PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Nilotinib Products Prior Authorization Policy
- Danziten™ (nilotinib tablets – Azurity)
- Tasigna® (nilotinib capsules – Novartis, generic)

REVIEW DATE: 03/26/2025; selected revision 06/04/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Nilotinib products, such as Tasigna and Danziten, are tyrosine kinase inhibitors (TKIs) indicated for the following uses:[1,9]

- **Chronic myeloid leukemia (CML)**, Philadelphia chromosome positive (Ph+), that is newly diagnosed, in chronic phase: Tasigna is approved for use in adults and pediatric patients ≥ 1 year of age. Danziten is approved for use in adults.
- **CML**, Ph+, chronic phase and accelerated phase: Tasigna and Danziten are approved for use **in adults** with resistance or intolerance to prior therapy that included imatinib.
- **CML**, Ph+, chronic phase and accelerated phase: Tasigna is approved for use in **pediatric patients** ≥ 1 year of age with resistance or intolerance to prior TKI therapy.

The prescribing information for Danziten notes that Novartis, the manufacturer of Tasigna, has marketing exclusivity rights in pediatric patients.[9] This is the reason Danziten is only FDA-approved in adults.

Dosing and Administration

Danziten may not be substitutable with other nilotinib products on a milligram per milligram basis.[9] Table 1 presents the Danziten and Tasigna dosage equivalence when switching between products. Danziten can be taken without regard to the timing of food intake. For Tasigna administration, no food should be taken for at least 2 hours before the dose is taken and for at least 1 hour after the dose is taken.

Table 1. Recommendations for Switching Between Danziten and Tasigna.[9]

Approved Indications	Danziten Dosage	Tasigna Dosage
Newly diagnosed Ph+ CML-CP	142 mg BID	300 mg BID
Resistant or intolerant Ph+ CML-CP and CML-AP	190 mg BID	400 mg BID

Ph+ – Philadelphia chromosome positive; CML – Chronic myeloid leukemia; CP – Chronic phase; BID – Twice daily; AP – Accelerated phase.

Guidelines

Nilotinib is addressed in guidelines from the National Comprehensive Cancer Network (NCCN):

- **Acute Lymphoblastic Leukemia (ALL):** NCCN guidelines for adults and adolescents (version 3.2024 – December 20, 2024) recommend nilotinib for Ph+ disease in many different clinical circumstances (e.g., induction, consolidation, maintenance, or relapsed or refractory disease) [category 2A].[2,8] The guidelines state that the ALL panel considers adolescents to be within the age range of 15 to 39 years. TKIs in combination with other agents (e.g., chemotherapy or corticosteroids) are recommended for induction therapy for Ph+ ALL. TKIs have also been incorporated into consolidation and maintenance therapy, as well as in the relapsed/refractory setting (category 2A). TKI options include: Bosulif® (bosutinib tablets), dasatinib, imatinib, nilotinib (Tasigna and Danziten), and Iclusig® (ponatinib tablets) [category 2A]. NCCN panel notes that not all TKIs have been directly studied within the context of each specific regimen and there are limited data for Bosulif in Ph+ ALL. Use of a specific TKI should account for anticipated/prior TKI intolerance and disease-related features. For adults and adolescents, Iclusig has activity against T315I mutations and/or in whom no other TKI is indicated (category 2A).
- **CML:** NCCN guidelines (version 3.2025 – November 27, 2024) mention in a footnote that TKIs (e.g., nilotinib) are available in different approved formulations, dosage forms, and strengths that are subject to different administration instructions. These products are noted not to be interchangeable. The guidelines recommend nilotinib as a "preferred" primary treatment for newly diagnosed chronic phase Ph+ or *BCR::ABL1*-mutation positive CML patients with a low-, intermediate-, or high-risk score (category 1).[3,8] Nilotinib is also recommended as an alternative TKI treatment after primary treatment [category 2A]. Nilotinib is also recommended in a variety of other situations, including post-allogeneic hematopoietic stem cell transplant (HSCT) [category 2A].
- **Gastrointestinal Stromal Tumor (GIST):** NCCN guidelines (version 2.2024 – July 31, 2024) recommend nilotinib as "useful in certain circumstances" after failure on approved therapies (category 2A).[4] Imatinib is a "preferred" regimen for first-line therapy (category 1) for sensitive mutations (excluding platelet-derived growth factor receptor alpha (*PDGFRA*) exon 18 mutations that are insensitive to imatinib including D842V mutation). Ayvakit® (avapritinib tablets) is also a "preferred" regimen (category 2A) for GIST with *PDGFRA* exon 18 mutations that are insensitive to imatinib, including the *PDGFRA* D842V mutation. Second-line therapies include sunitinib as "preferred" (category 1) or Qinlock® (ripretinib tablets) [for patients intolerant or sunitinib] and dasatinib as "other recommended regimen" (category

