POLICY NUMBER UM ONC_1284	**SUBJECT** Ninlaro™ (ixazomib)		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 3**
DATES COMMITTEE REVIEWED 03/23/16, 01/05/17, 01/10/18, 01/08/19, 12/11/19, 01/08/20	**APPROVAL DATE** January 8, 2020	**EFFECTIVE DATE** January 8, 2020	**COMMITTEE APPROVAL DATES** (latest version listed last) 03/23/16, 01/05/17, 01/10/18, 01/08/19, 12/11/19, 01/08/20	
PRIMARY BUSINESS OWNER: UM **APPROVED BY:** Dr. Andrew Hertler		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1		**NCQA STANDARDS** UM 2	**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** All	

I. PURPOSE

To define and describe the accepted indications for Ninlaro (ixazomib) usage in the treatment of cancer.

II. DEFINITIONS

Ninlaro (ixazomib): inhibits proteasomes reversibly which are enzyme complexes that regulate protein homeostasis within a cancer cell. This occurs specifically on the 20S proteasome activating a signaling cascade that eventually leads to cell-cycle arrest and apoptosis

Ninlaro (ixazomib) is the first approved oral proteasome and is FDA approved in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy.

Ninlaro (ixazomib) is available in 4mg, 3mg, and 2.3 mg oral capsules.

III. POLICY

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Ninlaro (ixazomib) may be considered medically necessary when any of the following selection criteria is met:

1. **PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:**
    a. When health plan Medicaid coverage provisions- including any applicable PDLs (Preferred Drug Lists)- conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the **Preferred Drug Guidelines OR**
    b. When health plan Exchange coverage provisions- including any applicable PDLs (Preferred Drug Lists)- conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the **Preferred Drug Guidelines OR**
    c. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the **Preferred Drug Guidelines shall follow NCH L1 Pathways** when applicable, otherwise shall follow NCH drug policies: http://pathways.newcenturyhealth.com **AND**
    d. Continuation requests of previously approved non-preferred medication are not subject to this provision **AND**
    e. When available, generic alternatives are preferred over brand-name drugs.
2. **Multiple Myeloma**
    a. Ninlaro (ixazomib) is being used for **ONE** of the following conditions:

i. Primary chemotherapy or for disease relapse after 6 months following primary chemotherapy with the same regimen:

   1. In combination with lenalidomide and dexamethasone **OR**
   2. In combination with cyclophosphamide and dexamethasone for transplant candidates **OR**

ii. Maintenance: as a single agent for transplant candidates.

iii. Relapse, progressive, or refractory disease:

   1. In combination with dexamethasone with or without lenalidomide.
   2. In combination with cyclophosphamide and dexamethasone.
   3. In combination with dexamethasone and pomalidomide for members who have received at least two prior therapies including an immunomodulatory agent and a proteasome inhibitor and who have demonstrated disease progression on or within 60 days of completion of the last therapy.

Exclusion Criteria: Ninlaro (ixazomib) is not considered medically necessary when any of the following selection criteria is met:

1. History of refractory disease on Ninlaro (ixazomib), proteasome inhibitor (i.e. bortezomib or carfilzomib), or immunodulatory agent (i.e. lenalidomide or pomalidomide). Refractory disease is defined as disease progression on treatment or progression within 60 days after the last dose of a given therapy.
2. Dosing exceeds single dose limit of 4 mg.
3. Treatment exceeds the maximum limit of 3 capsules (4 mg/3mg/2.3 mg) per month.
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Ninlaro (ixazomib) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration:** 4 mg oral capsule daily on days 1, 8, and 15 of a 28-day cycle. Doses should be given at least 1 hour before or 2 hours after food.
2. **Dosage Adjustments:**

   Renal: If the Creatinine clearance (CrCl) is < 30 mL /min (stage ≥ 4), reduce the initial dose to 3mg once weekly on days 1, 8, and 15 of the 28-day treatment therapy cycle. For patients with end stage renal disease (ESRD) please refer to the previous statement. Ninlaro (ixazomib) can be administered without regard to dialysis timing as it is not dialyzable.

   Hepatic: If the total bilirubin is > 1.5 times the ULN (moderate hepatic impairment) or > 3 time the ULN (sever hepatic impairment) reduce the initial dose to 3mg once weekly on days 1, 8, and 15 of the 28-day treatment therapy cycle.

   Other Toxicities: The first dose reduction is at 3mg. The second dose reduction is at 2.3 mg. If the member is unable to tolerate the 2.3 mg dose of the treatment therapy, then discontinue Ninlaro (ixazomib) all together.

3. **Monitoring**

   Monitor hepatic and renal function tests.

   Monitor platelet count monthly during therapy and adjust dosing for thrombocytopenia.

If ANC is < 500 mm^3 or platelet count is < 30,000 mm^3, withhold treatment therapy until ANC is greater than 500 mm^3 and resume at a reduced dose.

Monitor for severe diarrhea, constipation, nausea as vomiting and dose adjust as needed.

Monitor for symptoms of peripheral neuropathy.

Initiate a dose reduction for grade 2 and 3 toxicity and discontinue treatment therapy if the peripheral neuropathy is at grade 4.

Monitor for fluid retentions and consider dose adjusting in the presence of peripheral edema.

Monitor for rashes or other cutaneous reactions.

Discontinue treatment therapy if there is a grade 4 rash.

Monitor for hepatic enzymes for hepatotoxicity.

Monitor for embryo-fetal toxicity.

V. APPROVAL AUTHORITY

1. Review – Utilization Management Department
2. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. **PI prescribing information accessed on 1/8/19: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/208462lbl.pdf**
2. Clinical Pharmacology Elsevier Gold Standard. 2020.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2020.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2020.
5. **AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2020.**