ixazomib (Ninlaro®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO129

Description

Ixazomib (Ninlaro) is an orally administered reversible proteasome inhibitor that binds and inhibits chymotrypsin-like activity of the beta 5 subunit of the 20s proteasome.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
ixazomib (Ninlaro)	2.3 mg capsule	Previously treated multiple myeloma, in combination with lenalidomide and dexamethasone	3 capsules/28 days
	3 mg capsule		
	4 mg capsule		

Initial Evaluation

I. Ixazomib (Ninlaro) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with an oncologist or hematologist; **AND**
   C. A diagnosis of **Previously treated multiple myeloma** when the following are met:
      1. The member has relapsed or refractory disease; **AND**
      2. The member has progressed on at least one prior therapy (e.g., melphalan, thalidomide, bortezomib, stem cell transplant, etc.); **AND**
      3. The member has **not** previously progressed on or after lenalidomide (Revlimid); **AND**
      4. Ixazomib (Ninlaro) will be used in combination with lenalidomide (Revlimid) AND dexamethasone; **AND**
      5. Ixazomib (Ninlaro) will be **not** be used with any other oncolytic medication other than those noted above.

II. Ixazomib (Ninlaro) is considered investigational when used for all other conditions, including but not limited to:
   A. Graft-Versus-Host Disease
   B. AL Amyloidosis
   C. Non-Hodgkin lymphoma
   D. Follicular lymphoma
   E. Breast cancer

F. Mantle cell lymphoma
G. Sarcoma
H. Kidney cancer
I. Central nervous system cancers

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Ixazomib (Ninlaro) is prescribed by, or in consultation with, an oncologist or hematologist; **AND**
IV. Clinical documentation of response to treatment such as stabilization or improvement in disease or symptoms; **AND**
V. Will be used in combination with lenalidomide (Revlimid) AND dexamethasone; **AND**
VI. Will **not** be used in combination with any other oncolytic medication other than lenalidomide (Revlimid).

Supporting Evidence

I. The safety and efficacy of ixazomib (Ninlaro) was evaluated in a randomized, double-blind, placebo controlled trial.
    - Ixazomib (Ninlaro) was evaluated in combination with lenalidomide (Revlimid) and dexamethasone for multiple myeloma in adults. Subjects were relapsed or refractory to at least one prior therapy, with those who were refractory to lenalidomide (Revlimid) excluded from the trial. The label indicates 69% of participants in each group had previously progressed on bortezomib (Velcade), 44-47% had progressed on thalidomide (Thalomid), 80-81% had progressed on melphalan therapy, and 55-59% had previous stem cell transplantation.
    - A total of 722 subjects were randomized and treated until disease progression or unacceptable toxicity with ixazomib (Ninlaro)on days one, eight, and 15 of the 28-day cycles.
    - The primary endpoint was progression-free survival (PFS) according to the 2011 International Myeloma Working Group (IMWG) Consensus Uniform Response Criteria, assessed by a blinded independent review committee. The PFS for ixazomib (Ninlaro) was 20.6 months (17, NE) versus 14.7 months (12.9, 17.6) [HR 0.74 (0.59-0.94), p<0.012].
    - A statistically significant survival benefit has not been demonstrated with ixazomib (Ninlaro).
II. National Comprehensive Cancer Network guidelines indicate that treatment with a three drug regimen is standard of care; however, for those that have low performance status, initiation with a two-drug regimen may be appropriate until performance improves.

III. Clinical resources indicate ixazomib (Ninlaro) is approved for multiple myeloma maintenance therapy for newly diagnosed disease; however, the label does not indicate this use. A clinical trial for maintenance therapy after hematopoietic stem cell transplant shows preliminary results for PFS; however, clinically relevant data, such as overall survival, are unknown at this time.

Investigational or Not Medically Necessary Uses

I. Ixazomib (Ninlaro) has not been sufficiently studied for safety and efficacy, and/or are is currently being evaluated in clinical trials for the following indications:
   A. Graft-Versus-Host Disease
   B. AL Amyloidosis
   C. Non-Hodgkin lymphoma
   D. Follicular lymphoma
   E. Breast cancer
   F. Mantle cell lymphoma
   G. Sarcoma
   H. Kidney cancer
   I. Central nervous system cancers

References

1. Ninlaro [Package Insert]. Cambridge, MA: Millennium Pharmaceuticals, Inc. November 2016.
2. NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma. Version 2.2019 [Updated October 9, 2019]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf
3. National Institutes of Health. clinicaltrials.gov. Available from www.clinicaltrials.gov. Accessed November 2019.
4. Dimopolulos MA., Gay F., Schjesvold F., et al. Oral ixazomib maintenance following autologous stem cell transplant (TOURMALINE-MM3): a double-blind, randomized, placebo-controlled phase 3 trial. *Lancet*. 2019; 393(10168):253-264.

Policy Implementation/Update:

Date Created	December 2015
Date Effective	February, 2016
Last Updated	November 2019
Last Reviewed	11/2019

Action and Summary of Changes	**Date**
Prior authorization criteria transitioned to policy format. Age requirement added, as well as clarification on place in therapy and appropriate combination therapy. Renewal requirements changed to include specialist prescriber, and appropriate place in therapy and combination therapy.	11/2019