IMPORTANT DRUG WARNING

Bristol-Myers Squibb

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March 2011

Subject: Risk Evaluation and Mitigation Strategy (REMS) for YERVOY (ipilimumab) on the Risks of and Recommended Management for Severe Immune-mediated Adverse Reactions

Dear Healthcare Provider:

This letter is intended to inform you about the risk evaluation and mitigation strategy (REMS), developed by Bristol-Myers Squibb in collaboration with FDA, that is required to ensure that the benefits of YERVOY outweigh the risks of severe and fatal immune-mediated adverse reactions.

The YERVOY full Prescribing Information includes the following Boxed Warning:

WARNING: IMMUNE-MEDIATED ADVERSE REACTIONS

YERVOY can result in severe and fatal immune-mediated adverse reactions due to T-cell activation and proliferation. These immune-mediated reactions may involve any organ system; however, the most common severe immune-mediated adverse reactions are enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy. The majority of these immune-mediated reactions initially manifested during treatment; however, a minority occurred weeks to months after discontinuation of YERVOY.

Permanently discontinue YERVOY and initiate systemic high dose corticosteroid therapy for severe immune-mediated reactions. *[See Dosage and Administration (2.2)]*

Assess patients for signs and symptoms of enterocolitis, dermatitis, neuropathy and endocrinopathy and evaluate clinical chemistries including liver function tests and thyroid function tests at baseline and before each dose. *[See Warnings and Precautions (5.1, 5.2, 5.3, 5.4, 5.5)]*

This letter is not a comprehensive description of the risks associated with the use of YERVOY. The Boxed Warning summarizes the most common and severe immune-mediated adverse reactions. **Healthcare providers must read the boxed warning and accompanying full Prescribing Information for a complete description of these risks and their management.** You are advised to discuss the risks that may be associated with YERVOY therapy with patients and their caregivers. The YERVOY patient Medication Guide contains information about the known and potential risks of YERVOY.

REMS OVERVIEW

The YERVOY REMS consists of a Communication Plan to inform Healthcare Providers of the serious risks of YERVOY, to facilitate early identification of these risks, and an overview of recommended management of patients with moderate or more severe immune-mediated adverse reactions. Bristol-Myers Squibb will make available this Dear Healthcare Provider Letter and the following communication plan materials in print, electronic and web-based formats:

- *Immune-mediated Adverse Reaction Management Guide*
  - A booklet designed to inform healthcare providers of the signs, symptoms and management of YERVOY immune-mediated adverse reactions
- *Nursing Immune-mediated Adverse Reaction Checklist*
  - A checklist with key questions to ask patients and actions to take when assessing patients for YERVOY immune-mediated adverse reactions
- *Patient Wallet Card*
  - A foldable patient resource containing a list of symptoms associated with YERVOY adverse reactions and contact information for the patient's prescribing healthcare provider

For additional information regarding YERVOY or additional copies of the YERVOY REMS materials you may:

- Call the Bristol-Myers Squibb toll-free medical information line at 1-800-321-1335
- Visit the YERVOY web site at www.YERVOY.com/hcp/rems

REPORTING ADVERSE REACTIONS

Healthcare providers should report all suspected adverse reactions associated with the use of YERVOY. Please contact Bristol-Myers Squibb at 1-800-721-5072 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Sincerely,

John Tsai, MD
Vice President, Head of US Pharmaceuticals Medical
Bristol-Myers Squibb

This letter is required and approved by FDA as part of the YERVOY REMS.

References: YERVOY Full Prescribing Information, 03/11
731US11REMS00101 03/11