teriflunomide (ter-i-floo-noe-mide) Aubagio

**Classification**
Therapeutic: anti-multiple sclerosis agents
Pharmacologic: immune response modifiers, pyrimidine synthesis inhibitors

**Pregnancy Category** X

**Indications**
Management of relapsing forms of multiple sclerosis (MS).

**Action**
Inhibits an enzyme required for pyrimidine synthesis; has antiproliferative and anti-inflammatory effects. 

**Therapeutic Effects:**
Reduction in incidence and severity of relapses in MS, with a decrease in disability progression.

**Pharmacokinetics**

- **Absorption:** Well absorbed following oral administration.
- **Distribution:** Unknown.
- **Protein Binding:** 99%.
- **Metabolism and Excretion:** Eliminated via biliary excretion of unchanged drug with renal excretion of metabolites (37.5% in feces and 22.6% in urine), some metabolism occurs.
- **Half-life:** 18–19 days.

**TIME/ACTION PROFILE (decrease in disability progression)**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>3–6 mo</td>
<td>unknown</td>
<td>unknown</td>
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**Contraindications/Precautions**

- Contraindicated in: Severe hepatic impairment; Concurrent leflunomide treatment; Live virus vaccinations; Active acute or chronic infection; Severe immunodeficiency, bone marrow disease or severe uncontrolled infection; Hypertension (treat appropriately prior). 
- Cautious: Age > 60 yr, concurrent neurotoxic medications or diabetes mellitus (risk of peripheral neuropathy); OB: Women with childbearing potential. 

**Adverse Reactions/Side Effects**

- CV: Hypertension.
- Resp: INTERSTITIAL LUNG DISEASE (rare).
- GI: HEPATOXICITY, diarrhea, transaminases, nausea, diarrhea, nausea, vomiting.
- GU: acute renal failure (urate nephropathy).
- Derm: severe skin reactions including STEVENS-JOHNSON SYNDROME and TOXIC EPIDERMAL NECROLYSIS, alopecia.
- F and E: hyperkalemia, hypophosphatemia.
- Hemat: leukopenia, neutropenia, thrombocytopenia.
- Neuro: paresthesia, peripheral neuropathy. 

**Interactions**

- **Drug-Drug:** May ↑ levels and effects of drugs metabolized by the CYP2C8 enzyme system including paclitaxel, pioglitazone, repaglinide, and rosiglitazone. May ↓ levels and effectiveness of drugs metabolized by the CYP1A2 enzyme system including allopurinol, diltiazem, theophylline, and tizanidine. May ↓ response to and ↑ risk of adverse reactions from live vaccines (avoid live vaccinations and consider long half-life of teriflunomide before administering). May ↑ levels and effects of ethinylestradiol and levonorgestrel. May ↓ risk of bleeding with warfarin. May ↑ levels and effects of drugs metabolized by the CYP3A4 enzyme system including aminoglycosides, fluoroquinolones, and tizanidine. May ↑ risk of drug interactions with other immunosuppressants or antineoplastics (consider long half-life of teriflunomide). Levels and effects may be ↑ by breast cancer resistant protein (BCRP) inhibitors including cyclosporine, clofazimine, and gefitinib. May alter response to warfarin. May ↓ risk of adverse reactions and ↓ antibody response to live virus vaccines.

**Route/Dosage**

- **PO (Adults):** 7 or 14 mg once daily. 

**NURSING IMPLICATIONS**

**Assessment**

- Assess BP before starting and periodically during therapy. Treat hypertension as needed.

**Lab Test Considerations:** Monitor liver function tests (transaminases, bilirubin) within 6 months of starting therapy and monthly after teriflunomide discontinuation.
nomide therapy begins. Do not administer if ALT > upper limit of normal. Consider discontinuing therapy if serum transaminase > x5 - upper limit of normal is confirmed. Monitor serum transaminase and bilirubin in patients with symptoms of liver dysfunction. If liver injury is suspected, discontinue teriflunomide, begin accelerated elimination procedure, and monitor liver function tests weekly until normal.

- Obtain a pregnancy test from female patients prior to beginning therapy.
- Monitor CBC with platelet count within 6 months prior to starting and periodically during therapy based on signs and symptoms of infection. Mean decrease in WBC occurs during first 6 weeks and remains low during therapy.
- Monitor INR closely in patients taking warfarin, a decrease in warfarin peak may occur.

Potential Nursing Diagnoses
- Impaired physical mobility (Implications)
- Infection prevention (Implementation)

Implementation
- Administer a tuberculin skin test prior to administration of teriflunomide. Patients with active latent TB should be treated for TB prior to therapy.
- PO: Administer once daily without regard to food.

Drug Elimination Procedure: Either of the following procedures is recommended to achieve nondetectable plasma levels <0.02 mg/L after stopping treatment with teriflunomide: 1) Administer cholestyramine 8 g 3 times daily (every 8 hrs) for 11 days. If cholestyramine 8 g is not well tolerated, cholestyramine 4 g 3 times/day can be used; or 2) Administration of 50 g oral activated charcoal powder every 12 hr for 11 days. (Days do not need to be consecutive unless rapid lowering of levels is desired.) Verify plasma levels <0.02 mg/L by 2 separate tests at least 14 days apart. Plasma levels may take up to 2 years to reach nondetectable levels without drug elimination procedure.

Patient/Family Teaching
- Instruct patient to take teriflunomide as directed. Advise patient to read Medica-
- tion Guide before starting therapy and with each Rx refill in case of changes.
- Advise patient to notify health care professional promptly if symptoms of liver problems (nausea, vomiting, stomach pain, loss of appetite, tiredness, skin or whites of eyes yellowing, dark urine), serious skin problems (redness or peeling), infection (fever, chills, nausea, vomiting), or interstitial lung disease (cough, dyspnea, with or without fever) occur.
- Instruct patient to notify health care professional if symptoms of peripheral neuropathy (numbness and tingling in hands and feet different from symptoms of MS), fertility problem (blind pits, high prolactin level, amenorrhea or irregular heartbeat), or high BP occur.
- Instruct patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and consult health care professional before taking any new medications.
- Instruct patient to avoid vaccinations with live vaccines during and following therapy without consulting health care professional.
- Discuss the possibility of hair loss with patient. Explore methods of coping.
- Advise patient that teriflunomide is teratogenic. Effective birth control should be used during therapy and until blood levels of teriflunomide are low enough. If pregnancy is planned or suspected, or if breast-feeding while taking teriflunomide, accelerated elimination procedure may be used to decrease blood levels more rapidly. Male patients with female partners who plans to become pregnant may use effective birth control until blood levels are low enough. Male patients may be encouraged to use effective birth control until blood levels are low enough. Male patients who become pregnant without effective birth control may use effective birth control during pregnancy. Patients who become pregnant should be encouraged to enroll in the Aubagio Pregnancy Registry at 1-800-745-4447 to collect information about mother and baby's health.

Evaluation/Desired Outcomes
- Decrease in the number of MS flares (relapses) and slowing of physical problems caused by MS.

Why was this drug prescribed for your patient?