

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. 118778-001

v

Humana Insurance Company
Respondent

Issued and entered
this 4th day of December 2010
by Ken Ross
Commissioner

ORDER

I
BACKGROUND

On December 29, 2010, XXXXX (Petitioner) filed a request for an expedited external review with the Commissioner of Financial and Insurance Regulation under the Patient's Right to Independent Review Act (PRIRA), MCL 550.1901 *et seq.* On December 29, 2010, after a review of the material submitted, the Commissioner accepted the request for external review on an expedited basis.

The matter was assigned to an independent review organization, which provided its recommendation to the Office of Financial and Insurance Regulation on December 30, 2010.

II
FACTUAL BACKGROUND

Petitioner was diagnosed with membranous nephropathy in June 2010. After failing conservative treatment, Dr. XXXXX, a specialist in glomerulonephritis at the XXXXX recommended treatment with Rituxan was the drug best suited to treat his kidney disease.

Dr. XXXXX requested authorization from Humana to perform Rituxan infusions. Humana denied the request on that basis that Rituxan is not listed for use in kidney disease and is not listed as a drug to use for membranous glomerulonephritis.

The Petitioner appealed and was afforded an expedited internal grievance. At the conclusion of the internal grievance process Humana maintained its denial and issued a final adverse determination dated December 20, 2010.

III ISSUE

Did Humana properly deny authorization and coverage for Rituxan infusions under the terms of the certificate?

IV ANALYSIS

Petitioner's Argument

In a December 16, 2010, letter To Whom It May Concern, the Petitioner's physician explained the reasons for requesting treatment with Rituxan:

... [The Petitioner] was diagnosed with membranous nephropathy in June 2010. I saw the patient in November 2010. At that time he was still nephrotic despite maximum conservative therapy.

The best therapy for membranous nephropathy is the combined use of high dose [P]redisone with Cyclophosphamide. However, the patient has already elevated glucose levels and the use of [Prednisone is likely to make this much worse. In addition, the long-term toxicity of Cytoxan, e.g. bladder cancer, leukemia, etc., has relegated this treatment as rescue therapy in these patients.

Although considered experimental until recently there is considerable evidence that Rituxan is safe and effective in inducing remission of proteinuria in patient with membranous nephropathy. Our own experience with >35 patients treated with [R]ituximab for membranous nephropathy shows this drug to be of benefit in more than 70% of the patients, with an excellent side-effect profile: findings that are unheard of with the use of other available medications. . .

I would consider that allowing this patient's nephrotic syndrome to progress because of failure on your part to allow this patient the use of a medication that could put him into complete remission with minor side

effects to be short sighted to say the least. Should this patient be left untreated, the disease will progress and is likely to result in impairments to his quality of life, are inherent to these last two conditions.

Petitioner's physician notes that Petitioner failed antihypertensive agents, including angiotensin receptor blockers, and diuretics. For these reasons the Petitioner's physician wants Humana to authorize the Rituxan infusions as soon as possible.

Respondent's Argument

In its December 20, 2010, final adverse determination, Humana gave its reason for denying authorization for Rituxan infusions:

We were unable to approve [your] request for the Rituxan® infusion based on the report from the independent physician who reviewed all the information submitted for the expedite[d] appeal. This drug is listed in the Humana guideline for a variety of hematologic disease and certain types of arthritis, but it is not listed or use in kidney disease and is not listed as a drug to use for membranous glomerulonephritis.

In addition, the drug is not listed as first line therapy for membranous glomerulonephritis by up-to-date. Thus, this request for Rituxan® would be considered investigational for the member's diagnosis.

The Benefit Plan Document states:

LIMITATIONS AND EXCLUSIONS

Other limitation and exclusions

Unless specifically stated otherwise, no benefits will be provided for or on account of the following items:

Any drug, biological product, device, medical treatment, or procedure which is experimental, or investigational or for research purposes.

GLOSSARY

Experimental or investigational or for research purposes means a drug, biological product, device, treatment or procedure that meets any one of the following criteria, as determined by us:

Cannot be lawfully marketed without the final approval of the United States Food and Drug Administration (FDA) and which lacks such final FDA approval for the use or proposed use, unless (a) found to be accepted for that use in the most recently published edition of the United States Pharmacopeia-Drug Information for Healthcare Professional (USP-DI) or in the most recently published edition of the American Hospital Formulary Services (AHFS) Drug Information, or (b) identified as safe, widely used and generally accepted as effective for that use as reported in nationally recognized peer reviewed medical literature published in the English language as of the date of services; or (c) is mandated by state law.

- Is a device required to receive Premarket Approval (PMA) or 510K PPEOCL by the FDA but has not received a PMA or 510K approval;
- Is not identified as safe, widely used and generally accepted as effective for the proposed use as reported in nationally recognized peer reviewed medical literature published in the English language as of the date of service;
- Is the subject of a National Cancer Institute (NCI) Phase 1, II or III trial or a treatment protocol comparable to a NCI Phase I, II or III trial, or any trial not recognized by NCI regardless of ; or
- Is identified as not covered by the Centers for Medicare and Medicaid Services (CMS) Medicare Coverage Issues Manual, a CMS Operational Policy Letter or a CMS National Coverage Decision, except as required by state or federal law.

Humana contends the decision is in compliance with the terms of the certificate.

Commissioner's Review

Petitioner seeks coverage for Rituxan at two (2) 1-gram doses as a means to control his glomerulonephritis. Humana has denied the request based on its belief that Rituxan for Petitioner's condition was considered investigational; and its certificate excludes any drug which is experimental or investigational.

