

UNDERSTANDING HAIR THINNING/HAIR LOSS

INDICATION

AUBAGIO® (teriflunomide) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

IMPORTANT SAFETY INFORMATION

WARNING: HEPATOTOXICITY AND EMBRYOFETAL TOXICITY

- Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. Concomitant use of AUBAGIO with other potentially hepatotoxic drugs may increase the risk of severe liver injury.
- Obtain transaminase and bilirubin levels within 6 months before initiation of AUBAGIO therapy. Monitor ALT levels at least monthly for 6 months after starting AUBAGIO. If drug-induced liver injury is suspected, discontinue AUBAGIO and start an accelerated elimination procedure with cholestyramine or activated charcoal. AUBAGIO is contraindicated in patients with severe hepatic impairment. Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking AUBAGIO.
- AUBAGIO is contraindicated for use in pregnant women and in women of reproductive potential who are not using effective contraception because of the potential for fetal harm. Teratogenicity and embryoletality occurred in animals at plasma teriflunomide exposure lower than that in humans. Exclude pregnancy before the start of treatment with AUBAGIO in females of reproductive potential. Advise females of reproductive potential to use effective contraception during AUBAGIO treatment and during an accelerated drug elimination procedure after AUBAGIO treatment. Stop AUBAGIO and use an accelerated drug elimination procedure if the patient becomes pregnant.

Please see additional Important Safety Information on pages 5 and 6, and **Full Prescribing Information**, including **boxed WARNING**.


AUBAGIO®
(teriflunomide) 14mg
tablets

AUBAGIO is available in 14 mg and 7 mg tablets.

Transient, diffuse hair thinning/hair loss may be caused by many factors, including emotional and physiologic stress, autoimmune diseases, thyroid problems, vitamin deficiencies, inflammatory diseases, and certain drugs, including AUBAGIO® (teriflunomide).^{1,2}

Based on observations of patients in clinical trials, the presentation of hair thinning/hair loss during AUBAGIO use is characteristic of resting-phase hair loss (telogen effluvium). The exact mechanism of hair thinning/hair loss during AUBAGIO use is not fully understood.

Hair thinning/hair loss can be a significant concern for patients, particularly female patients. The following talking points are designed to help you discuss this potential side effect with your patients.

Some patients experienced hair thinning/hair loss in AUBAGIO clinical trials²⁻⁴

- In clinical trials, up to **14%** of patients treated with AUBAGIO experienced hair thinning/hair loss²

Most cases were mild to moderate and transient³

- No event was considered serious³
- Median time to onset was ~3 months³
- The average duration was less than 6 months³
- 87% of cases improved spontaneously while patients continued AUBAGIO therapy³

This side effect rarely led to discontinuation²⁻⁴

- In clinical trials, ~**1% of patients** discontinued AUBAGIO treatment due to hair thinning/hair loss²⁻⁴

Hair loss was NOT like chemotherapy-related hair loss³

- Hair thinning/hair loss in the clinical trials was described as diffuse and generalized over the scalp (ie, not patchy)³
- No cases of complete hair loss were reported in the entire clinical program³
- The presentation of hair thinning/hair loss during AUBAGIO use appears to be similar to the transient hair loss that can occur after pregnancy (telogen gravidarum)^{3,5,6}

For more information on AUBAGIO, please visit [AubagioHCP.com](https://www.aubagiohcp.com).

