PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Ninlaro® (ixazomib capsules – Takeda)

DATE REVIEWED: 02/26/2020

OVERVIEW

Ninlaro is an oral proteasome inhibitor (PI) indicated in combination with Revlimid® (lenalidomide capsules) and dexamethasone for treatment of patients with multiple myeloma who have received at least one prior therapy.[1] Ninlaro should be taken once a week on the same day and at approximately the same time for the first 3 weeks of a 4-week cycle. There are dose modification guidelines which are recommended to manage treatment-related adverse events, including platelet count, absolute neutrophil count (ANC), and other toxicities (e.g., rash, peripheral neuropathy). Treatment should be continued until disease progression or unacceptable toxicity. Safety and efficacy is not established in patients < 18 years of age.

Disease Overview

Multiple myeloma is a cancer formed by malignant plasma cells.[5] Often there are no symptoms of disease until it reaches an advanced stage. The most common signs and symptoms include: bone problems (e.g., pain, bone weakness, broken bones), decreased blood counts, hypercalcemia, nervous system symptoms due to spinal cord compression, nerve damage, hyperviscosity, kidney problems, and infections. A monoclonal immunoglobulin (M protein) is produced by myeloma cells and may be found in the blood or excreted in the urine of patients with multiple myeloma. If symptoms are suggestive of multiple myeloma, a diagnosis is made based on blood and urine testing, bone x-rays, and a bone marrow biopsy. Ninlaro is a reversible inhibitor of the chymotrypsin-like activity of the 20S proteasome.[1] Cancer cells have higher levels of proteasome activity vs. normal cells, making cancer cells more sensitive to the effects of Ninlaro.[2]

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines, which address diagnosis, treatment, and follow-up for patients with multiple myeloma (version 2.2020 – October 9, 2019), list multiple therapeutic regimens that may be used for primary therapy and previously treated multiple myeloma.[6] Ninlaro/Revlimid/dexamethasone is an Other recommended regimen (transplant and non-transplant candidates). Maintenance with Ninlaro is also listed among the alternatives for transplant candidates. For previously treated disease, multiple regimens are listed, including Ninlaro/Revlimid/dexamethasone (Preferred), Ninlaro/cyclophosphamide/dexamethasone, Ninlaro/dexamethasone, and Ninlaro/Pomalyst/dexamethasone. NCCN guidelines for systemic light chain amyloidosis (version 1.2020, December 6, 2019) list Ninlaro ± dexamethasone among the treatment options for patients who have relapsed/refractory disease.[7] NCCN guidelines for Waldenstrom macroglobulinemia/lymphoplasmacytic lymphoma list Ninlaro/rituximab/dexamethasone among the treatment options for primary therapy.[8]

Safety

As a class, the PIs are distinct in their specificities and affinities; thus, safety profiles differ within the class. Looking at the Warnings/Precautions for the PIs, thrombocytopenia and embryofetal toxicity are a concern for all of these agents (Ninlaro, Velcade® [bortezomib injection], and Kyprolis® [carfilzomib intravenous {IV} infusion]).[1,3-4] However, peripheral edema and cutaneous reactions are specific to Ninlaro, gastrointestinal toxicities and peripheral neuropathy are a concern for Ninlaro and Velcade, and hepatotoxicity is listed for Ninlaro and Kyprolis.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Ninlaro. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ninlaro is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Multiple Myeloma.** Approve for 3 years if the patient meets at least ONE of the following conditions (A, B, or C):
   - **A)** Ninlaro will be taken in combination with Revlimid (lenalidomide capsules) and dexamethasone; OR
   - **B)** The patient has received at least ONE prior regimen for multiple myeloma.
     Note: Examples include regimens containing Velcade (bortezomib injection), Kyprolis (carfilzomib infusion), Revlimid (lenalidomide capsules), Darzalex (daratumumab injection).); OR
   - **C)** The agent will be used following autologous stem cell transplantation (ASCT).

Other Uses with Supportive Evidence

2. **Systemic Light Chain Amyloidosis.** Approve for 3 years if the patient has tried at least one other regimen for this condition.
   Note: Examples of agents used in other regimens include Velcade (bortezumab injection), Revlimid (lenalidomide capsules), cyclophosphamide, and melphalan.

3. **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 3 years if used in combination with a rituximab product and dexamethasone.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Ninlaro has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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. Ninlaro® capsules [prescribing information]. Cambridge, MA: Takeda Pharmaceutical Company Limited; November 2016.
2. Moreau P, Richardson PG, Cavo M, et al. Proteasome inhibitors in multiple myeloma: 10 years later. *Blood*. 2012;120(5):947-959.
3. Velcade injection [prescribing information]. Cambridge, MA: Millennium Pharmaceuticals; June 2017.
4. Kyprolis injection [prescribing information]. Thousand Oaks, CA: Onyx Pharmaceuticals/Amgen; September 2018.
5. American Cancer Society. Multiple myeloma. Last updated: January 8, 2020. Available at: http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-key-statistics. Accessed on February 17, 2020.

6. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (Version 2.2020 – October 9, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 17, 2020.
7. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (Version 1.2020 – December 6, 2019). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 13, 2020.
8. The NCCN Waldenstrom Macroglobulinemia/Lymphoblastic Lymphoma Clinical Practice Guidelines in Oncology (Version 1.2020 – December 6, 2019). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 13, 2020.