In order to resolve the question of whether the Petitioner's prescription for Rituxan is medically necessary, the Commissioner obtained the recommendation of an independent review organization (IRO). The review was conducted by a physician who is certified by the practicing physician who is board certified in internal medicine and nephrology and has been in practice for more than 15 years.. The IRO reviewer referenced several articles in his recommendation to reverse Humana's denial of coverage for Rituxan.

The IRO report explained:

The MAXIMUS physician consultant noted that the member has been treated with antihypertensive agents, including angiotensin receptor blockers, and diuretics. The MAXIMUS physician consultant indicated that the member's medical records reports adverse affects from prednisone in the past, as well as a cough from an ACE inhibitor. The MAXIMUS physician consultant also indicated that in November 2010, the member's kidney function was well preserved, but his proteinuria was marked at 16 grams per 24 hours. The MAXIMUS physician consultant noted that the member has an elevated Hgb A1c of 6.2 and has had fasting glucose levels as high as 157. The MAXIMUS physician consultant also noted that the member has abnormal glucose tolerance and that some would consider him to be diabetic. The MAXIMUS physician consultant indicated that the member's weight is over 290 pounds and his body mass index is over 45. The MAXIMUS physician consultant also indicated that the member is morbidly obese and prednisone treatment is contraindicated. The MAXIMUS physician consultant noted that the member already has obstructive sleep apnea, which is likely related to his elevated body mass index.

The MAXIMUS physician consultant indicated that other treatment have been used for membranous nephropathy, including calcineurin inhibitors, such as cyclosporine and tacrolimus. The MAXIMUS physician consultant explained that one of the most common toxicities of these medications is kidney toxicity and fibrosis. The MAXIMUS physician consultant also explained that cyclophosphamide has also been used for treatment of membranous nephropathy, but has a number of serious toxicities. The MAXIMUS physician consultant indicated that Rituximab has been used at a number of centers for glomerulonephritis with significant success and a favorable side effect profile. The MAXIMUS physician consultant also indicated that the member has a number of poor prognostic factors in that he is male, over 50 years old and has nephritic proteinuria. The MAXIMUS physician consultant further indicated that the member is at high risk of progression to renal failure with this disease. The MAXIMUS physician noted that although some people develop spontaneous remission of this disease, the member has not developed remission over 6 months and his proteinuria has worsened despite conservative management. The MAXIMUS physician consultant explained that it is medically reasonable and necessary to add further treatment for the member at this time.

The MAXIMUS physician consultant indicated that Rituximab is an FDA approved medication (since 1997) for use in chronic lymphocytic leukemia and certain non-Hodgkins lymphomas. The MAXIMUS physician consultant noted that Rituximab has been used as a therapy for membranous nephropathy since 2002. Remuzzi G, et al. Rituximab for idiopathic membranous nephropathy. *Lancet*. 2002;360(9337):923-4. The MAXIMUS physician consultant indicated that several centers worldwide have demonstrated good success using Rituximab for membranous

nephropathy, so it has been listed as an alternate agent for use in the nephrology literature. (Ruggememti P, et al. Rituximab for idiopathic membranous nephropathy: who can benefit? *Clin J Am Soc Nephrol.* 2006;1(4):738-48. Fervenza FC, et al. Rituximab treatment of idiopathic membranous nephropathy. *Kidney Int.* 2008; 73(1): 117-25.) The MAXIMUS physician consultant also indicated that in the latest study, published in 2010 noted that after 2 year follow-up of 18 patients with membranous nephropathy, 4 were in complete remission, 12 were in partial remission, 1 had a limited response, and 1 patient relapsed and that in this study, "adverse effects were mainly infusion-related reactions and none were serious." (Fervenza F, et al. Rituximab Therapy in Idiopathic Membranous Nephropathy: A 2 year Study. *Clin J Am Soc Nephrol.* Accepted for publication July 8, 2010. In press.) The MAXIMUS physician consultant explained that although there have not been hundreds of patients with this condition treated with Rituximab, a high percentage of those who have received this treatment have benefitted. The MAXIMUS physician consultant also explained that Rituxan likely has a better side effect profile than other agents for membranous glomerulonephritis. The MAXIMUS physician consultant further explained that Rituximab meets the Michigan criteria for coverage of an off-label use of a drug in that it is an FDA approved medication which is prescribed for a chronic and seriously debilitating condition, and that more than 2 articles from major peer-reviewed medical journals present supporting the proposed off-label use or uses as generally safe and effective

Pursuant to the information set forth above and available documentation, the MAXIMUS physician consultant determined that Rituximab meets the Michigan criteria for coverage of an off-label use of a drug for treatment of membranous glomerulonephritis in that it is an FDA approved medication which is prescribed for a chronic and seriously debilitating condition, and that more than 2 articles from major peer-reviewed medical journals present [sic] supporting the proposed off-label use or uses as generally safe and effective.

The Commissioner finds that Humana's denial for Rituxan was incorrect under the terms of the certificate and Michigan law.

V ORDER

The Commissioner reverses Humana's December 20, 2010, final adverse determination. Humana is not required to authorize and cover the Petitioner's Rituxan infusions under the terms of the certificate. Humana Insurance Company shall provide coverage for the Rituxan infusions subject to limitations of the certificate (i.e., deductibles, copay or coinsurance) within

60 days of the Order and shall, within seven days of providing coverage, provide the Commissioner with proof it implemented this Order.

To enforce this Order, the Petitioner may report any complaint regarding the implementing to the Office of Financial and Insurance Regulation, Health Plans Division, toll free 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 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.