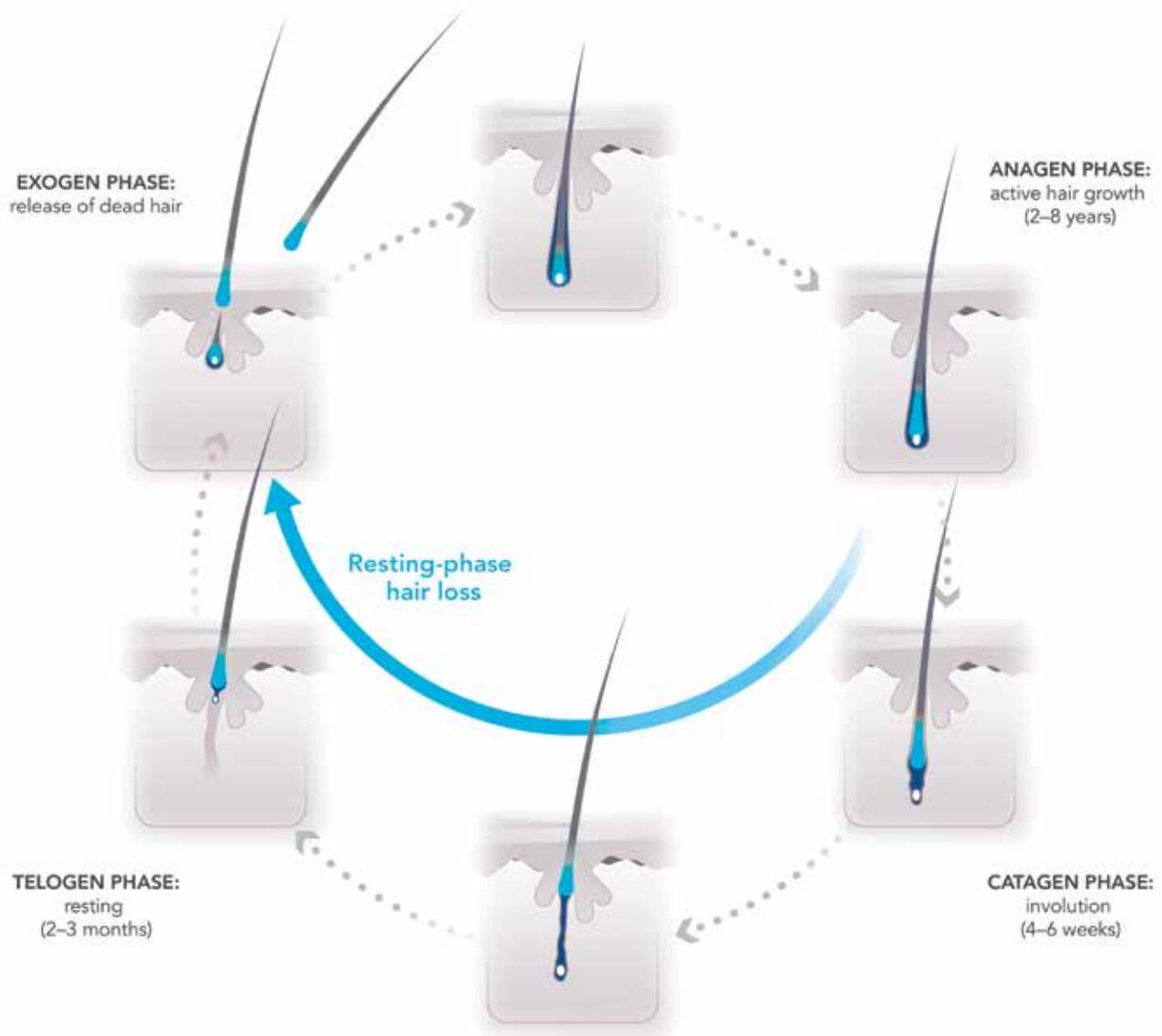
Please see Important Safety Information on pages 1, 5, and 6, and

2 Full Prescribing Information, including **boxed WARNING**.

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HAIR GROWS IN CYCLES, WITH PERIODS OF GROWTH AND REST¹



Adapted from: Harrison S, Bergfeld W. *Cleve Clin J Med.* 2009;76(6):361-367.

➤ Hair changes associated with AUBAGIO[®] (teriflunomide) appear to be characteristic of resting-phase hair loss^{3,5}

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RESTING-PHASE HAIR LOSS

Resting-phase (telogen) hair loss

- Each normal hair follicle cycles independently so that some hairs are growing, others are resting, and others are shedding¹
- In a normal hair cycle, we shed approximately 150 hairs per day¹
- In resting-phase (telogen) hair loss, a greater number of hairs transition prematurely to the resting phase^{1,5}
- These hairs fall out approximately 3 months later⁵
- Patients will usually notice an increased number of hairs beyond normal shedding on their hairbrush or in the shower and sometimes thinning of scalp hair⁵
- Hair grows back when follicles resume the normal hair cycle and start producing new hair⁵

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IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

- Patients with severe hepatic impairment.
- Pregnant women and females of reproductive potential not using effective contraception.
- Patients with a history of hypersensitivity reaction to teriflunomide, leflunomide, or to any of the inactive ingredients in AUBAGIO.
- Co-administration with leflunomide.

WARNINGS AND PRECAUTIONS

- **Hepatotoxicity:** Patients with pre-existing acute or chronic liver disease, or those with serum ALT >2 times the upper limit of normal (ULN) before initiating treatment, should not normally be treated with AUBAGIO. In clinical trials, if ALT elevation was >3 times the ULN on 2 consecutive tests, patients discontinued AUBAGIO and underwent accelerated elimination. Consider additional monitoring if co-administering AUBAGIO with other potentially hepatotoxic drugs; monitor patients who develop symptoms suggestive of hepatic dysfunction (eg, unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine).
- **Embryofetal Toxicity:** AUBAGIO may cause fetal harm when administered in pregnant women. Teratogenicity and embryofetal lethality occurred in animal reproduction studies in multiple animal species at plasma teriflunomide exposures similar to or lower than that in humans at the maximum human recommended dose of 14 mg/day. AUBAGIO is contraindicated for use in pregnant women and females of reproductive potential not using effective contraception.

Exclude pregnancy before starting AUBAGIO in females of reproductive potential. Advise females of reproductive potential to use effective contraception during AUBAGIO treatment and during an accelerated drug elimination procedure (AEP) after AUBAGIO treatment. If a woman becomes pregnant while taking AUBAGIO, stop treatment, apprise patient of the potential risk to a fetus, and perform an AEP to achieve an AUBAGIO plasma concentration of <0.02 mg/L. Upon discontinuing AUBAGIO, it is recommended all females of reproductive potential undergo an AEP.

