SUCCESSFUL TREATMENT STARTS WITH CLEAR COMMUNICATION

Discussing AUBAGIO® (teriflunomide) and family planning with your RMS patients

Discussing AUBAGIO with respect to family planning considerations

Understanding accelerated elimination when plans change

Clear communication between patients and HCPs

HCP=health care professional; RMS=relapsing forms of multiple sclerosis.

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

- **Clinically significant and potentially life-threatening liver injury, including acute liver failure requiring transplant, has been reported in patients treated with AUBAGIO in the postmarketing setting. Concomitant use of AUBAGIO with other 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 embryolethality 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 throughout and **Full Prescribing Information**, including **boxed WARNING.**

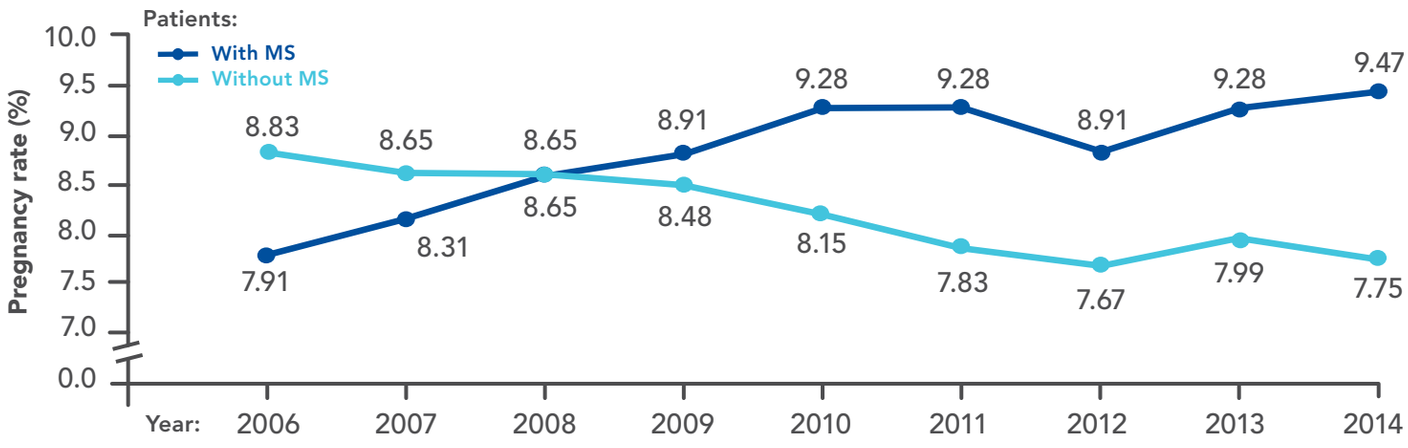
Once-daily
AUBAGIO®
(teriflunomide) 14 mg tablets

AUBAGIO is available in 14 mg and 7 mg tablets.

PREGNANCY IS POSSIBLE FOR PATIENTS WITH RMS

Pregnancy rates in women with RMS have increased, but remain under 10%[1]

Proportion of pregnant women from a U.S. claims database with and without MS by year[1]



Do you and your RMS patients of reproductive potential discuss family plans?

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:** Clinically significant liver injury, which could be life-threatening, can occur at any time during treatment with AUBAGIO. 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.

