

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. 148475-001

Blue Cross Blue Shield of Michigan,

Respondent.

---

Issued and entered  
this 28<sup>th</sup> day of July 2015  
by Randall S. Gregg  
Special Deputy Director

**ORDER**

**I. PROCEDURAL BACKGROUND**

On June 24, 2015, ██████████ authorized representative of ██████████ (Petitioner), filed a request with the Director of Insurance and Financial Services for an external review under the Patient's Right to Independent Review Act, MCL 550.1901 *et seq.* On July 1, 2015, after a preliminary review of the information submitted, the Director accepted the request.

The Petitioner receives health care benefits through a plan that is underwritten by Blue Cross Blue Shield of Michigan (BCBSM). The Director immediately notified BCBSM of the external review request and asked for the information it used to make its final adverse determination. BCBSM submitted the material on July 2, 2015.

The case involves medical issues so it was assigned to an independent review organization which submitted its recommendation on July 14, 2015.

**II. FACTUAL BACKGROUND**

At the time the medical service in dispute was rendered, the Petitioner's health care benefits were defined in BCBSM's *Community Blue Group Benefits Certificate*<sup>1</sup> (the certificate).

---

<sup>1</sup> BCBSM form no. 6225, approved 10/12.

The Petitioner has colitis and proctitis (inflammation of the rectum) that were treated with the prescription drug Humira (adalimumab). Her physician ordered the Anser ADA diagnostic test to monitor her response to the Humira. The test was performed on February 11, 2014, by [REDACTED] Laboratories, Inc., a non-participating provider. The charge for the test was \$2,500.00.

BCBSM denied coverage, saying the test was investigational in the treatment of the Petitioner's condition and therefore not a covered benefit. The Petitioner appealed the denial through BCBSM's internal grievance process. At the conclusion of that process BCBSM issued a final adverse determination dated April 27, 2015, affirming its denial. The Petitioner now seeks a review of that final adverse determination from the Director.

### III. ISSUE

Is the Anser ADA test investigational for the treatment of the Petitioner's condition?

### IV. ANALYSIS

#### BCBSM's Argument

In its final adverse determination, BCBSM's representative told the Petitioner's authorized representative:

. . . After review, I have determined that payment cannot be approved. The BCBSM/BCN Joint Uniform Medical Policy Committee (JUMP) has determined that the service is investigational.

\* \* \*

A board-certified M.D., in Family Practice reviewed the claim, the appeal, and [the Petitioner's] health care plan benefits for Blue Cross Blue Shield of Michigan (BCBSM). The medical consultant determined:

All of the submitted documentation was reviewed. Provider is appealing denial of 84999 (Anser ADA test) for a [REDACTED] year old member with diagnosis of colitis and proctitis who had the lab test Anser ADA performed in which Adalimumab (Humira) concentrations (levels) and antibodies were measured. According to BCBSM Medical Policy titled *Measurement of Serum Antibodies to Infliximab and Adalimumab*, measurement of antibodies to either infliximab or adalimumab in a patient receiving treatment with either infliximab or adalimumab, whether alone or as a combination test which includes the measurement of serum infliximab or adalimumab levels, is considered experimental/ investigational. The use of these tests has not been clinically proven to improve patient clinical outcomes or alter patient management.

\* \* \*

In this case, because the medical consultant determined that the service is considered experimental/investigational, and because experimental/investigational treatment is not covered by [the Petitioner's] terms of coverage, payment cannot be approved. I understand you disagree with this determination; however, I must adhere to the terms and conditions of coverage, and I cannot make an exception on [the Petitioner's] behalf.

### Petitioner's Argument

In a June 17, 2015 letter of appeal accompanying the external review request, the Petitioner's authorized representative said:

On 04/27/2015 [BCBSM] denied the [REDACTED] Answer ADA diagnostic test performed on 02/11/2014

as being Experimental/Investigational.

Anti-TNF agents, such as Humira (adalimumab), have demonstrated efficacy for induction and maintenance of remission in patients with moderate to severe CD or UC or both but the response is not universal. More than one third of patients do not respond to induction therapy (primary nonresponse) and even among initial responders, the response wanes over time. [REDACTED] has been treating [Petitioner] with Adalimumab for her IBD. She had begun to exhibit symptoms/ or loss of response that may be attributed to subtherapeutic levels of Adalimumab (ADA) and/or the presence of antibodies to Adalimumab (ATA).

