

July 18, 2006

Maximus
1040 First Avenue, Suite 200
King of Prussia, PA 19406

VIA FACSIMILE AND U.S. MAIL

RE: Request for Independent Review for XXXX
[Insert Address]
Member ID No. 208A21084
Telephone No.:
Medicare Part D Prescription Drug Plan: UniCare

Dear Sir/Madam:

On behalf of my patient and Medicare Part D enrollee, XXX, I am requesting from you a reconsideration (i.e., an independent review) of the May 19, 2006, denial (i.e., redetermination) by UniCare of Cymbalta. The unfavorable redetermination upheld the denial of coverage by UniCare of Mr. XXX's prescription on March 24, 2006.

Specifically, UniCare's denial stated as follows:

"The healthplan member is a 48 year old male who has received a large number of antidepressives but is now somewhat improved with 90 mg of duloxetine (Cymbalta). The clinical information provided does not support the medical necessity for doses greater than 60 mg for the treatment of major depressive disorders because larger doses do not appear to provide additional therapeutic benefit. While the optimum duration of therapy has not been established, it generally is agreed that acute depressive episodes require several months or longer of sustained antidepressant therapy.... In making this decision the health plan policy for medical necessity was utilized which is an internal document."

Copies of the unfavorable coverage determination and redeterminations are attached. In addition, I have attached the Form CMS-1696, Appointment of Representative, appointing me as Mr. XXX's representative to request an independent review.

1. Properly Considering Medical Necessity.

We strongly disagree with UniCare's conclusion regarding medical necessity. At issue here is the matter of whether the 90 mg dosage is medically necessary for Mr. XXX based on the clinical facts of his case. Determining medical necessity for psychotropic

drugs, such as Cymbalta, involves many variables, albeit the final evidence of medical need on an individual basis is straightforward (i.e., the patient's therapeutic response to the pharmacologic agent at the prescribed dose).

In my view there are several key elements that should guide the reconsideration decision as to medical necessity in this case: (i) the biological heterogeneous nature of depression and the heterogeneous characteristics of the medications needed to treat it; (ii) nationally recognized guidelines for the treatment of depression; (iii) the CMS regulations at 42 CFR Section 423.578(iii); and (iv) the fact that appropriate therapeutic response, after years of non-response, is prima facie evidence of medical necessity.

Depression is not a one dimensional medical reality. Patients vary widely in their symptoms, active and passive, and in their responses to treatment intervention (i.e., little or no response or non-adherence to prescribed protocols). This is especially true for individuals with chronic, not acute, major depressive conditions, such as Mr. XXX. Moreover, the class of medications (i.e., antidepressants) used to treat the condition also are highly variable in terms of their mechanism of action, their potential efficacy respecting any one individual, and their respective side effect profiles which may complicate treatment. Broad, sweeping statements about medical necessity for any one individual are inappropriate given the multifaceted nature of depression. By necessity, informed clinical judgment is required to create a medically individualized treatment for success.

Nationally recognized treatment guidelines, such as those published by the American Psychiatric Association, incorporate these realities and set forth a number of flexible protocols that appropriately keep treatment patient-centric rather than rule driven. Specifically regarding the pharmacological aspect of depression treatment, the key to assessment of whether the drug selected and/or its dosage is medically necessary is the actual therapeutic response of the patient. Therapeutic response can be measured by symptom reduction, resumption of functional activities (i.e., working), and so on.

The general rule about therapeutic response is that if the patient responds partially, the assumption would be that the drug has therapeutic value and that dosage can or should be increased to achieve a more complete response. If there is no response after several titration trials, the indication would be that another drug should be selected. It is well established that use of higher doses of antidepressant medication is an appropriate strategy to maximize the effectiveness of an initial treatment regimen.

CMS regulations embody these medical necessity principles by requiring that a dosage either be shown ineffective or that clinical judgment aver that the available doses are likely to be medically ineffective.

Mr. XXX has had a long history of depression, i.e., it is a chronic condition, and has tried numerous medications with little or no therapeutic response. Treatment with Cymbalta at 30 mg per day produced a partial response and when increased to a dose of 90 mg per day, Mr. XXX experienced a significant improvement, and is currently able to work and participate in family and personal activities. Mr. XXX's clinical progression supports the medical necessity of doses greater than 60 mg, and the Cymbalta, in this case, has been properly prescribed and titrated. Simply, Mr. XXX's therapeutic response to the 90 mg is prima facie evidence of the medical necessity for this dosage. Therefore, UniCare's denials should be overturned and Mr. XXX should receive his medication as prescribed.