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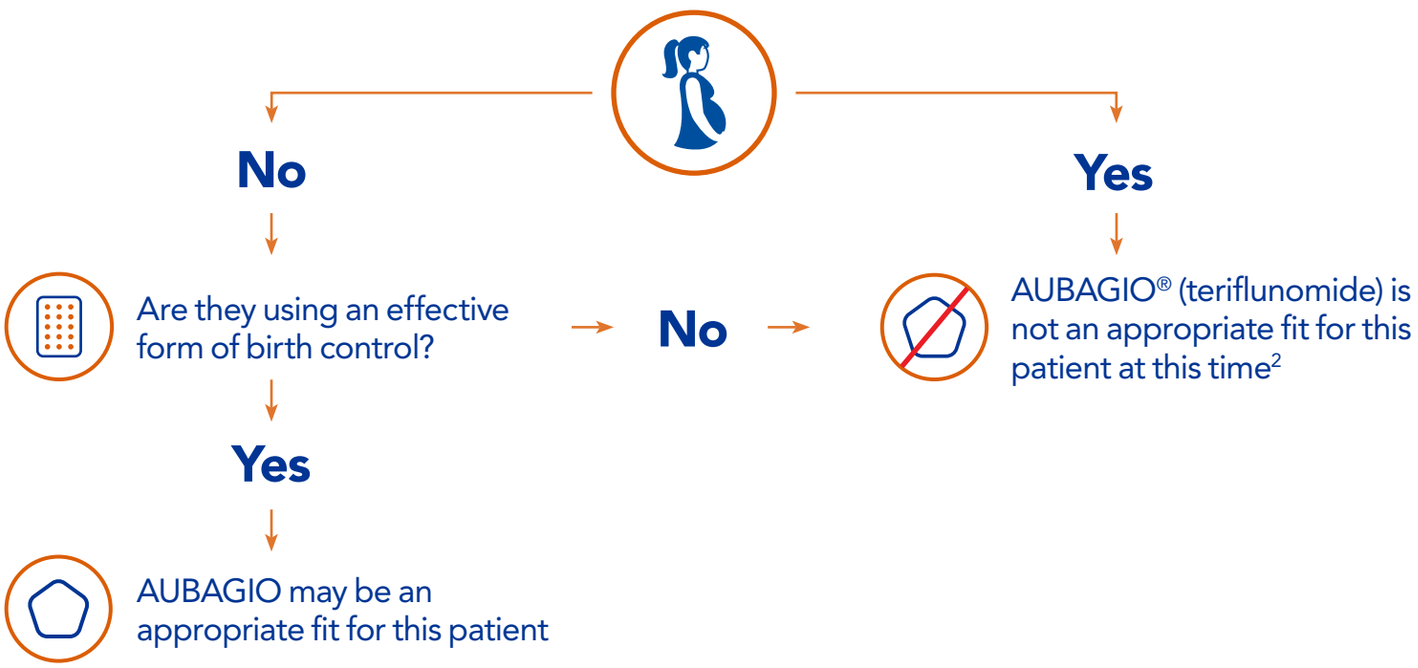
LEARN YOUR PATIENTS' PREGNANCY PLANS

Not every patient will want children—ask the following questions to learn about your patients' future plans

Are they actively trying to become pregnant?



Someone on effective contraception has decided not to become pregnant right now.

That's a potential AUBAGIO patient

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Embryofetal Toxicity:** 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.

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EARLY TREATMENT CONSIDERATIONS

Make communication an early part of treatment

Before treatment

Exclude pregnancy

- AUBAGIO® (teriflunomide) is contraindicated in pregnant women because of potential for fetal harm[2]

During treatment

Ensure patient is on effective contraception

- Females of reproductive potential should use effective contraception during AUBAGIO therapy[2]

Avoid pregnancy during treatment with AUBAGIO[2]

- If a patient has any reason to suspect pregnancy, she should inform her health care professional (HCP) immediately
- Pregnant women should not use AUBAGIO[2]

Start a conversation with your patient to set family planning expectations

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

- **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/mm^3, 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.

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LATER TREATMENT CONSIDERATIONS

Safety measures are in place if patients become, or want to become, pregnant

If patients want to start a family

Discontinue AUBAGIO® (teriflunomide) and perform an accelerated elimination procedure[2]

- There was a >98% decrease in plasma levels of teriflunomide with the accelerated elimination procedure at the end of 11 days[2]
- Blood levels <0.02 mcg/mL are thought to pose minimal risk to the fetus, based on animal data[2]

Continue using effective contraception until reduced drug levels are confirmed[2]

If patients inadvertently become pregnant

Discontinue AUBAGIO and perform an accelerated elimination procedure[2]

