

STATE OF MICHIGAN  
DEPARTMENT OF ENERGY, LABOR & ECONOMIC GROWTH  
OFFICE OF FINANCIAL AND INSURANCE REGULATION  
Before the Commissioner of Financial and Insurance Regulation

In the matter of

XXXXX

Petitioner

File No. 103972-001

v

Aetna Life Insurance Company  
Respondent

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Issued and entered  
this 22<sup>nd</sup> day of July 2009  
by Ken Ross  
Commissioner

**ORDER**

**I  
PROCEDURAL BACKGROUND**

On March 31, 2009, XXXXX (Petitioner) filed a request for external review with the Commissioner of the Office of Financial and Insurance Regulation under the Patient's Right to Independent Review Act, MCL 550.1901 *et seq.*

The Commissioner notified Aetna Life Insurance Company (Aetna) of the external review and requested the information used in making its adverse determination. Aetna provided the information on April 6, 2009.

The case involves medical issues so the Commissioner assigned it to an independent review organization which provided its recommendation to the Commissioner on April 21, 2009.

**II  
FACTUAL BACKGROUND**

The Petitioner's group health coverage is described in Aetna's Open Choice plan booklet (the certificate) and its Summary of Coverage.

In June 2008, during an extensive hospital stay, the Petitioner was diagnosed with Crohn's disease. Her gastroenterologist, Dr. XXXXX, started her on prednisone to control her condition and later placed her on Imuran as a "steroid sparing agent." Dr. XXXXX ordered thiopurine metabolite serologies to monitor her metabolite levels and regulate the doses of Imuran. These tests were provided August 8, 2008, September 18, 2008, and November 4, 2008.

Aetna denied coverage, asserting that the tests did not meet its medical policy criteria. The Petitioner appealed but Aetna maintained its denial and issued a final adverse determination dated February 13, 2009.

### **III ISSUE**

Was Aetna's denial of coverage for the Petitioner's serological tests correct under the terms of her coverage?

### **IV ANALYSIS**

#### **Petitioner's Argument**

Dr. XXXXX ordered the serological tests to help monitor the Imuran levels and insure the proper dosage. Dr. XXXXX explained the importance of the tests:

Once [the Petitioner] was started on Imuran I ordered metabolite levels to help direct the correct dosing of her Imuran. This is not an experimental test and is actually now considered standard of care in monitoring patients who are just being started on Imuran. This allows us to increase the dose to therapeutic levels while avoiding toxicity. Furthermore, I would note that after [Aetna] disallowed payment for these metabolite levels [the Petitioner] actually did run into complications from being placed on a higher Imuran dose. She developed neutropenia and anemia that required stopping the Imuran for a period of time.

The Petitioner believes Aetna's should cover the serological tests, saying they are not experimental or investigational. She argues that the tests are medically necessary because of her medical condition and needed to help her regain her health. The Petitioner believes Aetna should cover the tests.

Aetna's Argument

In its February 13, 2009, final adverse determination, Aetna defended its decision to deny coverage stating:

Based on our review..., we are upholding the previous decision to deny benefits for the laboratory test you had on August 8, 2008, September 18, 2008 and November 4, 2008 based on the information submitted not meeting coverage criteria of the Clinical Policy Bulletin for Inflammatory Bowel Disease: Serologic Markers and Pharmacogenomic and Metabolic Assessment of Thiopurine Therapy. Aetna does not cover this testing to determine therapeutic direction and monitoring of response. Also the [grievance] panel found no recent peer literature submitted with your appeal from your physician supporting the use of this testing for purposes of monitoring and therapeutic direction.

Aetna's clinical policy bulletin states in part:

Aetna considers 6-thioguanine nucleotide (6-TGN) and 6-methylmercaptopurine nucleotide (6-MMPN) (e.g., PRO-Predict<sup>R</sup> 6MP / azathioprine, PRO-Predict Metabolites) experimental and investigational to determine therapeutic direction and monitor response to 6-mercaptopurine and azathioprine therapy and for all other indications.

Aetna also cites the "General Exclusions" section of the certificate, which says:

Coverage is not provided for the following charges:

\* \* \*

- Those for or in connection with services or supplies that are, as determined by Aetna, to be experimental or investigational. A drug, a device, a procedure, or treatment will be determined to be experimental or investigational if:

there are insufficient outcomes data available from controlled clinical trials published in the peer reviewed literature to substantiate its safety and effectiveness for the disease or injury involved; or

if required by the FDA, approval has not been granted for marketing; or

a recognized national medical or dental society or regulatory agency has determined, in writing, that it is experimental, investigational, or for research purposes; or

the written protocol or protocols used by the treating facility, or the protocol or protocols of any other facility studying substantially the same drug, device, procedure, or treatment, or the written informed consent used by the treating facility or by another facility studying the same drug, device, procedure, or treatment states that it is

experimental, investigational, or for research purposes.

Aetna denied coverage for the tests because they do not meet the criteria of its medical policy and are considered to be experimental or investigational and therefore excluded under the terms of the certificate.

### Commission's Review

The Commissioner has carefully reviewed the arguments of the parties as well as the documents submitted and the certificate.

Because this case involves medical questions, the Commissioner asked for an analysis and recommendation from an independent review organization (IRO). The IRO physician who conducted the review is certified by the American Board of Internal Medicine with subspecialty certification in gastroenterology (diplomate) and is a member of the American College of Gastroenterology, the American College of Physicians, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy. The IRO reviewer is also published in the peer reviewed medical literature and is in active practice.

The IRO reviewer said:

The key enzyme in the breakdown pathway of azathioprine/6MP is thiopurine methyltransferase (TPMT). The measurement of either the TPMT gene or the enzyme activity of TPMT is medically necessary before initiation of azathioprine/6-MP treatment. It may also be done during treatment (if not previously done) in the event that a patient with abnormal blood count does not respond to dose reduction. Measurement of metabolite levels has been proposed as a mechanism to adjust the dose of azathioprine (AZA)/6-MP.

A study by Lowry et al, comparing 6-TG levels, leukocyte counts and disease activity showed poor correlation of metabolite level to either of the other two parameters. Another study by Goldenberg, et al likewise showed a poor correlation of 6-TG level to remission. \* \* \* The most cost-effective strategy was the measurement of TPMT enzyme activity. A commentary in the American Journal of Gastroenterology suggested that, "beyond use to assist in the determination of patient compliance, the measurement of metabolite levels requires further controlled trials. It should otherwise be considered to be experimental/investigational. Aetna's Clinical Policy Bulletin: Inflammatory Bowel Disease: Serologic Markers and Pharmacogenomic and Metabolic Assessment of Thiopurine Therapy Plan is well written and in agreement with the current standard of care.

The IRO reviewer recommended that Aetna's denial of coverage be upheld.

The Commissioner is not required in all instances to accept the IRO's recommendation. However, the Commissioner gives deference to the IRO's conclusion since it is based on extensive expertise and professional judgment. The Commissioner, discerning no reason to reject the IRO recommendation in this case, accepts the IRO reviewer's determination and finds that the thiopurine metabolite serologies are experimental or investigational and are therefore excluded from coverage under the terms of its certificate.

**V  
ORDER**

The Commissioner upholds Aetna Life Insurance Company's February 13, 2009, adverse determination. Aetna is not required to cover the Petitioner's August 8, 2008, September 18, 2008, and November 4, 2008, serological testing.

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 sixty 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 Commissioner of Financial and Insurance Regulation, Health Plans Division, Post Office Box 30220, Lansing, MI 48909-7720.