09-J1000-48

Original Effective Date: 01/01/12

Reviewed: 01/14/26

Revised: 02/15/26

Subject: Nilotinib Capsules (Nilceya and Tasigna) and Tablets (Danziten)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Nilotinib monohydrochloride monohydrate capsule (Tasigna), a second-generation tyrosine kinase inhibitor (TKI), was approved by the US Food and Drug Administration (FDA) in October 2007 for the treatment of adults with chronic-phase (CP) and accelerated-phase (AP) Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) resistant to or intolerant of prior treatment with imatinib (Gleevec). In December 2017, nilotinib became the first TKI to include information in the labeling regarding the eligibility of certain patients to discontinue treatment after 3 years. In March 2018, the indication was expanded to include the treatment of pediatric patients (1 year of age or older) with either newly diagnosed Ph+ CML in chronic phase, or chronic phase Ph+ CML with resistance or intolerance to prior TKI therapy. In September 2021, the pediatric CML indication was expanded to include accelerated-phase Ph+ CML. Per the National Comprehensive Cancer Network (NCCN) guidelines, nilotinib has also shown efficacy in the treatment of Ph+ acute lymphoblastic leukemia (ALL), myeloid/lymphoid neoplasms with eosinophilia and ABL1 rearrangement, gastrointestinal stromal tumors (GISTs), pigmented villonodular synovitis/tenosynovial giant cell tumor (PVNS/TGCT), and cutaneous melanoma with activating mutations of KIT. The FDA had previously granted nilotinib orphan designation status for the treatment of CML in 2006. The first generic version of Tasigna was launched by Apotex in May 2025, and then multiple additional generics launched at the end of 2025.

In November 2024, the FDA approved a novel tablet formulation of nilotinib, nilotinib tartrate tablets (Danziten). Danziten has improve bioavailability allowing for a lower dose while achieving similar nilotinib blood levels as Tasigna (i.e., bioequivalence). Danziten is available as 71 mg and 95 mg tablets, and it should not be substitutable with other nilotinib products on a milligram per milligram basis. In addition, Danziten has the convenience advantage of being able to be taken without regard to meals.

Tasigna must be taken on an empty stomach (i.e., no food should be consumed for at least 2 hours before the dose is taken and for at least 1 hour after the dose is taken).. Of note, Danziten does not include pediatric indications, due to Novartis Pharmaceuticals Corporation's marketing exclusivity rights for Tasigna until early 2029.

In February 2025, the FDA approved a 505(b)(2) capsule formulation of nilotinib D-tartrate manufactured by Cipla USA Inc. In July 2025, the FDA granted approval to Cipla USA Inc for inclusion of the proprietary name Nilceya. Nilceya is not considered a generic version of Tasigna (or Danziten) due to the novel D-tartrate salt formulation. D-tartrate is the dextrorotatory isomer of tartaric acid. Unlike Danziten tablets, Nilceya has the same recommended dosage as Tasigna, and is available in the same capsule strengths (50 mg and 150 mg) as Tasigna. Nilceya has the same restrictions as Tasigna that it must be taken on an empty stomach (i.e., no food should be consumed for at least 2 hours before the dose is taken and for at least 1 hour after the dose is taken). Similar to Danziten, Nilceya does not include pediatric indications.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of nilotinib monohydrochloride monohydrate capsules (Tasigna and generics), nilotinib D-tartrate capsules (Nilceya), and nilotinib tartrate tablets (Danziten) **meet the definition of medical necessity** when **ALL** of the following criteria are met:

A. **ONE** of the following to support clinical use is met ("1", "2", or "3"):
   1. **BOTH** of the following are met regarding FDA labeling or NCCN Compendium ("a" and "b"):
      a. **EITHER** of the following (indication and usage) ["i" or ii"]:
         i. Member is diagnosed with a condition that is consistent with an indication listed in the requested nilotinib product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
         ii. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation (see Table 2)
      b. **EITHER** of the following (diagnostic testing) ["i" or ii"]:
         i. The requested indication for the requested nilotinib product requires genetic/specific diagnostic testing per the FDA labeling* or NCCN Compendium, **AND BOTH** of the following are met:
            - The genetic/specific diagnostic testing has been completed

