

**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. 149241-001-SF**

████████████████████

**Plan Sponsor**

**and**

**Blue Cross and Blue Shield of Michigan, Plan Administrator  
Respondents**

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Issued and entered  
this 3<sup>rd</sup> day of September 2015  
by Randall S. Gregg  
Special Deputy Director

**ORDER**

**I. PROCEDURAL BACKGROUND**

On August 6, 2015, ██████████ authorized representative of ██████████ (Petitioner), filed a request with the Director of Insurance and Financial Services for an external review under Public Act No. 495 of 2006 (Act 495), MCL 550.1951 *et seq.* Act 495 authorizes the Director to conduct this external review as though the Petitioner were a covered person under the Patient's Right to Independent Review Act, MCL 550.1901 *et seq.* The Petitioner receives health care benefits through a plan sponsored by the ██████████ a self-funded governmental health plan as defined in Act 495. Blue Cross Blue Shield of Michigan (BCBSM) administers the plan. The benefits are described in BCBSM's *Community Blue Group Benefits Certificate*.

After a preliminary review of the material submitted, the Director accepted the Petitioner's request. The Director notified BCBSM of the external review request and asked for the information it used to make its final adverse determination. The Director received BCBSM's response on August 14, 2015.

The Director assigned an independent medical review organization to evaluate the medical issues in the case. The evaluation was submitted on August 26, 2015.

**II. FACTUAL BACKGROUND**

The Petitioner has Crohn's disease and is being treated with the drug Humira (adalimumab). His physician ordered the Anser IFX diagnostic test to monitor the Petitioner's response to Humira. The test was performed on June 23, 2014, by Prometheus Laboratories, Inc. The charge was \$2,500.00.

BCBSM denied coverage, ruling that the test was investigational and experimental as a part of the treatment for the Petitioner's condition. The Petitioner appealed the denial through BCBSM's internal grievance process. At the conclusion of that process, on July 14, 2015, BCBSM issued a final adverse determination affirming its denial. The Petitioner now seeks a review of that adverse determination from the Director.

### III. ISSUE

Was the Anser IFX test experimental or investigational as a part of the treatment of the Petitioner's Crohn's disease?

### IV. ANALYSIS

#### BCBSM's Argument

In its final adverse determination, BCBSM stated that the Petitioner's appeal was reviewed by a physician who is board-certified in internal medicine. The reviewer concluded that the denial of coverage should be affirmed. The reviewer stated:

Your appeal is for the denial of the PROMETHEUS Anser IFX test you had on June 23, 2014. Your doctor ordered the PROMETHEUS Anser IFX test for your Crohn's disease (an inflammatory bowel disease), to find out if the medication was helping control the disease. According to the Blue Cross Blue Shield of Michigan medical policy titled "Measurement of Serum Antibodies to Infliximab / 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.

#### Petitioner's Argument

In the request for external review, the Petitioner's authorized representative wrote:

We respectfully dispute all of the criteria that were used to deny Anser IFX testing for this patient. In our previous appeals we provided five peer-reviewed publications that address the importance of measuring levels of infliximab as well as antibodies to infliximab (ATI). There is an ever increasing body of evidence that demonstrates the impact that increasing levels of ATI can have on a patient's response to infliximab. Those publications, as well as the additional, published and peer reviewed literature listed below, clearly demonstrate that this technology cannot be considered unproven, experimental, nor not medically necessary. These, as well as many other publications provide support that the use of the data provided by this assay can be utilized by a clinician as "an effective management tool".

- Murthy S, Kevans D, Seow CH, et al. Association of serum infliximab and antibodies to infliximab to long-term clinical outcome in acute ulcerative colitis. *Gastroenterology*. 2012;142(5)(suppl1):S-388.
- Veres G, Kaplan JL, De Greef E, et al. New assay to detect infliximab levels and anti-infliximab antibodies from a single serum sample is useful in measuring efficacy of treatment with infliximab in children with IBD. *Gastroenterology*. 2012;142(5)(suppl 1):S-386.
- Kevans D, Murthy S, Iacono A, Silverberg MS, Greenberg GR. Accelerated clearance of serum infliximab during induction therapy for acute ulcerative colitis is associated with treatment failure. *Gastroenterology*. 2012;142(5)(suppl 1):S-385.
- Vande Casteele N, Cuypers L, Singh S, et al. Antibodies to infliximab can either be persistent or transient: a retrospective case-control study in IBD patients treated with infliximab maintenance therapy. *Gastroenterology*. 2012;142(5)(suppl 1):S- Velayos FS, Kahn JG, Sandborn WJ, Feagan BG. A test-based strategy is more cost effective than empiric dose-escalation for patients with Crohn's disease who lose responsiveness to infliximab [published online ahead of print January 25, 2013]. *Clin Gastroenterol Hepatol*. doi:10.1016/j.cgh.2012.12.035.
- Novel infliximab (IFX) and antibody-to-infliximab (ATI) assays are predictive of disease activity in patients with Crohn's disease (CD). *Gastroenterol Hepatol*. 2012;8(7)(suppl 4):3-4.

### Director's Review

The *Community Blue* certificate (page 6.3) excludes coverage for experimental treatment or services. The certificate (page 7.10) defines an experimental treatment as:

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 IFX test was experimental or investigational in the medical management of the Petitioner's condition was presented 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 who is board certified in gastroenterology and has been in practice for more than 15 years. The IRO report included the following analysis and recommendation:

[T]his is an unusual case, in which there was interruption of treatment with infliximab (Remicade). With restarting this medication, the member developed a possible lupus-like syndrome. There was significant concern that the member had an antigen-antibody complex, which was forming due to infliximab that was activating complement...[I]n these circumstances, it was reasonable to order testing of antibodies to infliximab. The result was negative and therefore, the etiology of the member's syndrome is unknown. However...biologics can be safely restarted in the future should the member need them.

Pursuant to the information set forth above and available documentation...the Prometheus Anser IFX test performed on 6/23/14 was not experimental/ investigational for diagnosis and treatment of the member's condition. ([www.uptodate.com/contents/infliximab-drug-information](http://www.uptodate.com/contents/infliximab-drug-information). Chalasani NP, et al. ACG Clinical Guideline: the diagnosis and management of idiosyncratic drug-induced liver injury. *Am J Gastroenterol.* 2014;109(7):950-66.)

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. The Director can discern no reason why the IRO's recommendation should be rejected in this case. Furthermore, it is not contrary to any provision of the Petitioner's certificate of coverage.

The Director finds that the Anser IFX test is not experimental/investigational as part of the Petitioner's treatment for Crohn's disease.

#### V. ORDER

The Director reverses BCBSM's final adverse determination of July 14, 2015. The Respondents shall immediately provide coverage for the Petitioner's Anser IFX test, and shall, within seven days of providing coverage, furnish the Director with proof that it has implemented this order.

To enforce this order, the Petitioner may report any complaint regarding its implementation to the Department of Insurance and Financial Services, Health Care Appeals Section, at this toll free telephone number: (877) 999-6442.

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:



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Randall S. Gregg  
Special Deputy Director