DRAFT—Appeal letter – Aubagio

Today's date

Medical Director/Pharmacy Director or other

Health Plan/Plan Administrator Entity

Health Plan Address

To Whom it May Concern:

This is a request for re-consideration of your denial/limitation of coverage for Aubagio *(teriflunomide)* for my patient **_____(patient name) _____,** who has been diagnosed with a relapsing form of multiple sclerosis. My prescription for Aubagio for this patient was based on my knowledge of (___**her /his____)** diagnosis, disease course and symptoms, and results of the recommended baseline liver function test that revealed no abnormalities.

Aubagio was approved by the U.S. Food and Drug Administration in September, 2012 as a once-a-day oral tablet for adult patients with relapsing forms of multiple sclerosis. Aubagio is a pyrimidine synthesis inhibitor that impedes the function of specific immune cells that have been implicated in MS.

A randomized trial of teriflunomide (TEMSO) involving 1088 people with relapsing MS reduced disease relapses compared with placebo over at least 108 weeks. Of two different doses tested (7 mg and 14 mg) the higher dose also slowed progression of disability.[1] Both doses also had a favorable effect on several MRI measures, including a smaller increase in total lesion volume and fewer new and actives lesions compared with placebo. Additional details about this study, its endpoints and other information useful to healthcare professionals and payers is compiled for easy online access by The Multiple Sclerosis Emerging Therapies Collaborative (http://www.mscoalition.org/emergingtherapies/medications/disease-modifying/teriflunomide-aubagio).

Recently, a second study (TOWER) confirmed the results seen in TEMSO, further supporting the value of this agent for treating relapsing forms of multiple Thank you for your prompt re-consideration of this recommended course of treatment.[2]

Sincerely,

John Smith, MD

Practice name or affiliation

[1]O'Connor P, Wolinsky JS, Confavreux C, Comi G, Kappos L, Olsson TP, Benzerdjeb H, Truffinet P, Wang L, Miller A, Freedman MS; TEMSO Trial Group. *Randomized trial of oral teriflunomide for relapsing multiple sclerosis.* N Engl J Med. 2011 Oct 6;365(14):1293-303.

Abstract

N Engl J Med. 2011 Oct 6;365(14):1293-303. doi: 10.1056/NEJMoa1014656.
Randomized trial of oral teriflunomide for relapsing multiple sclerosis.

O'Connor P, Wolinsky JS, Confavreux C, Comi G, Kappos L, Olsson TP, Benzerdjeb H, Truffinet P, Wang L, Miller A, Freedman MS; TEMSO Trial Group.

Source: University of Toronto, Toronto, ON, Canada. oconnorp@smh.ca

BACKGROUND: Teriflunomide is a new oral disease-modifying therapy for relapsing forms of multiple sclerosis.

METHODS: We concluded a randomized trial involving 1088 patients with multiple sclerosis, 18 to 55 years of age, with a score of 0 to 5.5 on the Expanded Disability Status Scale and at least one relapse in the previous year or at least two relapses in the previous 2 years. Patients were randomly assigned (in a 1:1:1 ratio) to placebo, 7 mg of teriflunomide, or 14 mg of teriflunomide once daily for 108 weeks. The primary end point was the annualized relapse rate, and the key secondary end point was confirmed progression of disability for at least 12 weeks.

RESULTS: Teriflunomide reduced the annualized relapse rate (0.54 for placebo vs. 0.37 for teriflunomide at either 7 or 14 mg), with relative risk reductions of 31.2% and 31.5%, respectively ($P<0.001$ for both comparisons with placebo). The proportion of patients with confirmed disability progression was 27.3% with placebo, 21.7% with teriflunomide at 7 mg ($P=0.08$), and 20.2% with teriflunomide at 14 mg ($P=0.03$). Both teriflunomide doses were superior to placebo on a range of end points measured by magnetic resonance imaging (MRI). Diarrhea, nausea, and hair thinning were more common with teriflunomide than with placebo. The incidence of elevated alanine aminotransferase levels (≥1 times the upper limit of the normal range) was higher with teriflunomide at 7 mg and 14 mg (54.0% and 57.3%, respectively) than with placebo (35.9%); the incidence of levels that were at least 3 times the upper limit of the normal range was similar in the lower- and higher-dose teriflunomide groups and the placebo group (6.3%, 6.7%, and 6.7%, respectively). Serious infections were reported in 1.6%, 2.5%, and 2.2% of patients in the three groups, respectively. No deaths occurred.

CONCLUSIONS: Teriflunomide significantly reduced relapse rates, disability progression (at the higher dose), and MRI evidence of disease activity, as compared with placebo. (Funded by Sanofi-Aventis; TEMSO ClinicalTrials.gov number, NCT00134563).

[2]Miller A, Kappos L, Comi G, Confavreux C, Freedman M, Olsson T, Wolinsky J, Bagulho T, Delhay J-L, Zheng Y, Truffinet P, O'Connor P.

Abstract from Academy of Neurology 2013
S01 Multiple Sclerosis: Clinical Trials I

Teriflunomide Efficacy and Safety in Patients with Relapsing Multiple Sclerosis: Results from TOWER, a Second, Pivotal, Phase 3 Placebo-Controlled Study (S01.004)

Miller A, Kappos L, Comi G, Confavreux C, Freedman M, Olsson T, Wolinsky J, Bagulho T, Delhay J-L, Zheng Y, Truffinet P, O'Connor P.

OBJECTIVE: To assess the efficacy and safety of teriflunomide in patients with relapsing forms of multiple sclerosis (RMS) in a second Phase 3 clinical trial (TOWER, NCT00751881).

BACKGROUND: Teriflunomide is a novel, once-daily, oral, disease-modifying therapy recently approved in the US for treatment of RMS. In the TEMSO study (NCT00134563), teriflunomide 14mg reduced the annualized relapse rate (ARR) by 31.5% ($p<0.001$ vs placebo) and risk of sustained disability progression (confirmed for at least 12 weeks) by 29.8% ($p=0.028$ vs placebo). Teriflunomide 7mg reduced ARR by 31.2% ($p<0.001$ vs placebo), without a statistically significant effect on disability progression. Teriflunomide was generally well tolerated with a well-characterized safety profile.

DESIGN/METHODS: In TOWER, a double-blind, parallel-group study, 1169 patients with RMS (18–55 years old, Expanded Disability Status Scale score $\leq$5.5 at screening, and $\geq$1 or $\geq$2 relapses in the 12 or 24 months prior to randomization, respectively) were randomized to once-daily placebo, teriflunomide 7mg or 14mg. TOWER had variable treatment duration; the study ended when the last patient randomized completed 48 weeks of treatment. The primary and key secondary endpoints were ARR and 12-week disability progression, respectively. Safety analyses included treatment-emergent adverse events (TEAE), laboratory evaluations, and vital signs.

RESULTS: Teriflunomide 14mg significantly reduced ARR by 36.3% ($p<0.001$) and 12-week disability progression by 31.5% ($p=0.044$), compared with placebo. A significant reduction in ARR (22.3%; $p=0.018$) was observed with teriflunomide 7mg, with no significant effect on 12-week disability progression. Commonly reported TEAEs included headache, alanine aminotransferase elevations, hair thinning, diarrhea, and nausea. There were 4 deaths (placebo: respiratory infection; teriflunomide: motor vehicle accident, suicide, sepsis).

CONCLUSIONS: Teriflunomide 14mg significantly reduced ARR and 12-week disability progression compared with placebo; 7mg significantly reduced ARR. Teriflunomide has a well-characterized safety profile. These results confirm those of TEMSO and support teriflunomide as a treatment option for patients with RMS.