2A). Stivarga® (regorafenib tablets) is a "preferred" third-line therapy (category 1). Qinlock® (ripretinib tablets) is a "preferred" fourth-line therapy (category 1).

- **Melanoma: Cutaneous:** NCCN guidelines (version 2.2025 – January 28, 2025) recommend nilotinib as "useful in certain circumstances" for metastatic or unresectable disease with an activating *KIT* mutation as second-line or subsequent therapy for disease progression, intolerance, and/or projected risk of progression with *BRAF*-targeted therapy (category 2A).[5]
- **Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions:** NCCN guidelines (version 1.2025 – February 21, 2025) recommend nilotinib as a "Preferred" agent for *ABL1* rearrangements in chronic or blast phase (category 2A).[6] It is also recommended as treatment in combination with ALL- or acute myeloid leukemia-type induction chemotherapy followed by allogeneic HSCT (if eligible) for lymphoid, myeloid, or mixed lineage neoplasms with eosinophilia and *ABL1* rearrangement in blast phase (category 2A).[8]
- **Soft Tissue Sarcomas:** NCCN guidelines (version 5.2024 – March 10, 2025) recommend nilotinib as "useful in certain circumstances" as single-agent therapy for the treatment of pigmented villonodular synovitis/tenosynovial giant cell tumor (category 2A).[7] Turalio® (pexidartinib capsules) and Romvimza™ (vimseltinib capsules) are the preferred regimen (category 1) and imatinib is also cited as "useful in certain circumstances" (category 2A).

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of nilotinib products. All approvals are provided for the duration noted below.

- **Danziten™ (nilotinib tablets – Azurity)**
- **Tasigna® (nilotinib capsules - Novartis, generic)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Chronic Myeloid Leukemia.** Approve for 1 year if the patient meets ONE of the following (A or B):
   A) Patient has Philadelphia chromosome-positive chronic myeloid leukemia; OR
   B) Patient has *BCR::ABL1*-mutation positive chronic myeloid leukemia.

Other Uses with Supportive Evidence

2. **Acute Lymphoblastic Leukemia.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 15 years of age; AND
   B) Patient has Philadelphia chromosome-positive acute lymphoblastic leukemia.

3. **Gastrointestinal Stromal Tumor.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried ALL of the following (i, ii, iii, and iv):
      i. Imatinib or Ayvakit (avapritinib tablets); AND
      ii. Sunitinib or dasatinib; AND
      iii. Stivarga (regorafenib tablets); AND

iv. Qinlock (ripretinib tablets).

4. **Melanoma, Cutaneous.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has metastatic or unresectable disease; AND
   C) Patient has an activating *KIT* mutation; AND
   D) Patient has tried at least one systemic regimen.
   Note: Examples of a systemic regimen include: Opdivo (nivolumab intravenous infusion) + Yervoy (ipilimumab intravenous infusion), Opdualag (nivolumab/relatlimab-rmbw intravenous infusion), Keytruda (pembrolizumab intravenous infusion), Opdivo, Tafinlar (dabrafenib capsules and tablets for suspension) + Mekinist (trametinib tablets), Zelboraf (vemurafenib tablets) + Cotellic (cobimetinib tablets), Braftovi (encorafenib capsules) + Mektovi (binimetinib tablets).