- AUBAGIO is contraindicated for use in pregnant women and females of reproductive potential not using effective contraception because of the potential for fetal harm, based on animal data[2]
- There are human data, based on >150 pregnancies in patients treated with teriflunomide and >300 pregnancies in patients treated with leflunomide, available in the Prescribing Information for AUBAGIO[2]
  - — The prospectively reported data (from clinical trials and postmarketing reports) have not demonstrated an increased rate of congenital malformations or miscarriage following teriflunomide exposure in the early first trimester when followed by an accelerated elimination procedure
  - — Specific patterns of major congenital malformations in humans have not been observed
- There are limitations to these data[2]:
  - — Inadequate number of reported pregnancies from which to draw conclusions
  - — The short duration of drug exposure in reported pregnancies, which precludes a full evaluation of the fetal risks, incomplete reporting
  - — The inability to control for confounders (such as underlying maternal disease and use of concomitant medications)

Confirmation of elimination is available via a LabCorp assay paid for by Sanofi Genzyme*

*The blood draw and assay are paid for by Sanofi Genzyme only when they are performed through the Sanofi Genzyme/LabCorp program.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Bone Marrow Effects/Immunosuppression Potential/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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USING THE FAMILY PLANNING DISCUSSION GUIDE

A tool for conversations with RMS patients about future plans

The information below can be used for conversations with patients about AUBAGIO® (teriflunomide) and pregnancy. It condenses relevant information about pregnancy, contraception, and accelerated elimination into 3 simple points.

AUBAGIO patients should use effective contraception[2]

- Patients intending to get pregnant should continue using effective contraception until AUBAGIO is eliminated[2]

HCPs should be notified if plans change

- Patients should contact their HCP in the event of an unexpected pregnancy or change in family plans[2]

The elimination of AUBAGIO can be accelerated[2]

- There was a >98% decrease in plasma levels of teriflunomide with the accelerated elimination procedure at the end of 11 days[2]

Safety is our first priority

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

- **Hypersensitivity Reactions:** AUBAGIO can cause anaphylaxis and severe allergic reactions. Signs and symptoms have included dyspnea, urticaria, and angioedema including lips, eyes, throat, and tongue. Inform patients of the signs and symptoms of anaphylaxis and angioedema.
- **Serious Skin Reactions:** Cases of serious skin reactions, sometimes fatal, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported with AUBAGIO. Fatal outcomes were reported in one case of TEN and one case of DRESS. Inform patients of the signs and symptoms of a serious skin reaction and instruct them to discontinue AUBAGIO and seek immediate medical care. Unless the reaction is clearly not drug-related, discontinue AUBAGIO and begin accelerated elimination immediately. In such cases, patients should not be re-exposed to teriflunomide.
- **Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS):** DRESS, also known as multiorgan hypersensitivity, has occurred with AUBAGIO. One fatal case of DRESS that occurred within 34 days of initiation of AUBAGIO treatment has been reported in the postmarketing setting. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy and/or facial swelling, in association with other organ system involvement, such as hepatitis, nephritis, hematologic abnormalities, myocarditis, or myositis, sometimes resembling an acute viral infection. Eosinophilia is often present. This disorder is variable in its expression, and other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity (eg, fever, lymphadenopathy) may be present even though rash is not evident. If such signs or symptoms are present, the patient should be evaluated immediately.

  Discontinue AUBAGIO, unless an alternative etiology for the signs or symptoms is established, and begin an accelerated elimination procedure immediately. In such cases, patients should not be re-exposed to teriflunomide.

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DISCUSSING FAMILY PLANNING AND AUBAGIO IS IMPORTANT

If your patients need more information, they can visit Aubagio.com or contact MS One to One® at 1-855-676-6326

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

- **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 (≥10% and ≥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.

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

References: 1. Houtchens MK, Edwards NC, Schneider G, et al. Pregnancy rates and outcomes in women with and without MS in the United States. *Neurology*. 2018;91:e1559-e1569. doi: 10.1212/WNL.0000000000006384. **2.** AUBAGIO (teriflunomide) [package insert]. Cambridge, MA: Genzyme Corporation.

Colorado Prescribers may click here for Wholesale Acquisition Cost Price Disclosure.

Vermont Prescribers may click here for Average Wholesale Price Disclosure.

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