR < 65 years of age without substantial comorbidities; **AND**

        - Used in a multiagent chemotherapy regimen for induction or consolidation therapy; **OR**
        - Used in combination with a corticosteroid for induction or; **OR**
        - Used in combination with vincristine and dexamethasone for induction therapy; **OR**
    - Patient is ≥ 65 years of age OR with substantial comorbidities; **AND**
        - Used as induction therapy as part of one of the following regimens:
            - As a single agent or in combination with a corticosteroid; **OR**
            - In combination with vincristine and dexamethasone; **OR**
            - In combination with a multiagent chemotherapy regimen

Gastrointestinal Stromal Tumors (GIST) ‡ [2,7,17]

- Patient has unresectable, recurrent/progressive, or metastatic disease; **AND**
    - Used as a single agent for disease that has progressed on prior treatment with approved therapies including each of the following: imatinib, sunitinib OR dasatinib, regorafenib, AND ripretinib; **OR**
- Used as reintroduction therapy as a single agent for palliation of symptoms in patients who previously tolerated nilotinib with an effective response

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes ‡ [2,15,16]

- Patient has eosinophilia and ABL1 rearrangement; **AND**
    - Patient chronic or blast phase myeloid or lymphoid neoplasms; **AND**
        - Used as a single agent; **OR**
    - Patient has blast phase lymphoid, myeloid, or mixed lineage neoplasms; **AND**
        - Used in combination with ALL- or AML-type induction chemotherapy followed by allogeneic HCT (if eligible)

Soft Tissue Sarcoma (STS) ‡ [2,6]

- Patient has pigmented villonodular synovitis/tenosynovial giant cell tumor (PVNS/TGCT); **AND**
- Used as single-agent therapy

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-4,6]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status

etc. identified in Section III; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: electrolyte abnormalities (hypophosphatemia, hypokalemia, hyperkalemia, hypocalcemia, hyponatremia), myelosuppression (neutropenia, thrombocytopenia, anemia), QT prolongation, cardiac and arterial vascular occlusive events, pancreatitis and elevated serum lipase, hepatotoxicity (severe changes in liver function tests), tumor lysis syndrome, hemorrhage, fluid retention, growth retardation in pediatric patients, etc. **AND**

Acute Lymphoblastic Leukemia (ALL)

- Treatment response or stabilization of disease as indicated by CBC, bone marrow cytogenic analysis, QPCR, or FISH

Chronic Myelogenous Leukemia (CML)

- Re-initiation of treatment:
  - Patient lost molecular response (MMR or MR4.0) after discontinuation of therapy with nilotinib; **OR**
- Treatment response as indicated by one of the following BCR-ABL1 (IS) transcript levels:
  - > 0.1% to 10% at 3 months or 6 months; **OR**
  - > 0.1% to 1% at 12 months and beyond (if treatment goal is long-term survival); **OR**
  - ≤ 0.1% at 12 months and beyond (if treatment goal is treatment-free remission)

NOTE: cytogenetic assessment of response may be used if quantitative RT-PCR (QPCR) using International Scale (IS) for *BCR-ABL1* is not available

Gastrointestinal Stromal Tumors (GIST)

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes

- Disease response as evidenced by at least one of the following:
  - Decrease in spleen size or improvements in other myelofibrosis symptoms (such as fatigue, bone pain, frequent infections, fever, night sweats, easy bruising/bleeding, etc.)
  - Stabilization or improvement as evidenced by a complete response [CR] (i.e. morphologic, cytogenetic or molecular complete response CR), complete hematologic response, or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH

Soft Tissue Sarcoma (STS)

