

**STATE OF MICHIGAN**  
**DEPARTMENT OF INSURANCE AND FINANCIAL SERVICES**  
**Before the Director of Insurance and Financial Services**

**In the matter of:**

██████████  
**Petitioner**

**v**

**File No. 152106-001-SF**

**University of Michigan, Plan Sponsor**  
**and**  
**MedImpact Healthcare Systems, Inc., Plan Administrator**  
**Respondents**

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Issued and entered  
this 11<sup>th</sup> day of February 2016  
by **Randall S. Gregg**  
**Special Deputy Director**

**ORDER**

**I. PROCEDURAL BACKGROUND**

On February 8, 2016, ██████████, authorized representative of ██████████ (Petitioner), filed a request for an expedited external review with the Director of Insurance and Financial Services under the Patient's Right to Independent Review Act, MCL 550.1901 *et seq.*, appealing the denial of coverage for a prescription drug. The denial was issued by MedImpact Healthcare Systems, Inc. (MedImpact), the administrator of the Petitioner's prescription drug benefit plan. The benefit plan is a self-funded plan sponsored by the University of Michigan.

Public Act No. 495 of 2006 (Act 495), MCL 550.1951 *et seq.*, requires the Director to provide external reviews to a person covered by a self-funded health plan that is established or maintained by a state or local unit of government. The Director's review is performed "as though that person were a covered person under the Patient's Right to Independent Review Act." (MCL 550.1952). The Petitioner's prescription drug benefit plan is such a plan.

The Director notified MedImpact of the request and asked for the information used to make its final adverse determination. MedImpact furnished its response and the Director accepted the request for external review on February 8, 2016.

To address the medical issue in this case, the Director assigned it to an independent review organization which provided its analysis and recommendation on February 9, 2016.

**II. FACTUAL BACKGROUND**

The Petitioner is ██████ years old and has multiple myeloma. He has failed multiple medication therapy and a stem cell transplant. His oncologist recommended treatment with Ninlaro (ixazomib).

MedImpact denied coverage for the drug ruling that the medication is not medically necessary.

The Petitioner's authorized representative appealed the denial through MedImpact's internal grievance process. At the conclusion of that process, MedImpact issued a final adverse determination dated February 2, 2016, affirming its denial. The Petitioner now seeks a review of that adverse determination from the Director.

### III. ISSUE

Is MedImpact required to provide prescription drug coverage for Ninlaro?

### IV. ANALYSIS

#### Respondents' Argument

In its February 2, 2016, final adverse determination MedImpact's appeals coordinator wrote to the Petitioner:

Your request for a second level review of an adverse benefit determination [was] sent to Advanced Medical Reviews (AMR), an External Review Organization (ERO). The ERO has completed its review of your appeal regarding Ninlaro 4mg which was prescribed by [REDACTED], MD. Your appeal was not approved. A specialist in Internal Medicine, Oncology, and Hematology at AMR reviewed the case and made the following determination:

Based on the evidence-based literature, the request for ixazomib (Ninlaro) 4 mg is not medically necessary for this patient. It is not consistent with the accepted standard of practice and is not supported by sufficient evidence in published peer-reviewed medical literature."

#### Petitioner's Argument

In a letter dated February 5, 2016, the Petitioner's oncologist wrote:

[Petitioner] has been previously treated with Revlimid/dexamethasone, Revlimid/Dexamethasone/Velcade (RVD), autologous stem cell transplant; Revlimid with Biaxin, and Revlimid alone. [Petitioner] most recently progressed on RVD + Biaxin treatment and was switched to pomalidomide/dexamethasone/Velcade on 10/21/2015. Proteasome inhibition has shown benefit in both initial and relapsed myeloma. Until the approval of Ninlaro (ixazomib), proteasome inhibitors were only available for intravenous and subcutaneous administration. Ixazomib is the first oral proteasome inhibitor indicated for use in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy. My plan for [Petitioner] is to give all oral agents with the regimen Ninlaro/Pomalidomide/Dexamethasone.

Ninlaro is preferred NCCN Category 1 combination with lenalidomide and dexamethasone for patients who have received at least 1 prior therapy for relapse or for progressive or refractory disease and is also a category 2A as a single agent or with dexamethasone alone.

Pomalidomide is also NCCN Category 1 for patients who have received at least two prior therapies, including bortezomib and an immunomodulatory agent (in this case lenalidomide).

A phase 2 trial of ixazomib showed promising activity and favorable toxicity in relapsed myeloma in patients not refractory to Velcade. This new route of administration has been shown to be beneficial in older, more frail patients and those with more indolent relapses. Additionally, ixazomib has demonstrated an excellent response rate and safety in combination with pomalidomide and dexamethasone. This is not surprising as it is standard of practice that we often use the immune modulating agents (lenalidomide, thalidomide, and pomalidomide) interchangeably based on toxicity profile and patient characteristics.

