VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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

TAC APPROVAL DATE: 02/20/2019

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] The recommended starting dose is 4 mg administered orally once a week on Days 1, 8, and 15 of a 28-day cycle. It is recommended to taken with Revlimid (recommended starting dose is 25 mg once daily on Days 1 through 21) and dexamethasone (recommended starting dose of 40 mg once daily on Days 1, 8, and 22). 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.

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 2.2019 – November 16, 2018), list multiple therapeutic regimens that may be used for previously treated multiple myeloma.[6] Preferred Regimens include Revlimid/dexamethasone given in combination with one of the following agents: Velcade, Kyprolis, Darzalex, Empliciti, or Ninlaro. Other Preferred Regimens include Kyprolis/dexamethasone and Darzalex/Velcade/dexamethasone. In addition, there are 21 Other Regimens for previously treated multiple myeloma, including Ninlaro/dexamethasone and Ninlaro/Pomalyst/dexamethasone. For primary treatment of transplant and non-transplant patients, Ninlaro/Revlimid/dexamethasone is listed as an Other Recommended Regimen. NCCN guidelines for systemic light chain amyloidosis (version 1.2019, October 26, 2019) list Ninlaro ± dexamethasone among the treatment options for patients who have relapsed/refractory disease.[7]

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 the following conditions (A and B):
   - **A)** Ninlaro will be taken in combination with Revlimid (lenalidomide capsules) and dexamethasone; AND
   - **B)** The patient has received at least ONE previous regimen for multiple myeloma (e.g., a regimen containing Velcade [bortezomib injection], Kyprolis [carfilzomib intravenous {IV} infusion], Thalomid® [thalidomide capsules], Revlimid [lenalidomide capsules], Pomalyst® [pomalidomide capsules], Alkeran® [melphalan], dexamethasone, prednisone).

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 (e.g., regimens containing Velcade [bortezomib injection], cyclophosphamide, and/or Revlimid [lenalidomide capsules]).

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 2015.
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: February 28, 2018. Available at: http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-key-statistics. Accessed on January 15, 2019.
6. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (Version 1.2019 – November 16, 2018). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 15, 2019.
7. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 15, 2019.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No changes to criteria.	01/18/2017
Annual revision	No changes to criteria.	02/07/2018
Annual revision	**Multiple Myeloma:** Clarify criteria are to approve if the patient has tried a previous regimen for multiple myeloma (previously worded as tried another therapy). **Systemic Light Chain Amyloidosis:** Add criteria to approve for 3 years for this off-label indication, if the patient has previously tried another regimen.	02/20/2019

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx.