PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 05/01/2024; selected revision 06/12/2024, 12/04/2024

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 why 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]

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

Guidelines

Nilotinib products are addressed in guidelines/compendium from National Comprehensive Cancer Network (NCCN).[2-8] Other than the FDA-approved indication of CML, the NCCN compendium recommends Danziten for acute lymphoblastic leukemia and soft tissue sarcoma. Other off-label uses in the compendium for Tasigna do not yet include Danziten.

- **Acute Lymphoblastic Leukemia (ALL):** NCCN guidelines for adults and adolescents (version 4.2023 – February 5, 2024) recommend nilotinib for Ph+ disease in many different clinical circumstances (e.g., induction, consolidation therapy, 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), Sprycel® (dasatinib tablets), 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+ 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 with imatinib, Bosulif® [bosutinib tablets], or Sprycel® [dasatinib tablets]) [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 1.2024 – March 8, 2024) recommend Tasigna 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 Sprycel 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 2.2024 – April 3, 2024) recommend Tasigna 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 1.2024 – December 21, 2023) recommend Tasigna 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 1.2024 – April 26, 2024) 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) is 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of nilotinib products is recommended in those who meet one of the following criteria. The condition of approval for each product is specified for the indications:

FDA-Approved Indication

1. **Chronic Myeloid Leukemia.** Approve Tasigna or Danziten for 1 year if the patient has Philadelphia chromosome-positive chronic myeloid leukemia.

Other Uses with Supportive Evidence

2. **Acute Lymphoblastic Leukemia.** Approve Tasigna or Danziten 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 Tasigna 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 Sprycel (dasatinib tablets); AND
      iii. Stivarga (regorafenib tablets); AND
      iv. Qinlock (ripretinib tablets).

4. **Melanoma, Cutaneous.** Approve Tasigna 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), Opdivo + 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 Tasigna 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 Tasigna or Danziten for 1 year if the patient meets ONE of the following (A or B):
   A) Patient has tried Turalio (pexidartinib capsules); OR
   B) According to the prescriber, patient cannot take Turalio.
   Note: Examples of reasons for not being able to take Turalio include patients with elevated liver enzymes or concomitant use of medications that are associated with hepatotoxicity.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of nilotinib products is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new 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 4.2023 – February 5, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 29, 2024.
3. The NCCN Chronic Myeloid Leukemia Clinical Practice Guidelines in Oncology (version 2.2024 – December 5, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 29, 2024.
4. The NCCN Gastrointestinal Stromal Tumors Guidelines in Oncology (version 1.2024 – March 8, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 29, 2024.
5. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 2.2024 – April 3, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 29, 2024.
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9. Danziten® tablets [prescribing information]. Woburn, MA: Azurity; November 2024.