

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. 147839-001

Blue Cross Blue Shield of Michigan
Respondent

Issued and entered
this 9th day of June 2015
by Randall S. Gregg
Special Deputy Director

ORDER

I. PROCEDURAL BACKGROUND

On May 12, 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 May 19, 2015, after a preliminary review of the information submitted, the Director accepted the request.

The Petitioner receives health care benefits through a plan underwritten by Blue Cross Blue Shield of Michigan (BCBSM) for the Michigan Education Special Services Association (MESSA). The terms of coverage are defined in BCBSM's *MESSA Choices/Choices II* benefit booklet. The Director 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 May 27, 2015.

The case involves medical issues so it was assigned to an independent review organization which submitted its recommendation on June 2, 2015.

II. FACTUAL BACKGROUND

The Petitioner has ulcerative colitis. She has been treated with the drug Remicade (infliximab). Her physician ordered a test known as the Anser IFX to monitor her response to Remicade. The test was performed on February 1, 2014, by Prometheus Laboratories, Inc. The charge for the test was \$2,500.00.

BCBSM denied coverage, saying the test was investigational or experimental for 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 March 11, 2015, affirming its denial. The Petitioner now seeks a review of that final adverse determination from the Director.

III. ISSUE

Was the Anser IFX test experimental or investigational for the treatment of the Petitioner's condition?

IV. ANALYSIS

BCBSM's Argument

In its final adverse determination, BCBSM stated that the Petitioner's appeal had been reviewed by a medical doctor board certified in family practice who concluded:

According to BCBSM Medical Policy titled "Measurement of Serum Antibodies to Infiximab 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.

Petitioner's Argument

In an April 30, 2015 letter included with the request for an 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...clearly demonstrate that this technology cannot be considered unproven, experimental, or 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 "an effective management tool".
[References omitted.]

Director's Review

The *MESSA Choices/Choices II* benefit booklet (page 54) excludes coverage for “experimental treatment or services related to experimental treatment except as approved by the BCBSM.” “Experimental treatment” is defined in the booklet (page 71) as

Treatment that has not been scientifically proven to be as safe and effective for treatment of the patient’s condition as conventional treatment. Sometimes it is referred to as “experimental services.”

The question of whether the Anser IFX test was experimental or investigational for 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 in active practice who is certified by the American Board of Internal Medicine with a subspecialty in gastroenterology. The reviewer is a member of the American College of Gastroenterology, the American College of Physicians, and the American Gastroenterology Association and is published in peer reviewed medical literature. The IRO report included the following analysis and recommendation:

This case involves a forty seven (47) year old female, with a history of ulcerative colitis complicated by sclerosing cholangitis. The enrollee has previously been treated with azathioprine, which was discontinued due to acute hepatic toxicity. She had previously required the use of corticosteroids, with weight gain related to that class of medications. An Anser IFX panel was ordered. It demonstrated detectable serum levels of infliximab, and no detectable antibodies to infliximab. When seen in follow-up on April 17, 2014, the enrollee’s symptoms were well controlled on infliximab every eight (8) weeks.

* * *

The Anser IFX panel consists of two (2) separate serological levels: antibodies to infliximab and serum infliximab levels. As noted above, the measurement of serum infliximab levels has been suggested as a cost-effective follow-up to the adjustment of infliximab dosing, without measurement of antibodies to infliximab. The use of this test panel is not part of the routine management as noted in the specialty society guidelines for the treatment of inflammatory bowel disease. The laboratory testing in question is not subject to Federal Food and Drug Administration (FDA) approval, as it has been developed and validated by the performing lab. It is also not the subject of a current investigational new device application for the same reason.

The use of the Anser IFX serological testing has not been shown to be medically necessary for this enrollee. Based on the current medical literature, such testing

has remained experimental and/or investigational. As noted in a study specifically aimed at determining the clinical utility of the measurement of these parameters, "In patients with irritable bowel disease (IBD) who lose response to infliximab, clinical improvement may occur upon intensification of infliximab therapy, irrespective of infliximab serum concentration or presence of antibodies to Infliximab (ATI)." These results are counter-intuitive to those of a previous study in Rheumatoid Arthritis (RA) patients, in [which] it was stated "Specific and neutralizing anti-infliximab antibodies develop in RA patients treated with infliximab, and that low trough levels of functional infliximab are associated with the presence of such antibodies." Although a preliminary evaluation by Yanai and Hanauer states that the combination of ATI's and Infliximab serum level measurement can have an impact in the care of patients, it is further stated that this hypothesis requires prospective evaluation. As noted in a review of the subject of the usefulness of monitoring both ATI's and serum infliximab levels, "Serum IFX concentrations are related to response in luminal or fistulizing Crohn's disease, as well as in ulcerative colitis. Those patients receiving maintenance IFX who had detectable trough concentrations of IFX had a higher rate of clinical remission, a lower serum C-reactive protein, and a higher rate of endoscopic improvement, irrespective of ATI status or concomitant immunosuppression." This sentiment was echoed in an Ulcerative Colitis study published in Gut; "An undetectable trough serum infliximab, irrespective of antibody status, is associated with less favourable outcomes." It has been suggested that serum infliximab levels alone may be an appropriate test to be performed in response to a loss of clinical effectiveness of the medication.

The predominant opinion in the literature is that this test panel requires further evaluation and controlled studies. As noted, further controlled prospective studies have been recommended in the literature regarding the utility of this test panel. The use of this panel has not been demonstrated in controlled studies to be more beneficial than available standard health care services. For this reason, the use of the Anser IFX panel would be considered investigational/experimental, and therefore not medically necessary. [References omitted]

Recommendation:

It is the recommendation of this reviewer that the denial issued by Blue Cross Blue Shield of Michigan for the Anser IFX diagnostic test performed on February 1, 2014 be upheld.

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, discerning no reason why the IRO's recommendation should be rejected in this case, finds that the Anser IFX test is experimental/investigational for the management of the Petitioner's condition and is therefore not a benefit under the terms of the booklet.

V. ORDER

The Director upholds BCBSM's final adverse determination of March 11, 2015.

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:



Randall S. Gregg
Special Deputy Director