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

§ Consider discontinuation of treatment in patients with Ph+ CML-CP	
Newly diagnosed Ph+ CML-CP who have: – been treated with Tasigna for at least 3 years – maintained a molecular response of at least MR4.0 (corresponding to = BCR-ABL/ABL ≤ 0.01% IS) for one year prior to discontinuation of therapy – achieved an MR4.5 for the last assessment taken immediately prior to discontinuation of therapy – been confirmed to express the typical BCR-ABL transcripts (e13a2/b2a2 or e14a2/b3a2) – no history of accelerated phase or blast crisis – no history of prior attempts of treatment-free remission discontinuation that resulted in relapse.	Ph+ CML-CP that are resistant or intolerant to treatment with imatinib who have achieved a sustained molecular response (MR4.5) on Tasigna who have: – been treated with Tasigna for a minimum of 3 years – been treated with imatinib only prior to treatment with Tasigna – achieved a molecular response of MR.4.5 (corresponding to = BCR-ABL/ABL ≤ 0.0032% IS) – sustained an MR4.5 for a minimum of one year immediately prior to discontinuation of therapy – been confirmed to express the typical BCR-ABL transcripts (e13a2/b2a2 or e14a2/b3a2) – no history of accelerated phase or blast crisis – no history of prior attempts of treatment-free remission discontinuation that resulted in relapse.

V. Dosage/Administration [1,5,7,8,16,18]

Indication	Dose
Chronic Myelogenous Leukemia (CML)	*Adults with newly diagnosed chronic phase CML* 300 orally twice daily *Adults with resistant or intolerant chronic or accelerated phase CML* 400mg orally twice daily *Pediatrics* 230 mg/m^2 orally twice daily (rounded to the nearest 50mg dose to a maximum single dose of 400 mg and up to a maximum daily dose of 800 mg)
Acute Lymphoblastic Leukemia (ALL)	400 mg orally twice daily
Gastrointestinal Stromal Tumors (GIST)	400 mg orally twice daily
Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes	400 mg orally twice daily
Soft Tissue Sarcoma (STS)	400 mg orally twice daily

VI. Billing Code/Availability Information

HCPCS Code:

- J8999: Prescription drug, oral, chemotherapeutic, not otherwise specified

NDC:

- Tasigna 50 mg capsule: 00078-0951-xx
- Tasigna 150 mg capsule: 00078-0592-xx

- Tasigna 200 mg capsule: 00078-0526-xx

VII. References

1. Tasigna [package insert]. East Hanover, NJ; Novartis Pharm. Corp; September 2021. Accessed June 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for nilotinib hydrochloride monohydrate. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2022.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Acute Lymphoblastic Leukemia. 1.2022. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2022.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Chronic Myeloid Leukemia 3.2022. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2022.
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6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Soft Tissue Sarcoma 2.2022. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2022.
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14. Hijiya N, Maschan A, Rizzari C, et al. Phase 2 study of nilotinib in pediatric patients with Philadelphia chromosome-positive chronic myeloid leukemia. Blood. 2019;134(23):2036-2045. doi:10.1182/blood.2019000069.
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17. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Gastrointestinal Stromal Tumors. Version 1.2022. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2022.

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C49.A0	Gastrointestinal stromal tumor, unspecified site
C49.A1	Gastrointestinal stromal tumor of esophagus
C49.A2	Gastrointestinal stromal tumor of stomach
C49.A3	Gastrointestinal stromal tumor of small intestine
C49.A4	Gastrointestinal stromal tumor of large intestine
C49.A5	Gastrointestinal stromal tumor of rectum
C49.A9	Gastrointestinal stromal tumor of other sites
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C83.50	Lymphoblastic (diffuse) lymphoma, unspecified site
C83.51	Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.53	Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
C83.54	Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
C83.55	Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb
C83.56	Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
C83.57	Lymphoblastic (diffuse) lymphoma, spleen
C83.58	Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
C83.59	Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse
C92.10	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission

C92.11	Chronic myeloid leukemia, BCR/ABL-positive, in remission
C92.12	Chronic myeloid leukemia, BCR/ABL-positive, in relapse
C94.8	Other specified leukemias
C94.80	Other specified leukemias not having achieved remission
C94.81	Other specified leukemias, in remission
C94.82	Other specified leukemias, in relapse
C95.1	Chronic leukemia of unspecified cell type
C95.10	Chronic leukemia of unspecified cell type not having achieved remission
C95.11	Chronic leukemia of unspecified cell type, in remission
C95.12	Chronic leukemia of unspecified cell type, in relapse
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
D48.1	Neoplasm of uncertain behavior of connective and other soft tissue
Z85.831	Personal history of malignant neoplasm of soft tissue

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
15	KY, OH	CGS Administrators, LLC