- The results of the testing indicate nilotinib therapy is appropriate – documentation must be submitted

ii. The requested indication for the requested nilotinib product does **NOT** require specific genetic/diagnostic testing per FDA labeling or NCCN Compendium

**FDA Companion Diagnostics: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools*

2. The requested nilotinib product is designated as an orphan drug by the FDA for the requested indication, **AND** the indication is not included in the FDA labeling or the NCCN compendium as a 1 or 2A recommendation (i.e., "Designated") [orphan drug designations can be found at http://www.accessdata.fda.gov/scripts/opdlisting/oopd/]
3. The indication and usage is supported by the results of **TWO** or more published clinical studies – the prescriber must submit full text copies of each article

   NOTE:
   - Case reports, posters, and abstracts (including published meeting abstracts) are **NOT** accepted as evidence to support use
   - Clinical studies must be supportive of use for a similar patient population (e.g., indication, diagnosis, disease severity, genetic or tumor mutations) and for the intended treatment plan, including any concomitant therapy

B. For the diagnosis of chronic-phase, Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) **ONLY** – **ANY** of the following ("1", "2", or "3")**:

1. **BOTH** of the following ("a" and "b"):
   a. Member has a low-risk Sokal, Hasford (EURO), or EUTOS long-term survival (ELTS) score as determined prior to treatment initiation
   b. **ANY** of the following:
      i. Member has received imatinib and was unable to achieve treatment goals
      ii. Member has a known imatinib-resistance mutation (confirmatory laboratory documentation of the mutation must be submitted) or an FDA-labeled contraindication to imatinib, **AND** member has an FDA-labeled contraindication to, persistent intolerable adverse effects despite appropriate dose modification, or was unable to achieve treatment goals with dasatinib – if applicable, the specific adverse effect or contraindication(s) must be provided
      iii. Member has FDA-labeled contraindication(s) to and/or persistent intolerable adverse effects despite appropriate dose modification to **BOTH** imatinib **AND** dasatinib that are not expected to occur with the requested nilotinib product - the specific adverse effect(s) and/or contraindication(s) must be provided
2. **BOTH** of the following ("a" and "b"):
   a. Member has an intermediate- or high-risk Sokal, Hasford (EURO), or EUTOS long-term survival (ELTS) score as determined prior to treatment initiation (at least one calculated score must be provided)

b. Member has an FDA-labeled contraindication to, persistent intolerable adverse effects despite appropriate dose modification, or was unable to achieve treatment goals with dasatinib - the specific adverse effect or contraindication must be provided

3. Member has an F317L/V/I/C, T315A, or V299L mutation (confirmatory laboratory documentation of the mutation must be submitted)

***Step therapy requirement does **NOT** apply if a prior health plan paid for the medication - documentation of a paid claim within the past 90 days must be submitted*

C. For brand Tasigna capsule, Danziten (nilotinib tartrate) tablets, Nilceya (nilotinib D-tartrate) capsules **ONLY – EITHER** of the following ("1" or "2"):

1. Member has a contraindication to nilotinib monohydrochloride monohydrate capsules (generic for Tasigna), and the contraindication is **NOT** applicable to the requested nilotinib product – the specific contraindication(s) and rationale for using the requested nilotinib product must be provided

2. Member has tried and had intolerable adverse effects to nilotinib monohydrochloride monohydrate capsules (generic for Tasigna), and the intolerance is not expected to occur with the requested nilotinib product - the specific intolerance(s) and rationale for using the requested nilotinib product must be provided. Also, **BOTH** of the following are required:

   a. A completed Medwatch reporting form (FDA 3500) must be submitted: https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda

   b. A completed Naranjo Adverse Drug reaction probability scale must be submitted: https://assets.guidewell.com/m/2736e82ff52fe22d/original/mcg-naranjo-algorithm.pdf

D. The dosage of the requested nilotinib product does not exceed the maximum FDA-approved dose and frequency with the following exceptions ("1" or "2"):

1. Dose and frequency for the indication are supported by standard reference compendia (see NCCN Compendium or other compendia in Table 3)

2. Dose and frequency for the indication are supported by the results of **TWO** or more published clinical studies – the prescriber must submit full text copies of each article

   NOTE: Dose ranging studies, case reports, posters, and abstracts (including published meeting abstracts) are not accepted as evidence to support use