An increasing number of studies have assessed the relationship between Adalimumab levels and the presence of ATA's with outcomes in patients with IBD. . . .

\* \* \*

Advantages of the Anser ADA assay include:

- Detection of all antibody isotypes and subclasses of IgG, and antibodies with low binding affinity, yielding fewer false negative results
- Data demonstrating no significant interference in both assays from common endogenous components of human serum and drug, generating fewer false positive results thereby reducing likelihood of unnecessary changes in management
- Analytical validation of both the ATA and Adalimumab assays with robust performance data (99% specificity and 100% sensitivity for ATI, 97% specificity and 100% sensitivity for ADA)

In summary, there is a growing consensus that measuring ADA drug levels as well as ATA's is important in the management and treatment of patients to identify those who:

- Have clinical symptoms that may not correlate with active IBD
- Have antibodies to antibodies to adalimumab
- Exhibits therapeutic levels of adalimumab, but the inflammation is not TNF-driven

Based on [Petitioner's] symptoms, the clinician's medical findings and assessment as well as the evidence presented above we are asking that you overturn the denial of this service as Experimental/Investigational and provide coverage at an in-network benefit level. This patient should not be penalized for obtaining a test which her physician believed could play a critical role in assessing and managing her response to Humira. [References omitted]

### Director's Review

The certificate (p. 6.3) excludes coverage for experimental treatment:

#### Services That Are Not Payable

We do not pay for experimental treatment (including experimental drugs or devices) or services related to experimental treatment, except as explained under "Services That Are Payable" below.<sup>2</sup> In addition, we do not pay for administrative costs related to experimental treatment or for research management.

"Experimental treatment" is defined in the certificate (p. 7.10):

Treatment that has not been scientifically proven to be as safe and effective for treatment of the patient's conditions as conventional treatment. Sometimes it is referred to as "investigational" or "experimental services."

The question of whether the Anser ADA test was experimental or investigational for the Petitioner's condition was presented to an independent review organization (IRO) for analysis and a recommendation as required by section 11(6) of the Patient's Right to Independent Review Act, MCL 550.1911(6).

The IRO physician reviewer is board certified in internal medicine and gastroenterology, and is in active clinical practice. The IRO report included the following analysis and recommendation:

#### **Recommended Decision:**

---

<sup>2</sup> None of the exceptions apply in this case.

The MAXIMUS physician consultant determined that the Anser ADA testing performed on 2/11/14 was experimental/investigational for diagnosis and treatment of the member's condition.

**Rationale:**

The results of the consultant's review indicate that this case involves a now [REDACTED] year-old female who has a history of ulcerative colitis. At issue in this appeal is whether the Anser ADA testing performed on 2/11/14 was experimental/investigational for diagnosis and treatment of the member's condition.

The member had been treated with Humira along with a thiopurine drug. A note from March 2014 stated that the member was having worsening proctitis symptoms with diarrhea and urgency and that she was also having dysphagia as well. In February 2014, the member underwent the Anser ADA assay, which revealed detectable levels of adalimumab and undetectable antibodies.

Monitoring patients on adalimumab with measurement of adalimumab levels and antibodies to adalimumab levels remains an area of clinical interest. In generally (sic), adalimumab levels correlate inversely with disease activity. The presence of antibodies may portend or explain loss of response. However, the MAXIMUS physician consultant explained that the target level of adalimumab necessary to achieve clinical benefit remains unknown. The physician consultant also explained that there are no controlled data which have identified the optimal drug level to date. This issue remains speculative. The physician consultant indicated that issues of how a patient is doing on the drug, whether the patient is responding or losing response are more important than drug level. The consultant also indicated there are no prospective controlled data to validate the use of the Anser ADA test in directing treatment.

Pursuant to the information set forth above and available documentation, the MAXIMUS physician consultant determined that the Anser ADA testing performed on 2/11/14 was experimental/investigational for diagnosis and treatment of the member's condition. [References 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 extensive 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 why the IRO's recommendation should be rejected in this case, finds that the Anser ADA test was experimental or investigational for the treatment of the Petitioner's condition and therefore was not a benefit under the terms of the certificate.

**V. ORDER**

The Director upholds BCBSM's April 27, 2015 final adverse determination.

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 Michigan 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:

A handwritten signature in black ink, appearing to read 'RSG', is written over a horizontal line.

Randall S. Gregg  
Special Deputy Director