

<b>Case Number:</b>	CM14-0024117		
<b>Date Assigned:</b>	06/11/2014	<b>Date of Injury:</b>	07/31/2001
<b>Decision Date:</b>	08/05/2014	<b>UR Denial Date:</b>	01/14/2014
<b>Priority:</b>	Standard	<b>Application Received:</b>	02/25/2014

### HOW THE IMR FINAL DETERMINATION WAS MADE

MAXIMUS Federal Services sent the complete case file to an expert reviewer. He/she has no affiliation with the employer, employee, providers or the claims administrator. The expert reviewer is Board Certified in Internal Medicine and is licensed to practice in Washington DC and Virginia. He/she has been in active clinical practice for more than five years and is currently working at least 24 hours a week in active practice. The expert reviewer was selected based on his/her clinical experience, education, background, and expertise in the same or similar specialties that evaluate and/or treat the medical condition and disputed items/services. He/she is familiar with governing laws and regulations, including the strength of evidence hierarchy that applies to Independent Medical Review determinations.

### CLINICAL CASE SUMMARY

The expert reviewer developed the following clinical case summary based on a review of the case file, including all medical records:

This is a 61 year old patient who sustained injury on July 31 2001. There is limited documentation provided. ██████ saw the patient on Sept 25 2013 and Nov 5 2013 for continued total body pain, chronic fatigue and insomnia. He was thought to have rheumatoid arthritis and acute gouty arthropathy. He was instructed to continue enbrel, naproxen, flurbiprofen and tramadol topical. ██████ saw the patient on Dec 20 2013 for continued total body pain, chronic fatigue and insomnia. He was thought to have rheumatoid arthritis and acute gouty arthropathy. He was instructed to continue enbrel, naproxen, flurbiprofen and tramadol topical. At some point, the use of trexall was prescribed for this patient.

### IMR ISSUES, DECISIONS AND RATIONALES

The Final Determination was based on decisions for the disputed items/services set forth below:

**TREXALL 2.5MG #24:** Overturned

**Claims Administrator guideline:** The Claims Administrator did not cite any medical evidence for its decision.

**MAXIMUS guideline:** The Expert Reviewer did not base their decision on the MTUS. Decision based on Non-MTUS Citation Other Medical Treatment Guideline or Medical Evidence: <http://www.uptodate.com/contents/use-of-methotrexate-in-the-treatment-of-rheumatoid-arthritis>.

**Decision rationale:** From the clinical documentation provided, the patient was diagnosed with rheumatoid arthritis (RA). The patient had persistent symptoms despite initial medical therapy. Methotrexate is used to treat RA. This drug is not reviewed by ACOEM or MTUS so alternate sources were sought. For this patient, it is medicated indicated and appropriate. Methotrexate (MTX) is commonly used for the treatment of patients with rheumatoid arthritis (RA). The use of MTX in RA is also associated with a beneficial effect on survival. (See 'Possible survival benefit' below.) Healing of erosive disease has been observed with MTX, but the magnitude of the response is inferior to that observed with tumor necrosis factor (TNF) inhibition. There is substantial evidence of clinical benefit, which is discussed below. (See 'Efficacy for arthritis' below.) Efficacy for arthritis. The short-term efficacy of MTX in the treatment of RA was initially demonstrated in a few small, randomized, placebo-controlled trials [23,24]. The longer-term efficacy was subsequently evaluated in a number of observational studies [25-30]. The following illustrate the range of findings: A prospective multicenter study evaluated the effectiveness of MTX over a five-year period in 123 patients with RA. When compared with the assessment at study entry, MTX was associated with significant improvement in all clinical disease variables (such as joint pain/tenderness and joint swelling index), measures of functional status, and the erythrocyte sedimentation rate (ESR). An 84-month prospective study of 26 patients demonstrated that the benefit continued beyond the short-term; significant improvement in joint symptoms in this cohort was still present after 36 months of therapy with weekly MTX [25]. Of the 12 patients remaining in the study at the 84-month visit, there were persistent reductions in the number of painful joints, the number of swollen joints, joint pain index, joint swelling index, and physician and patient global assessments. A significant reduction in prednisone dose was also achieved in the 14 patients taking prednisone at study entry. Ten patients withdrew from the study between 0 and 36 months, and four patients between 36 and 84 months. Drug toxicity required discontinuation in 11.5 percent. In a series of 24 patients with new-onset RA (11 and 13 patients with and without radiographic erosions, respectively), the use of MTX as the first disease-modifying antirheumatic drug (DMARD) halted disease progression in approximately 50 percent of patients, particularly among those without baseline erosions. Not all studies have found consistent long-term radiographic benefits with MTX. In one study, 271 patients with RA in whom another DMARD was ineffective were treated with MTX and followed for periods of up to 108 months [31]. Although improvement was observed in the affected joint count and the ESR, the assessment of joint radiographs via the Larsen score revealed progressive disease despite continued therapy. Possible survival benefit -- Several studies have suggested that MTX use is associated with reduced mortality. As examples: A cohort study of 1240 patients with RA at one clinical center in North America addressed the question of a possible survival benefit among those treated with MTX. During follow-up, 191 patients died. MTX was prescribed for 588 patients; treatment decisions were not made in a randomized fashion. The group that received MTX had poorer prognostic indicators and more frequent prednisone use than the MTX-naïve group (37 versus 22 percent, respectively). Approximately 70 percent of both groups were women, and the average age was 57 years. After adjustment for possible confounding factors including age, gender, marital status, disease duration, body mass index, disability score, blood pressure, presence of absence of diabetes, and use of cholesterol-lowering drugs, the hazard ratio for all cause mortality among MTX treated patients was 0.4 (95% CI 0.2-0.8). When deaths were divided into those due to cardiovascular disease and other causes, the hazard ratios were 0.3 and 0.6, respectively. The reduction in cardiovascular risk was statistically significant, while that of non-cardiovascular mortality was

not. The patients in this study were treated beginning in the 1980s and 1990s, prior to the general availability of anticytokine therapy. Use of traditional DMARDs other than MTX did not appear to have a similar survival advantage (hazard ratio 1.0). Improved survival with MTX was also found in a study involving 5,626 patients from 10 large North American practices. Patients were followed with mailed questionnaires. A total of 666 patients (12 percent) died during follow-up (median 4.2 years, interquartile range 1.7-9.6 years, and total observation period of 40.772 patient-years). Propensity-matching for MTX use was used to constitute comparable groups for analysis. The use of MTX was associated with a significant reduction in mortality (adjusted hazard ratio 0.30, 95% CI 0.09-1.03). Only MTX use for greater than one year was associated with lower risk of mortality. It is possible that MTX may achieve an anti-atherogenic effect by improving the efficiency of reverse cholesterol transport from foam cells, although both total cholesterol and LDL do increase in patients starting MTX.