Women receiving AUBAGIO who wish to become pregnant must discontinue AUBAGIO and undergo an AEP, until plasma concentrations of AUBAGIO are <0.02 mg/L. Men wishing to father a child should also stop AUBAGIO and either undergo an AEP or wait until plasma concentration of AUBAGIO is <0.02 mg/L.

Women who become pregnant while taking AUBAGIO may enroll in the AUBAGIO pregnancy registry by calling 1-800-745-4447, option 2.

- **Procedure for Accelerated Elimination of Teriflunomide:** Teriflunomide is eliminated slowly from the plasma—it takes an average of 8 months, or up to 2 years, to reach plasma concentrations <0.02 mcg/mL. Elimination may be accelerated by administration of cholestyramine or activated charcoal, but this may cause disease activity to return in patients who were responding to AUBAGIO.
- **Bone Marrow Effects/Immunosuppression Potential/Infections:** Decreases in white blood cell counts, mainly of neutrophils and lymphocytes, and platelets have been reported with AUBAGIO. Thrombocytopenia, including rare cases with platelet counts less than 50,000/mm³, has been reported in the postmarketing setting. Obtain a complete blood cell count within 6 months before starting treatment, with further monitoring based on signs and symptoms of bone marrow suppression. AUBAGIO is not recommended for patients with severe immunodeficiency, bone marrow disease, or severe uncontrolled infections. Tuberculosis (TB) has been observed in clinical studies of AUBAGIO. Before starting treatment, screen patients for latent TB infection with a tuberculin test. Treatment in patients with acute or chronic infections should not be started until the infection(s) is resolved. Administration of live vaccines is not recommended. The risk of malignancy, particularly lymphoproliferative disorders, or infection may be increased with the use of some medications with immunosuppressive potential, including teriflunomide.

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IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Hypersensitivity and Serious Skin Reactions:** AUBAGIO can cause anaphylaxis and severe allergic reactions. Signs and symptoms have included dyspnea, urticaria, and angioedema including lips, eyes, throat, and tongue. Cases of serious skin reactions, including Stevens-Johnson syndrome and a fatal case of toxic epidermal necrolysis, have been reported with AUBAGIO. Very rare cases of Drug Reaction with Eosinophilia and Systemic Symptoms have also been reported with leflunomide. If a severe skin reaction develops with AUBAGIO, stop treatment and begin accelerated elimination. In such cases, patients should not be re-exposed to teriflunomide.
- **Peripheral Neuropathy:** Peripheral neuropathy, including polyneuropathy and mononeuropathy, has been reported with AUBAGIO. Age >60 years, concomitant neurotoxic medications, and diabetes may increase the risk. If peripheral neuropathy is suspected, consider discontinuing treatment and performing accelerated elimination.
- **Increased Blood Pressure:** Blood pressure increases and hypertension have occurred with AUBAGIO. Measure blood pressure at treatment initiation and manage any elevations during treatment.
- **Respiratory Effects:** Interstitial lung disease (ILD), including acute interstitial pneumonitis, has been reported with AUBAGIO. ILD may be fatal and may occur acutely at any time during therapy with a variable clinical presentation. If discontinuation of the drug is necessary, consider initiation of an accelerated elimination procedure.

Adverse Reactions: The most frequent adverse reactions ($\geq 10\%$ and $\geq 2\%$ greater than placebo) with AUBAGIO 7 mg and 14 mg and placebo, respectively, were headache (18% and 16% vs 15%), ALT increased (13% and 15% vs 9%), diarrhea (13% and 14% vs 8%), alopecia (10% and 13% vs 5%), and nausea (8% and 11% vs 7%).

Drug Interactions: Monitor patients when teriflunomide is coadministered with warfarin, or with drugs metabolized by CYP1A2, CYP2C8, substrates of OAT3 transporters, substrates of BCRP, or OATP1B1/1B3 transporters.

Use in Specific Populations: Women should not breastfeed during treatment with AUBAGIO.

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References: 1. Harrison S, Bergfeld W. Diffuse hair loss: Its triggers and management. *Cleve Clin J Med*. 2009;76(6):361-367. 2. AUBAGIO (teriflunomide) [package insert]. Cambridge, MA: Genzyme Corporation. 3. Data on file, Sanofi Genzyme. 4. O'Connor P, Wolinsky JS, Confavreux C, et al; for the TEMSO Trial Group. Randomized trial of oral teriflunomide for relapsing multiple sclerosis. *N Engl J Med*. 2011;365(14):1293-1303. 5. Mounsey A, Reed S. Diagnosing and treating hair loss. *Am Fam Physician*. 2009;80(4):356-362. 6. Data on file, Sanofi Genzyme. Clinical study report HMR1726-EFC6049-teriflunomide. January 12, 2011.

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6 SAUS.AUBA.19.08.4311 (10/19)

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