

Teriflunomide (Aubagio)

Criteria for Use

VHA Pharmacy Benefits Management Services, Medical Advisory Panel and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or <http://vaww.pbm.va.gov> for further information.

Exclusion Criteria (if any box is checked the patient DOES NOT qualify for teriflunomide)

- Patient is diagnosed with primary progressive multiple sclerosis
- Patient has secondary progressive MS with no clinical or MRI evidence of relapses
- Patient is currently responsive to and tolerating another immune system modifying drugs for MS
- Pregnancy [i.e., known pregnancy or positive pregnancy test]
- Total bilirubin, ALT, or AST greater than 2 times the upper limit of normal
- Patient currently receiving treatment with leflunomide

Inclusion Criteria

- Patient has relapsing MS^a characterized by disease activity defined as one or more relapses in the two years prior to therapy or gadolinium positive lesions on MRI^b, or new T2 lesions on MRI despite disease modifying therapy (DMT)
- Or
- Patient is receiving natalizumab and is at risk for developing PML (refer to the natalizumab CFU at [Natalizumab\(Tysabri\) Criteria for Use](#))
- Or
- Patient developed intolerance or has a contradiction to the other DMT used in MS

Dosage Recommendations

Teriflunomide is FDA approved at a 7 and 14 mg daily dose. It is recommended that the daily dose be 14mg as clinical outcomes from the pivotal trials were demonstrated uniformly with the higher dose. The 7 mg daily dose did not document the same robust outcomes.

Issues for Consideration

- Severe liver injury, including fatal liver failure has been reported in rheumatoid arthritis patients receiving leflunomide, which is the parent drug of teriflunomide. Concomitant use of teriflunomide with other potentially hepatotoxic drugs may increase the risk of liver injury.
- Rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in patients with rheumatoid arthritis receiving leflunomide. A similar risk would be expected for teriflunomide. If a patient taking teriflunomide develops any of these conditions, stop therapy and perform an accelerated elimination procedure.
- Obtain CBC, transaminase and bilirubin levels within 6 months before initiation of teriflunomide. Monitor liver function tests monthly for the first six months of therapy.
- If pregnancy or liver injury occurs (increase of total bilirubin, ALT or AST greater than 2 times the upper limit of normal), immediately stop teriflunomide and initiate an accelerated elimination procedure with cholestyramine 8 grams given every 8 hours for 11 days (if this regimen is not well tolerated, 4 gram given 3 times a day can be used) or oral activated charcoal powder 50 grams every 12 hours for 11 days should be initiated. If either elimination procedure is poorly tolerated, treatment days do not need to be consecutive unless there is a need to lower teriflunomide plasma concentration rapidly.
- Patients may be considered for first line use of teriflunomide if they have a history of treatment resistant or suicidal depression or are unable to master self-injection technique or lack a caregiver who can perform the injections.
- There is no evidence available to support the use of leflunomide in the treatment of MS. Additionally, no evidence exists which defines an equivalent dose of leflunomide for a 14 mg dose of teriflunomide.
- The use of teriflunomide in clinically isolated syndrome and as adjunct therapy with other disease modifying therapies is not supported by currently available evidence. These trials are in progress with final results pending.
- Prior to initiating teriflunomide, screen patients for latent tuberculosis infection with a tuberculin skin test. Teriflunomide has not been studied in patients with a positive tuberculosis screen, and the safety of teriflunomide in individuals with latent tuberculosis infection is unknown
- In placebo-controlled studies of teriflunomide, no overall increase in the risk of serious infections was observed with teriflunomide 7 mg (1.4%) or 14 mg (2.2%) compared with placebo (2.1%). However, the product labeling advises not initiating therapy in patients with acute or chronic infections. Teriflunomide may cause a degree of immunosuppression and white blood cell lowering that could put patients at a higher risk of adverse outcome. The risk benefit ratio should be reviewed for individual patients.

^a Diagnosis is made using the McDonald Criteria ^b gadolinium should not be used in patients with CrCl \leq 30 ml/min or those on dialysis