E. The dose will be achieved using the fewest number of capsules or tablets per day

Approval duration: 6 months

Continuation of nilotinib monohydrochloride monohydrate capsules (Tasigna and generics), nilotinib D-tartrate capsules (Nilceya), and nilotinib tartrate tablets (Danziten) **meet the definition of medical necessity** when **ALL** of the following criteria are met:

A. Nilotinib has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met **ALL** indication-specific criteria

B. For brand Tasigna capsule and Nilceya (nilotinib D-tartrate capsules) **ONLY – EITHER** of the following ("1" or "2"):

1. Member has a contraindication to nilotinib monohydrochloride monohydrate capsules (generic for Tasigna), and the contraindication is not applicable to the requested nilotinib product – the specific contraindication(s) and rationale for using the requested nilotinib product must be provided
2. Member has tried and had intolerable adverse effects to nilotinib monohydrochloride monohydrate capsules (generic for Tasigna), and the intolerance is not expected to occur with the requested nilotinib product - the specific intolerance(s) and rationale for using the requested nilotinib product must be provided. Also, **BOTH** of the following are required:
    a. A completed Medwatch reporting form (FDA 3500) must be submitted: https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda
    b. A completed Naranjo Adverse Drug reaction probability scale must be submitted: https://assets.guidewell.com/m/2736e82ff52fe22d/original/mcg-naranjo-algorithm.pdf

C. The dosage of the requested nilotinib product does not exceed the maximum FDA-approved dose and frequency with the following exceptions:
    i. Dose and frequency for the indication are supported by standard reference compendia (see NCCN Compendium or Table 3)
    ii. Dose and frequency for the indication are supported by the results of **TWO** or more published clinical studies – the prescriber must submit full text copies of each article

    NOTE: Dose ranging studies, case reports, posters, and abstracts (including published meeting abstracts) are not accepted as evidence to support use

D. The dose of nilotinib will be achieved using the fewest number of capsules or tablets per day

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved:

- Tasigna - indicated for the following: (1) the treatment of adult and pediatric patients greater than or equal to 1 year of age with newly-diagnosed Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP), (2) the treatment of adult patients with CP and accelerated phase (AP) Ph+ CML resistant or intolerant to prior therapy that included imatinib, and (3) the treatment of pediatric patients greater than or equal to 1 year of age with CP and AP Ph+ CML with resistance or intolerance to prior TKI therapy. The recommended adult dose is 300 mg orally twice daily for newly diagnosed Ph+ CML-CP and 400 mg twice daily for resistant or intolerant Ph+ CML-CP and CML-AP. The recommended dose for pediatric patients is 230 mg/m^2 twice daily, rounded to the nearest 50 mg dose (to a maximum single dose of 400 mg) [see Table 1 in the product labeling for dosage recommendations for different body surface area (BSA) ranges]. If needed, attain the desired dose by combining different strengths of capsules. Tasigna should be administered approximately 12 hours apart and must be taken on an empty stomach. The capsules

should be swallowed whole with water. Discontinuation of treatment can be considered for certain patient who have received treatment for at least 3 years. See the package labeling for the recommended criteria and monitoring requirements. Patients, who stop therapy and lose response, should be re-initiated on treatment within 4 weeks at the previous dose level.