5. **Myeloid/Lymphoid Neoplasms with Eosinophilia.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) The tumor has an *ABL1* rearrangement.

6. **Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor.** Approve for 1 year if the patient meets ONE of the following (A or B):
   A) Patient has tried Turalio (pexidartinib capsules) or Romvimza (vimseltinib capsules); OR
   B) According to the prescriber, patient cannot take Turalio or Romvimza.
   Note: Examples of reasons for not being able to take Turalio or Romvimza include elevated liver enzymes or concomitant use of medications that are associated with hepatotoxicity.

CONDITIONS NOT COVERED

Nilotinib products is not recommended in the following situations:

- **Danziten™ (nilotinib tablets – Azurity)**
- **Tasigna® (nilotinib capsules (Novartis, generic)**

is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as newly published data are available):

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as newly published data are available.

REFERENCES

1. Tasigna® capsules [prescribing information]. East Hanover, NJ: Novartis; February 2024.
2. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 3.2024 – December 20, 2024 © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 21, 2025.
3. The NCCN Chronic Myeloid Leukemia Clinical Practice Guidelines in Oncology (version 3.2025 – November 27, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 21, 2025.

4. The NCCN Gastrointestinal Stromal Tumors Guidelines in Oncology (version 2.2024 – July 31, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 18, 2025.
5. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 2.2025 – January 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 21, 2025.
6. The NCCN Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions Clinical Practice Guidelines in Oncology (version 1.2025 – February 21, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 21, 2025.
7. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 5.2024 – March 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 21, 2025.
8. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Search term: nilotinib. Accessed on March 21, 2025.
9. Danziten™ tablets [prescribing information]. Woburn, MA: Azurity; November 2024.
10. Nilotinib capsules [prescribing information]. Toronto, Ontario: Apotex; March 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Acute Lymphoblastic Leukemia:** The criterion requiring trial of at least one other tyrosine kinase inhibitor for Philadelphia chromosome-positive acute lymphoblastic leukemia was removed. **Melanoma, Cutaneous:** This new condition of approval was added to "Other Uses With Supportive Evidence" section based on NCCN guideline recommendations.	05/31/2023
Annual Revision	No criteria changes.	05/01/2024
Selected Revision	**Acute Lymphoblastic Leukemia:** The age requirement was changed from ≥18 years of age to ≥ 15 years of age.	06/12/2024
Selected Revision	**Danziten:** This new formulation of nilotinib was added to the policy and criteria, as applicable: Chronic Myeloid Leukemia, Acute Lymphoblastic Leukemia, Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor. **Policy name** was changed from "Oncology – Tasigna PA Policy" to "Oncology – Nilotinib Products PA Policy."	12/04/2024
Annual Revision	**Danziten:** The following indications of approval were added for this drug: Gastrointestinal Stromal Tumor, Melanoma, Cutaneous, Myeloid/Lymphoid Neoplasms with Eosinophilia. **Chronic Myeloid Leukemia**: The following option for approval was added, "patient has *BCR::ABL1*-positive chronic myeloid leukemia." **Melanoma, Cutaneous:** The following example of systemic regimen in the Note was modified from Opdivo + Opdualag (nivolumab/relatlimab-rmbw intravenous infusion) to Opdualag (nivolumab/relatlimab-rmbw intravenous infusion). **Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor:** Romvimza (vimseltinib capsules) was added as an option of a medication that patient has to try or that patient cannot take. Romvimza was added to the Note as well.	03/26/2025
Selected Revision	Generic nilotinib capsule was added to the policy and criteria.	06/04/2025