[Petitioner] progressed on lenalidomide thus it would be inappropriate to prescribe lenalidomide for him hence the reason for pomalidomide. It is standard of practice to substitute in pomalidomide or thalidomide when a patient has progressed or is intolerant to lenalidomide. [Petitioner's] response to pomalidomide has been slow and given the evidence, we would like to optimize this response and add in ixazomib as the response rate in this combination was 62%. Given the data, providing it makes therapeutic and economical sense to change his Velcade to ixazomib. It is important to note that [Petitioner] has already completed one cycle of treatment with Ninlaro + pomalidomide + dexamethasone as the drug approved the first cycle. He has tolerated it well and the drug plan has approved an additional month supply while we await this decision. [References omitted.]

### Director's Review

To determine whether Ninlaro (ixazomib) is medically necessary for treatment of the Petitioner's condition, the Director presented the issue to an independent review organization (IRO) for analysis, as required by Section 11(6) of the Patient's Right to Independent Review Act, MCL 550.1911(6).

The IRO reviewer is a physician in active practice for more than 12 years who is board certified in hematology and oncology. The reviewer is familiar with the medical management of patients with the Petitioner's condition. The IRO report included the following analysis and recommendation:

[T]his case involves a [REDACTED] year-old male with a stage IIIA, IgG kappa multiple myeloma. At issue in this appeal is whether Ninlaro (ixazomib) is medically necessary treatment of the member's condition.

The member had progression of disease on most recent therapy consisting of Revlimid, bortezomib (Velcade) and dexamethasone (RVD) in October 2015, for which he was started on pomalidomide, bortezomib and dexamethasone on 10/21/15. Prior treatment consisted of 4 cycles of Revlimid and dexamethasone, then RVD followed by an autologous stem cell transplant in December 2007. Post-transplant, the member received Revlimid/dexamethasone followed by Revlimid. Biaxin was added. The member was observed from May to August 2012 and later restarted on Revlimid and dexamethasone on 8/17/12 and stopped on 5/21/13. RVD was started on 5/22/13 and in January 2015, Biaxin was added for which 29 cycles were completed and discontinued on 10/13/15 for progression of disease. Ixazomib is requested as a substitution for bortezomib (Velcade), since it is oral.

Ixazomib is Food and Drug Administration (FDA) approved for the treatment of multiple

myeloma in combination with lenalidomide (Revlimid) and dexamethasone based on a phase 1 and a phase 3 trials....[T]he combination of ixazomib with dexamethasone and pomalidomide is not supported by current medical guidelines and the medical literature and is not yet considered a standard of care. According to UpToDate, the choice of immunomodulatory agents is based upon the therapies that a patient has already tried and side effect profiles and are not necessarily interchangeable....[I]n addition, the combination of ixazomib, pomalidomide and dexamethasone is currently the subject of 4 clinical trials that are open to enrollment at present within the United States, making this combination of drugs experimental/investigational and not a standard of care at this time....

Pursuant to the information set forth above and available documentation...Ninlaro (ixazomib) is not medically necessary treatment of the member's condition. [Citations omitted.]

The Director is not required to accept the IRO's recommendation. *Ross v Blue Care Network of Michigan*, 480 Mich 153 (2008). However, the recommendation is afforded deference by the Director. In a decision to uphold or reverse an adverse determination, the Director must cite "the principal reason or reasons why the [Director] did not follow the assigned independent review organization's recommendation." MCL 550.1911(16)(b). The IRO's analysis is based on experience, expertise, and professional judgment. In addition, the IRO's recommendation is not contrary to any provision of the Petitioner's certificate of coverage. MCL 550.1911(15).

The Director, discerning no reason to reject the IRO's recommendation, finds that prescription drug Ninlaro (ixazomib) is not medically necessary for treatment of the Petitioner's conditions and therefore, is not a covered benefit.

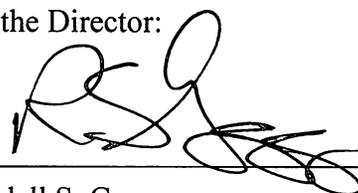
## V. ORDER

MedImpact's final adverse determination of February 2, 2016, is upheld.

This is a final decision of an administrative agency. Under MCL 550.1915, any person aggrieved by this order may seek judicial review no later than 60 days from the date of this order in the circuit court for the county where the covered person resides or in the circuit court of Ingham County. A copy of the petition for judicial review should be sent to the Department of Insurance and Financial Services, Office of General Counsel, Post Office Box 30220, Lansing, MI 48909-7720.

Patrick M. McPharlin  
Director

For the Director:



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Randall S. Gregg  
Special Deputy Director