2. Introduction and Background.

a. Mr. XXX's Diagnosis and Brief Medical and Prescription History.

Mr. XXX is a 48 years old, dual eligible, and has been suffering from ADHD, depression, personality disorder not specified, and cannabis abuse for most of his life. In the past, without appropriate medication, Mr. XXX required hospitalization and treatment at day treatment centers. However, over the past six (6) months, I have been able to appropriately treat him with medication and outpatient therapy and he has seen a decrease in his symptoms and a significant increase in his functional ability, actively participating in his family's life and working part-time. A key to this treatment has been the use of Cymbalta at 90mg per day.

Prior to taking Cymbalta, Mr. XXX tried a number of medications without any significant therapeutic response. A list of these medications is attached for your review. Since 2004, I have employed multiple treatment strategies to improve Mr. XXX's depressive symptoms and functional level. My notes from Mr. XXX's medical record reflect that in 2004 Mr. XXX was prone to self injury and smoked cannabis regularly. He had chronic depression, suicidal ideation, and anxiety/rumination. Mr. XXX did not seek routine medical care and his marriage was in disrepair because he was unable to hold down a job and participate in family activities and household chores.

With medication and ongoing supportive therapy, I was able to help Mr. XXX make small, but significant improvements with Mr. XXX. He decreased his cannabis use; worked, albeit infrequently; and agreed to see a primary care physician. However, as of late 2005, Mr. XXX complained of paranoia, extreme fatigue, hopelessness, a failing marriage, and feelings of abandonment. I attempted to improve his functional level and activity by adjusting his medications. By February of 2006, I saw some improvements in Mr. XXX, but his overall symptoms and functioning were still inadequate. I thought further improvement was necessary. I therefore decided to try Cymbalta with Mr. XXX and prescribed it at an initial dose of 30 mg/day. My goal was to see if the Cymbalta

could improve his symptoms and allow me to taper his other medications (Lamictal, Strattera, Wellbutrin, and Ambien).

By March of 2006, Mr XXX reported that he felt somewhat better. He could watch T.V. and believed that he did not feel as depressed (e.g., he did not have to cry about everything). He said he was still a bit anxious, but for the first time he saw hope. In accordance with clinical treatment guideline, seeing this improvement in Mr. XXX after we initiated Cymbalta, I increased the dose to 60mg/day and decreased his Lamictal.

Although I increased Mr. XXX's prescribed dose of Cymbalta to 60mg/day, Mr. XXX thought I told him to take 120 mg/day and he took 120 mg/day. When I saw Mr. XXX at his next visit in April 2006, he was smiling and relaxed. For the first time, Mr. XXX was upbeat and hopeful. He said he felt well, and had no suicide thoughts or thoughts of self harm. I was impressed by the dramatic improvement in Mr. XXX, but acknowledged that the dose he had been taking was a bit high, so I reduced his dose of Cymbalta to 90mg/day.

I examined Mr. XXX in May and June of 2006 and have documented the continued substantial symptom reduction and the dramatic improvement in his functional ability. He has energy and participates around the house and with his children. He is relaxed, smiles, and says he does not feel stress. He is now working at a part-time job doing computer repair. He has no suicidal thoughts or desire to injure himself. Mr. XXX reports that he has not felt this good in years. Based on my years of clinical experience, I can only attribute this substantial therapeutic response (nearly complete) to the 90 mg of Cymbalta that he is currently taking each day. Mr XXX's therapeutic achievements face a high probably of regression if he is forced to re-undergo trials at doses that produce only partial therapeutic response.

b. Mr. XXX's Prescription of Cymbalta Was Denied by UniCare.

On April 21, 2006, JW, a nurse in my practice, attempted to obtain prior authorization from UniCare for 90 mg of Cymbalta. On April 24, 2006, UniCare responded by denying this request, stating in part that "[t]he clinical information provided does not support the medical necessity for doses greater than 60 mg for the treatment of major depressive disorders because larger doses do not appear to provide additional therapeutic benefit. "

On May 2, 2006, Ms. W requested a reconsideration and independent review of the denial by UniCare. On May 12, 2006, UniCare responded by stating that they needed to see evidence that Ms. W was Mr. XXX's authorized representative. This evidence was sent to UniCare on May 15, 2006.