- Nilceya - indicated for the following: (1) the treatment of adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase, and (2) the treatment of adult patients with chronic phase and accelerated phase Philadelphia chromosome positive chronic myelogenous leukemia (Ph+ CML) resistant or intolerant to prior therapy that included imatinib. Additional pediatric use information is approved for Novartis Pharmaceuticals Corporation's Tasigna (nilotinib) capsules. However, due to Novartis Pharmaceuticals Corporation's marketing exclusivity rights, this drug product is not labeled with that pediatric information. The recommended adult dose is 300 mg orally twice daily for newly diagnosed Ph+ CML-CP and 400 mg twice daily for resistant or intolerant Ph+ CML-CP and CML-AP. Nilceya should be administered approximately 12 hours apart and must be taken on an empty stomach. The capsules should be swallowed whole with water. Discontinuation of treatment can be considered for certain patient who have received treatment for at least 3 years. See the package labeling for the recommended criteria and monitoring requirements. Patients, who stop therapy and lose response, should be re-initiated on treatment within 4 weeks at the previous dose level.
- Danziten - indicated for the following: (1) the treatment of adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase, and (2) the treatment of adult patients with chronic phase and accelerated phase Philadelphia chromosome positive chronic myelogenous leukemia (Ph+ CML) resistant or intolerant to prior therapy that included imatinib. Additional pediatric use information is approved for Novartis Pharmaceuticals Corporation's Tasigna (nilotinib) capsules. However, due to Novartis Pharmaceuticals Corporation's marketing exclusivity rights, this drug product is not labeled with that pediatric information. The recommended dose is 142 mg mg orally twice daily at approximately 12-hour intervals (with or without food) for newly diagnosed Ph+ CML-CP and 190 mg orally twice daily at approximately 12-hour intervals (with or without food) for resistant or intolerant Ph+ CML-CP and CML-AP. The tablets should be swallowed whole with water. Discontinuation of treatment can be considered for certain patient who have received treatment for at least 3 years. See the package labeling for the recommended criteria and monitoring requirements. Patients, who stop therapy and lose response, should be re-initiated on treatment within 4 weeks at the previous dose level. Danziten may not be substitutable with other nilotinib products on a milligram per milligram basis. When switching between Danziten tablets and Tasigna capsules, use the dosage conversion table in the product labeling.

Approved Indications	Danziten dosage	Tasigna dosage
Newly diagnosed Ph+ CML-CP	142 mg orally twice daily	300 mg orally twice daily
Resistant or intolerant Ph+ CML-CP and CML-AP	190 mg orally twice daily	400 mg orally twice daily

Dose Modifications: Refer to the product labeling for either Tasigna, Nilceya, or Danziten

Drug Availability:

- Tasigna (and generics) - available as 50 mg, 150 mg, and 200 mg capsules
- Danziten – available as 71 mg (pink) and 95 mg (red) tablets supplied in blister packs

- Nilceya – available as 50 mg, 150 mg, and 200 mg capsules

PRECAUTIONS:

CONTRAINDICATIONS

- Do not use in patients with hypokalemia, hypomagnesemia, or long QT syndrome.

BOXED WARNING:

- Nilotinib prolongs the QT interval. Prior to administration and periodically, monitor for hypokalemia or hypomagnesemia and correct deficiencies. Obtain ECGs to monitor the QTc at baseline, seven days after initiation, and periodically thereafter, and follow any dose adjustments.
- Sudden deaths have been reported in members receiving nilotinib. Do not administer to members with hypokalemia, hypomagnesemia, or long QT syndrome.
- Avoid use of concomitant drugs known to prolong the QT interval and strong CYP3A4 inhibitors.
- Members should avoid food two hours before and one hour after taking dose [DOES NOT INCLUDE DANZITEN].

WARNINGS

- **Myelosuppression:** Treatment with nilotinib can cause severe thrombocytopenia, neutropenia, and anemia. Perform complete blood cell counts (CBCs) every 2 weeks for the first 2 months and then monthly thereafter, or as clinically indicated. Reversible by withholding dose; dose reduction may be required.
- **QT prolongation:** Nilotinib prolongs the QT interval. Correct hypokalemia or hypomagnesemia prior to administration and monitor periodically. Avoid concomitant administration of drugs known to prolong the QT interval and strong CYP3A4 inhibitors. Use with caution in patients with hepatic impairment. Obtain ECGs at baseline, seven days after initiation, and periodically thereafter. The same monitoring should be done following any dose adjustments.
- **Sudden deaths:** Sudden deaths have been reported in members with resistant or intolerant CML treated with nilotinib in clinical studies (0.3%). The relative early occurrence of some of the deaths relative to the initiation of nilotinib suggests the possibility that ventricular repolarization abnormalities may have contributed to their occurrence.
- **Cardiac and Arterial Vascular Occlusive Events:** Events including ischemic heart disease, peripheral arterial occlusive disease and ischemic cerebrovascular events have been reported in patients with newly diagnosed Ph+ CML receiving nilotinib. Cardiovascular status should be evaluated, and cardiovascular risk factors monitored and managed during therapy.
- **Pancreatitis and elevated serum lipase:** Check serum lipase monthly or as clinically indicated. If lipase elevations are accompanied by abdominal symptoms, interrupt doses and consider appropriate diagnostics to exclude pancreatitis. Administer with caution to persons with a history of pancreatitis.
- **Hepatotoxicity:** The use of nilotinib may result in elevations in alkaline phosphatase, AST/ALT, and bilirubin. Grade 3-4 elevations of bilirubin, AST, and ALT were reported at a higher frequency in pediatric than in adult patients. Check hepatic function tests monthly or as clinically indicated.
- **Tumor lysis syndrome:** Cases have been reported in nilotinib treated patients with resistant or intolerant CML. Due to potential for tumor lysis syndrome, maintain adequate hydration and correct uric acid levels prior to initiating therapy.

