VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

Aubagio (teriflunomide)

Date Developed: 1/25/13 by A. Reeves, MD
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Aubagio, a pyrimidine synthesis inhibitor, is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS).[1] The recommended dose of Aubagio is 7 mg once daily (QD) or 14 mg QD. Aubagio should not be used in patients with severe hepatic impairment, women who are pregnant, or in those concurrently receiving leflunomide. The most common adverse reactions with Aubagio (≥ 10% and 2% ≥ than placebo) include increases in alanine aminotransferase (ALT), alopecia, diarrhea, influenza, nausea, and paresthesia. Transaminase and bilirubin levels should be obtained 6 months before initiation of Aubagio. Monitor ALT levels at least monthly for 6 months after commencing Aubagio treatment. Obtain a complete blood count (CBC) within 6 months before the initiation of Aubagio therapy. Conducted further monitoring based on signs and symptoms of infection. Prior to starting Aubagio, screen patients for latent tuberculosis (TB) infection with a tuberculin skin test. Monitor blood pressure before initiating Aubagio therapy and periodically thereafter. Elimination of Aubagio can be accelerated by administration of cholestyramine or oral activated charcoal for 11 days. Aubagio is in pregnancy category X.

Authorization Criteria:

i. relapsing forms of multiple sclerosis (MS; relapsing- remitting multiple sclerosis [RRMS], secondary-progressive multiple sclerosis [SPMS] with relapses, and progressive-relapsing multiple sclerosis [PRMS] --AND- The patient has tried one of the following: Avonex, Rebif, Betaseron, Extavia, Copaxone, Gilenya, or Tysabri-or- patient is unable to administer injections due to dexterity issues or visual impairment)

ii. approval requires Aubagio to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Coverage of Aubagio is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

2. **Patients with relapsing forms of MS who have not received Aubagio.** Approve for patients who meet the following criteria (a, b, and c):

a) The patient has a relapsing form of MS (relapsing forms of MS include relapsing-remitting multiple sclerosis [RRMS], secondary-progressive multiple sclerosis [SPMS] with relapses, and progressive-relapsing multiple sclerosis [PRMS]); AND
b) The agent is prescribed by, or in consultation with, a neurologist or a physician who specializes in the treatment of MS; AND
c) The patient meets ONE of the following conditions (i or ii):
    i. The patient has tried one of the following: Avonex, Rebif, Betaseron, Extavia, Copaxone, Gilenya, or Tysabri; OR
    ii. The patient is unable to administer injections due to dexterity issues or visual impairment.

3. Patients with relapsing forms of MS who are currently receiving Aubagio. Approve if the patient meets the following criteria (a and b):
a) Patient has a relapsing form of MS, (relapsing forms of MS are RRMS, SPMS with relapses, and PRMS); AND
b) The agent is prescribed by, or in consultation with, a neurologist or a physician who specializes in the treatment of MS.

Note: Patients who have been receiving Aubagio ONLY as samples (carton of 5 tablets in one blister card) must follow criteria number 1 (a, b, and c)

VCHCP requires that this medication be prescribed by neurologist or a physician specializing in MS.

Dosing: Adult

Multiple sclerosis (MS): Adults: Oral: 7 mg or 14 mg once daily

Dosing: Renal Impairment

No dosage adjustment is needed in patients with mild-to-severe renal impairment.

Dosing: Hepatic Impairment

Mild-to-moderate impairment: No dosage adjustment needed.

Severe impairment: Use contraindicated (has not been studied).

Dosing: Adjustment for Toxicity
ALT elevations >3 times ULN:

Dosage Forms: U.S.

Excipient information presented when available (limited, particularly for generics).

Consult specific product labeling.

Tablet, oral:

Aubagio®: 7 mg, 14 mg

Generic Equivalent Available: U.S.