We did not hear anything after this evidence was sent until Ms. W called UniCare on May 23, 2006, and spoke with Toni Olivarey, a UniCare supervisor. At that time, Ms. Olivarey informed Ms. W that there had been a May 19, 2006, decision to uphold the denial. Ms. Olivarey encouraged Ms. W to submit a letter requesting that UniCare provide another review of its decision. Ms. W submitted the requested letter on May 23, 2006.

Having received no response to this letter, Ms. W called UniCare again on June 5, 2006. At this time, she was told that UniCare had once again upheld its reconsideration and denied Mr. XXX's Cymbalta. They claimed that they sent this letter on May 30, 2006.

I have since obtained and been able to review the denials of reconsideration. The May 19, 2006, letter from UniCare simply stated that "...it has been determined that the denial of this drug be upheld. Your appeal request for the coverage for a quantity override of Cymbalta under your Medicare Prescription Part D drug benefit was denied." The May 30, 2006, letter was substantially similar in content. The black box medical necessity protocols employed by UniCare were never disclosed or adequately stated. Moreover, the factual recounting of Mr. XXX's condition as acute, rather than chronic, belies any basic clinical understanding of Mr. XXX's condition. Lastly, given the well accepted reality that the medical condition of chronic depression is biologically heterogeneous and that patient response is highly idiosyncratic to any intervention, it follows that the dosage and the duration of a trial will, invariably, be different from individual to individual. UniCare's assertion that doses greater than 60 mg "do not appear to provide additional therapeutic benefit" is a conclusory miscalculation based on their internal rules rather than on the clinical evidence from Mr. XXX's treatment.

3. Statement of Disagreement.

a. Cymbalta is Medically Necessary for Treatment of Mr. XXX's Condition.

I strongly disagree with UniCare's decision to deny the Cymbalta as I prescribed it (90 mg daily) and am seeking a favorable decision from you to overturn the denials by UniCare. As I understand it, with the exception of certain statutorily excluded medications, Medicare Part D covers all drugs that are reasonable and necessary for the treatment of an illness. All plans must allow plan participants to access medically necessary drugs that treat the enrollee's medical conditions.

Cymbalta at this dose level is an essential and medically necessary component of the clinical treatment of XXX. While the dose of 90 mg per day is a different dose than that indicated in FDA recommendations, when medically necessary this dose is consistent with the doses that practicing psychiatrists use to treat patients with chronic and persistent depression who have had an inadequate treatment response to lower doses. Failure to provide the drug as I have prescribed it is substantially likely to adversely

affect the health of Mr. XXX. Mr. XXX is now, after years with no therapeutic response, a functioning member of society.

In addition, UniCare's refusal to provide the drug is inconsistent with the Medicare regulations that govern the exceptions process. CMS, in its Medicare Part D regulations related to exceptions and appeals, anticipated that physicians would request doses for drugs that exceed the recommendations set forth in package inserts and provided a process by which enrollees and their physicians could obtain an exception, and therefore, receive doses higher than indicated in the package insert.

At 42 CFR §423.578 (b)(5)(iii), the Medicare regulations state that in his/her supporting statement for an exception, a physician must show that the drug is medically necessary to treat an enrollee's disease. In a case where the physician is requesting a dose in excess of a dose restriction, the physician may prove that a dose is medically necessary by showing that the number of doses that is available under a dose restriction for the drug either *(a)* has been ineffective in the treatment of the enrollee's disease, or *(b)* based on clinical evidence and medical and scientific evidence, the known and relevant physical and mental characteristics of the enrollee and the known characteristics of the drug regimen, is likely to be ineffective or adversely effect the drug's effectiveness or patient compliance. There is no requirement that the physician establish medical necessity by proving both *(a)* and *(b)*.

The operative criterion in Mr. XXX's case is criteria *(a)*. Therefore, in accordance with these regulations, as a physician seeking an exception to a dose and/or quantity limitation, I have provided oral and written supporting statements that the requested prescription drug is medically necessary because "the number of doses that is available under a dose restriction for the prescription drug has been ineffective in the treatment of the enrollee's disease or medical condition." In all of our telephone conversations with UniCare and in our written correspondence to UniCare, we have provided an appropriate supporting statement that Cymbalta is medically necessary for Mr. XXX and that lower doses were not completely effective in his treatment in the past.