- **Electrolyte abnormalities:** The use of nilotinib can cause hyperkalemia, hypocalcemia, hypokalemia, hyponatremia, and hypophosphatemia. Electrolyte abnormalities must be corrected prior to initiating nilotinib. Monitor these electrolytes periodically during therapy.
- **Drug interactions:** Avoid concomitant use of strong inhibitors or inducers of CYP3A4. If patients must be coadministered a strong CYP3A4 inhibitor, dose reduction should be considered, and the QT interval should be monitored closely.
- **Total gastrectomy:** The exposure of nilotinib is reduced in members with total gastrectomy. Consider more frequent follow-up of these patients. Consider dose increase or alternative therapy in patients with total gastrectomy.
- **Food effects**: Food increases blood levels of nilotinib. Avoid food 2 hours before and 1 hour after a dose [DOES NOT INCLUDE DANZITEN].
- **Lactose intolerance:** Because the capsules contain lactose, nilotinib is not recommended for persons with rare hereditary problems of galactose intolerance, severe lactase deficiency with a severe degree of intolerance to lactose-containing products, or glucose-galactose malabsorption [DOES NOT INCLUDE DANZITEN].
- **Hepatic function impairment:** Nilotinib exposure is increased in patients with impaired hepatic function. Use a lower starting dose for patients with mild to severe hepatic impairment (at baseline) and monitor the QT interval frequently.
- **Hemorrhage**: Hemorrhage from various sites was reported in patients with newly diagnosed CML and observed in the postmarketing reports of patients receiving nilotinib therapy.
- **Fluid retention**: Pericardial effusion, pleural effusion, and severe fluid retention have occurred in patients receiving nilotinib. Monitor patients for signs and symptoms such as unexpected rapid weight gain, swelling, and shortness of breath.
- **Effects on Growth and Development in Pediatric Patients**: Growth retardation has been reported in pediatric patients with Ph+ CML in chronic phase treated with nilotinib. Growth deceleration was more pronounced in children who were less than age 12 at baseline. Monitor growth and development in pediatric patients receiving treatment.
- **Embryo-fetal toxicity**: Fetal harm can occur when administered to a pregnant woman. Women should be advised not to become pregnant when taking nilotinib.

BILLING/CODING INFORMATION:

HCPCS Coding

J8999	Prescription drug, oral, chemotherapeutic, nos

ICD-10 Diagnosis Codes That Support Medical Necessity

C43.0 – C43.9	Malignant melanoma of skin
C49.10 – C49.12	Malignant neoplasm of connective and soft tissue of upper limb, including shoulder
C49.20 – C49.22	Malignant neoplasm of connective and soft tissue of lower limb, including hip
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C49.A0 – C49.A9	Gastrointestinal stromal tumor

C83.50 – C83.59	Lymphoblastic (diffuse) lymphoma
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
C94.80 – C94.82	Other specified leukemias
C95.10 – C95.12	Chronic leukemia of unspecified cell type
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
D48.19	Other specified neoplasm of uncertain behavior of connective and other soft tissue

REIMBURSEMENT INFORMATION:

Refer to section entitled POSITION STATEMENT**.**

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Accelerated Phase CML: is a phase of chronic myelogenous leukemia in which the disease is progressing.

Acute lymphoblastic leukemia: an aggressive (fast-growing) type of leukemia (blood cancer) in which too many immature white blood cells are found in the blood and bone marrow. Also called acute lymphocytic leukemia and ALL.

