Tasigna® (nilotinib)
(Oral)

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I. Length of Authorization

Coverage will be provided for six 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) [Pharmacy Benefit]:

- 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) [Medical Benefit]:

- 800 mg per day

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 18 years old (unless otherwise specified); **AND**
- Patient does not have a history of long QT-syndrome; **AND**

Chronic Myelogenous Leukemia (CML) †

- Patient's disease is confirmed by either a Philadelphia chromosome-positive (Ph+) or *BCR-ABL1* positive laboratory test result; **AND**
  - Patient is resistant, or intolerant, or had an inadequate response to prior tyrosine kinase inhibitor (TKI) therapies, consisting of a 3 month trial or longer, with any of the following: omacetaxine, imatinib, bosutinib, ponatinib, dasatinib, etc. † ; **AND**
    - Patient has accelerated phase disease; **OR**
    - Patient is at least 1 year old and has chronic phase disease

- Primary Treatment †
  - Used as single agent for newly diagnosed chronic phase disease in patients at least 1 year old †; **OR**
  - Used as single agent for myeloid blast phase or accelerated phase disease; **OR**
  - In combination with steroids for lymphoid blast phase disease; **OR**
  - In combination with induction chemotherapy for lymphoid or myeloid blast phase disease
- Switch Therapy ‡
  - Initial therapy was one of the following: imatinib, bosutinib, or dasatinib; **AND**
  - Patient has *BCR-ABL1* transcript levels:
    - >1% to 10% at 12 or >15 months
    - >10% at any response milestone
- Continued Therapy ‡
  - Patient has *BCR-ABL1* transcript levels:
    - ≤0.1% at any response milestone
    - >1% to 10% at 3, 6, or 12 months
    - >10% at 3 months
- Post-allogeneic hematopoietic stem cell transplant (HCT) ‡
  - Used in patients with a complete cytogenetic response (CCyR) for accelerated or blast phase disease; **OR**
  - Used in patients with molecular relapse (BCR-ABL1 transcript positive) following CCyR; **OR**
  - Used in patients with relapse or those who are not in CCyR
- Used in patients with F317L/V/I/C, T315A, or V299L BCR-ABL1 mutations
- Re-initiation of treatment †
  - Patient lost molecular response (MMR or MR4.0) after discontinuation of therapy with nilotinib

Acute Lymphoblastic Leukemia (ALL) ‡

- Patients disease is Philadelphia chromosome-positive(Ph+); **AND**
  - Relapsed-Refractory Treatment
    - Used as a single agent therapy; **OR**
    - Used in combination with an induction therapy not previously used; **OR**
    - Used in patients with F317L/V/I/C, T315A, or V299L BCR-ABL1 mutations
  - Induction Treatment
    - Patient's age is at least 15 years old; **AND**
      - Used in combination with corticosteroids; **OR**
      - Used in combination with dexamethasone and vincristine; **OR**

- Used as a component of cyclophosphamide, daunorubicin, vincristine and prednisone as induction/consolidation therapy; **OR**
- Patient's age is at least 65 years old; **AND**
  - Used with or without corticosteroids as low-intensity therapy; **OR**
  - Used in EWALL; as part of a moderate-intensity multiagent chemotherapy regimen (vincristine, dexamethasone, methotrexate, cytarabine, asparaginase)

- Maintenance Treatment
  - Used in combination with vincristine and prednisone; **OR**
  - Used in patients who are post-hematopoietic stem cell transplant

Gastrointestinal stromal tumors (GIST) ‡

- Patient's disease is progressive after prior therapies, consisting of a 3 month trial or longer, with at least ONE of the following: imatinib, regorafenib or sunitinib

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s)

IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Patient continues to meet criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: electrolyte abnormalities (hypomagnesemia, hypokalemia); cardiac toxicity (long QT syndrome); myelosuppression (neutropenia, thrombocytopenia, and anemia); metabolic toxicity (increase lipase, pancreatitis); hepatotoxicity (severe changes in liver function tests); tumor lysis syndrome; electrolyte abnormalities, hemorrhage, etc. **AND**
- Patient has been adherent to therapy; **AND**

Acute lymphoblastic leukemia (ALL) only:

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

Chronic Myelogenous Leukemia (CML) only:

- 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:
  - ≤ 10% at 3 months; **OR**
  - ≤ 10% at 6 months; **OR**
  - < 1% at 12 months; **OR**
  - < 0.1% beyond 12 months

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) only:

- 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

Indication	Dose
Chronic Myelogenous Leukemia (CML)	*Adults* 300 – 400 mg 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

VI. Billing Code/Availability Information

HCPCS code:

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

- C9399: Unclassified drugs or biologicals *(Hospital Outpatient Use ONLY)*

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; July 2018. Accessed June 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for nilotinib hydrochloride monohydrate. National Comprehensive Cancer Network, 2019. 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 2019.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Acute Lymphoblastic Leukemia. 2.2019. National Comprehensive Cancer Network, 2019. 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 2019
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Chronic Myeloid Leukemia 1.2019. National Comprehensive Cancer Network, 2019. 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 2019
5. Kim DY, Joo YD, Lim SN, et al. Nilotinib combined with multiagent chemotherapy for newly diagnosed Philadelphia-positive acute lymphoblastic leukemia. Blood 2015; 126:746-756

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
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
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) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-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): 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