Notwithstanding the foregoing, given the known and relevant physical and mental characteristics of the enrollee, and his clinical history, the doses available under the UniCare quantity limit are highly likely to be ineffective and adversely affect the drug's effectiveness. In addition, there is research literature that demonstrates efficacy for Cymbalta at greater than 60 mg. The recognition by the Drug Compendia of efficacy at higher doses, in principle, provides additional evidence to support my clinical judgment in this case, which is based on the principle that patients who do not adequately respond at a low dose should be titrated to a higher dose and maintained at the dose that proves therapeutic.

As is set forth above, prior to February 2006, Mr. XXX had been treated with a variety of medications. Although provided in appropriate doses over an appropriate length of time, these medicines failed to produce an appropriate treatment response. In February 2006, Cymbalta was added to his drug regimen, and a titration process to 30mg three times daily was commenced. He has had an incredible response to this process and this regimen of 30 mg of Cymbalta three times a day has proved effective. Mr. XXX has been stabilized with no active symptoms (i.e., paranoia, anger, or thought disruptions).

b. Medical Practice Supports the Refill of Mr. XXX's Cymbalta Prescription.

As is set forth above, CMS understood that there would be a need for exceptions to dose limitations and by regulation provided for a method that would allow an enrollee to obtain a covered drug at a dose prescribed at a different dose than on the drug plan's formulary. In addition, although the dose of 90 mg daily is higher than the FDA recommended dosage, prescribing at higher doses than recommended by FDA labeling is a widespread and a well accepted part of medical practice. In fact, professionally recognized treatment guidelines specifically address the issue of higher dosing when there is an inadequate treatment response; i.e., it is medically necessary. See, for example, *The Expert Consensus Guideline Series, "Optimizing Pharmacologic Treatment of Psychotic Disorders"*, *The Journal of Clinical Psychiatry*, Vol. 64, Supplement 12 (2003). See also the American Psychiatric Association's *"Practice Guideline for the Treatment of Patients with Schizophrenia, 2nd Edition"*, *The American Journal of Psychiatry*, Vol. 161, No. 2, February 2, 2004.

In psychiatry, the process to determine whether a drug elicits a therapeutic response begins with trying the drug. If the patient has no therapeutic response to the medication, the medication is stopped. If the patient has some therapeutic response, the dose is increased to determine whether a better therapeutic response can be achieved. This process of titrating up the dose, even to levels beyond the FDA recommended dosage, is common psychiatric practice.

This is the exact process that was used to treat Mr. XXX. When I introduced Cymbalta, Mr. XXX's condition seemed to improve somewhat. I therefore increased his dose of Cymbalta and found that his condition was substantially better. On the increased dose, Mr. XXX has become a functioning member of society. Therefore, Cymbalta at 90 mg/day is a medically necessary component of his treatment.

4. Conclusion.

UniCare's denial of Mr. XXX's medication should be overturned. As stated, XXX is a Medicare beneficiary entitled to benefits under the Part D prescription drug program. He suffers from a medically diagnosed mental illness condition, chronic and severe

major depression, and has seen a significant therapeutic response since being treated with 90 mg of Cymbalta daily. I, therefore, respectfully request that the prescription denial be overturned and that he receive the medically necessary medications that he has been using to treat his condition .

If you have any questions or need any further information, please let me know.

Sincerely,

YYYYYY, M.D.

LIST OF MEDICATIONS TRIED IN THE PAST BY MR. XXX

Stelazine

Desipramine (up to 200mg between 1993-1995)

Wellbutrin (up to 450 mg between 1998 - 2000)

Trazodone (PRN for sleep)

Klonopin

Zoloft

Effexor (up to 300 mg between 1996 - 1998)

Vistaril (PRN)

Dilantin

Ritalin

Cylert

Norpramin

Benadryl (on and off throughout the years)

Paxil (up to 40 mg between 2000 - 2001)

Tenex (3 mg in 1998)

Celexa (up to 40 mg between 2001 - 2002)

Lexapro (up to 10 mg in 2003)

Strattera (80 mg currently)

Lamictal (up to 200 mg between 2004-2006)

Provigil (up to 200 mg)

Cymbalta (up to 90 mg)

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