Blast Phase CML: is the final phase in the evolution of CML, and behaves like an acute leukemia, with rapid progression and short survival.

Chronic Phase CML: approximately 85% of members with CML are in the chronic phase at the time of diagnosis. During this phase, members are usually asymptomatic or have only mild symptoms of fatigue, left side pain, joint and/or hip pain, or abdominal fullness.

Chronic Myelogenous Leukemia (CML): also known as chronic myeloid leukemia and chronic granulocytic leukemia (CGL), is a cancer of the white blood cells. It is a form of leukemia characterized by the increased and unregulated growth of predominantly myeloid cells in the bone marrow and the accumulation of these cells in the blood.

Cytogenetic: is a branch of genetics that is concerned with the study of the structure and function of the cell, especially the chromosomes. It includes routine analysis of G-banded chromosomes, other cytogenetic banding techniques, as well as molecular cytogenetics such as fluorescent in situ hybridization (FISH) and comparative genomic hybridization (CGH).

Induction Chemotherapy: the use of drug therapy as the initial treatment for patients presenting with advanced cancer that cannot be treated by other means.

Philadelphia chromosome or Philadelphia translocation: is a specific chromosomal abnormality that is associated with chronic myelogenous leukemia (CML).

Relapse: the return of a disease or the signs and symptoms of a disease after a period of improvement. Specifically, for CML a relapse is defined as "any sign of loss response" (defined as hematologic or cytogenic relapse). A 1-log increase in BCR-ABL transcript levels with loss of MMR should prompt bone marrow evaluation for loss of complete cytogenic response is not itself defined as relapse.

Refractory: cancer that does not respond to treatment; the cancer may be resistant at the beginning of treatment, or it may become resistant during treatment. Also called resistant cancer.

RELATED GUIDELINES:

Allogeneic Bone Marrow and Stem Cell Transplantation, 02-38240-01
Bosutinib (Bosulif) Tablets, 09-J1000-84
Oral Oncology Medications, 09-J3000-65

OTHER:

Table 1: CML Risk Scores

Score	Calculation	Risk Definition by Calculation
Sokal score	Exp 0.0116 x (age - 43.4) + (spleen size - 7.51) + 0.188 x [(platelet count/700)^2 - 0.562] + 0.0887 x (blast cells - 2.10)	• Low: <0.8 • Intermediate: 0.8 to 1.2 • High: >1.2
Hasford (EURO) score	[0.666 when age ≥50 + (0.042 x spleen size) + 1.0956 when platelet count ≥1,500 x 10^3/L + (0.0584 x blast cells) + 0.2039 when basophils ≥3% + (0.0413 x eosinophils)] x 1,000	• Low: ≤780 • Intermediate: >780 to 1,480 • High: >1,480

EUTOS long-term survival (ELTS) score	$0.0025 \times (age/10)^3 + 0.0615 \times$ spleen size $+ 0.1052 \times$ blast cells $+ 0.4104 \times (platelet\ count/1{,}000)^{-0.5}$	• Low: ≤1.5680 • Intermediate: >1.5680 to ≤2.2185 • High: >2.2185

Age is in years. Spleen is in centimeters below the costal margin (maximum distance). Blast cells, eosinophils, and basophils are in percent of peripheral blood differential. All factors must be collected prior to any treatment.

Online calculator for Sokal and Hasford (EURO) scores can be found at: https://www.leukemia-net.org/content/leukemias/cml/euro__and_sokal_score/index_eng.html

Online calculator for the ELTS score can be found at: https://www.leukemia-net.org/content/leukemias/cml/elts_score/index_eng.html

Table 2

NCCN Categories of Evidence Consensus	
Category 1	Based upon high-level evidence; there is uniform NCCN consensus that the intervention is appropriate
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate
Category 2B	Based upon lower-level evidence, there NCCN consensus that the intervention is appropriate
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Table 3

Other Compendia	
Compendium	**Covered Uses**
AHFS-DI	Narrative text is supportive
Clinical Pharmacology	Narrative text is supportive
Lexicomp	Evidence rating A, B or G
Thomson Micromedex DrugDex	Meets requirements for **BOTH** of the following: • Strength of recommendation: Class I (Recommended) or IIa (Recommended, In Most Cases) • Efficacy: Class I (Effective) or IIa (Evidence Favors Efficacy)
AHFS-DI - American Hospital Formulary Service Drug Information	

Table 4

Lexicomp Recommendation Ratings	
A	Consistent evidence from well-performed randomized, controlled trials or overwhelming evidence of some other form (e.g., results of the introduction of penicillin treatment) to support the off-label use. Further research is unlikely to change confidence in the estimate of benefit.