No

Adverse Reactions Significant

>10%:

Central nervous system: Headache (19% to 22%)
Dermatologic: Alopecia (10% to 13%)
Endocrine & metabolic: Hypophosphatemia (5% to 18%)
Gastrointestinal: Diarrhea (15% to 18%), nausea (9% to 14%)
Hematologic: Neutropenia (2% to 15%)
Hepatic: ALT increased (12% to 14%)
Miscellaneous: Influenza (12%)

1% to 10%:

Cardiovascular: Hypertension (4%), palpitation (2% to 3%)
Central nervous system: Anxiety (3% to 4%)
Dermatologic: Pruritus (3% to 4%), acne (3%), burning sensation (2% to 3%)
Endocrine & metabolic: Hyperkalemia (1%)
Gastrointestinal: Abdominal pain (5% to 6%), toothache (4%), viral gastroenteritis (2% to 4%), weight loss (2% to 3%), abdominal distension (1% to 2%)
Genitourinary: Cystitis (2% to 4%)
Hematologic: Thrombocytopenia (10%), lymphocytopenia (7% to 10%), leukopenia (1% to 2%)
Hepatic: GGT increased (3% to 5%), AST increased (2% to 3%)
Neuromuscular & skeletal: Paresthesia (9% to 10%), musculoskeletal pain (4% to 5%), myalgia (3% to 4%), sciatica (3%), carpal tunnel syndrome (1% to 3%), peripheral neuropathy (1% to 2%)
Ocular: Blurred vision (3%), conjunctivitis (3%)
Renal: Renal failure (transient, 1%)
Respiratory: Upper respiratory tract infection (9%), bronchitis (8%), sinusitis (6%)
Miscellaneous: Herpes simplex (4%), seasonal allergy (2% to 3%)

<1% (Limited to important or life-threatening): Cytomegalovirus hepatitis reactivation, jaundice, infection, MI

Contraindications

Severe hepatic impairment; concomitant use with leflunomide; women of childbearing age who will not use contraception reliably; pregnancy

Warnings/Precautions

Boxed warnings:

- Hepatotoxicity: See "Concerns related to adverse effects" below.
- Pregnancy/women of childbearing potential: See "Special populations" below.

Concerns related to adverse effects:

Hepatotoxicity: **[U.S. Boxed Warning]: Use of leflunomide has been associated with rare reports of hepatotoxicity, hepatic failure, and death, therefore, a similar risk is expected with teriflunomide. Treatment should not be initiated in patients with pre-existing acute or chronic liver disease or ALT >2 x ULN; use is contraindicated in patients with severe impairment. Use caution in patients with concurrent exposure to potentially hepatotoxic drugs. Monitor ALT levels at least monthly for first 6 months during therapy; discontinue if ALT >3 x ULN occurs and, if hepatotoxicity is likely teriflunomide-induced, start drug elimination procedures** (eg, cholestyramine, activated charcoal) and monitor liver function tests weekly until normalized.

Concurrent drug therapy issues:

- Immunosuppressants: If coadministered with other potential immunosuppressive agents or switching from teriflunomide to another known immunosuppressant, increased monitoring for hematological adverse effects is necessary.

Special populations:

- Pregnancy/women of childbearing potential: **[U.S. Boxed Warning]: Based on animal data, teriflunomide may cause major birth defects if used in pregnant women. Teriflunomide is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Pregnancy must be avoided during therapy or prior to completing the accelerated elimination treatment protocol. Pregnancy must be excluded prior to initiating treatment.**

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Monitoring Parameters

CBC within 6 months of initiation and periodically thereafter based on signs/symptoms of infection; serum potassium, serum creatinine, serum transaminase and bilirubin within 6 months of initiation of therapy and monthly during the initial 6 months of treatment. In addition, monitor for signs/symptoms of severe infection, abnormalities in hepatic function tests, symptoms of hepatotoxicity, and blood pressure (baseline and periodically thereafter). Screen for tuberculosis and pregnancy prior to therapy.

REFERENCES

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5. Freedman MS, Wolinsky JS, Wamil B, et al, for the teriflunomide multiple sclerosis trial group and the MRI analysis center. Teriflunomide added to interferon-β in relapsing multiple sclerosis. A randomized phase II trial. *Neurology*. 2012;78:1877-1885.
6. Freedman MS, Wolinsky JS, Wamil B, et al. Oral teriflunomide plus glatiramer acetate in relapsing multiple sclerosis [abstract p17]. *Int J MS Care*. 2011;13(Suppl 3):9

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