B	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate.
C	Evidence from observational studies (e.g., retrospective case series/reports providing significant impact on patient care), unsystematic clinical experience, or from potentially flawed randomized, controlled trials (e.g., when limited options exist for condition). Any estimate of effect is uncertain.
G	Use has been substantiated by inclusion in at least one evidence-based or consensus-based clinical practice guideline.

Table 5

Thomson Micromedex DrugDex Recommendation Ratings: Strength of Recommendation		
Class I	Recommended	The given test or treatment has been proven to be useful, and should be performed or administered
Class IIa	Recommended, in most cases	The given test or treatment is generally considered to be useful and is indicated in most cases.
Class IIb	Recommended in some cases	The given test or treatment may be useful, and is indicated in some, but not most, cases
Class III	Not recommended	The given test or treatment is not useful and should be avoided
Class Indeterminate	Evidence Inconclusive	

Table 6

Thomson Micromedex DrugDex Recommendation Ratings: Efficacy		
Class I	Effective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is effective
Class IIa	Evidence favors efficacy	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion favors efficacy.
Class IIb	Evidence is inconclusive	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion argues against efficacy.
Class III	Ineffective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is ineffective

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/14/26.

GUIDELINE UPDATE INFORMATION:

01/01/12	New Medical Coverage Guideline.

11/15/12	Review and revision to guideline; consisting of updating position statement, adding contraindications, updating precautions, coding, program exceptions, related guidelines and references.
03/15/13	Review and revision to guideline; consisting of reformatting and revising position statement to include treatment of acute lymphoblastic leukemia; reformatting and revising description, dosage/administration, and precautions sections; adding definitions and related guidelines; and updating coding and references.
03/15/14	Review and revision to guideline; consisting of reformatting/revising position statement; reformatting precautions section; updating program exceptions and references.
03/15/15	Review and revision to guideline; consisting of revising position statement and updating the description, dosage/administration, warnings, and references.
11/01/15	Revision: ICD-9 Codes deleted.
03/15/16	Review and revision to guideline consisting of description, position statement, definitions, and references.
09/15/16	Revision to guideline consisting of updating the position statement and definitions.
10/01/16	Revision: ICD-10 code updates.
01/15/17	Revision to guideline consisting of updating the description section, position statement, and references based on updated NCCN guidelines.
03/15/17	Review and revision to guideline consisting of updating the position statement, description section, dosage/administration section, precautions section, and references.
02/15/18	Review and revision to guideline consisting of updates to description, position statement, dosage/administration, billing/coding, definitions, and references sections.
05/15/18	Revision to guideline consisting of updates to description, dosage/administration, and references sections based on the new FDA-approved indication for pediatric patients.
02/15/19	Review and revision to guideline consisting of updates to description, position statement, dosage/administration, billing/coding, definitions, other, and references sections.
02/15/20	Review and revision to guideline consisting of updates to description, warnings/precautions, billing/coding, and references.
02/15/21	Review and revision to guideline consisting of updates to the description, position statement, billing/coding, other section, related guidelines, and references.
02/15/22	Review and revision to guideline consisting of updates to the description, dosage/administration, warnings/precautions, and references.
02/15/23	Review and revision to guideline consisting of updates to the related guidelines and references.
02/15/24	Review and revision to guideline consisting of updates to the description, billing/coding, and references.
02/15/25	Review and revision to guideline consisting of updates to the references.
04/01/25	Revision to guideline consisting of updates to the description section, position statement, dosage/administration, warnings/precautions, and references based on the addition Danziten tablets.

10/01/25	Revision to guideline consisting of updates to the description section, position statement, dosage/administration, warnings/precautions, and references based on the addition of Nilceya capsules.
02/15/26	Review and revision to guideline consisting of updates to the description section, position statement, related guidelines, and references.