Initial REMS Approval: 03/2011

BLA 125377 YERVOY (ipilimumab) Injection, for intravenous infusion

Human cytotoxic T-lymphocyte antigen-4 (CTLA-4)-blocking monoclonal Antibody

Bristol-Myers Squibb Company
P.O. Box 4000
Princeton, NJ 08543

Contact:
Phone: 609-897-5854
Fax: 609-897-3627

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

The goal of the YERVOY REMS is to inform healthcare providers about the serious risks associated with YERVOY, including risks of severe and fatal immune-mediated adverse reactions such as fatal immune-mediated enterocolitis (including gastrointestinal perforation), fatal immune-mediated hepatitis (including hepatic failure), fatal immune-mediated toxicities of skin (including toxic epidermal necrolysis), fatal nervous system toxicity, and endocrinopathies, and the management of these reactions.

II. REMS ELEMENTS

A. Communication Plan

Bristol-Myers Squibb Company (Bristol-Myers Squibb) will implement a communication plan to healthcare providers to support implementation of this REMS.

The communication plan will include:

1. At least one week prior to first availability of YERVOY to healthcare providers, and every six months for three years thereafter, Bristol-Myers Squibb will send a communication via direct mail and via electronic delivery to U.S. cancer treatment infusion centers, and to the following U.S.-licensed healthcare providers: oncologists, surgical oncologists, oncology nurses, oncology pharmacists, infusion nurses, and cancer treatment infusion nurses. and health-system pharmacists. Recipients will include members of the following organizations:

a. American Society of Clinical Oncology (ASCO)
b. Hematology Oncology Pharmacist Association (HOPA)
c. Infusion Nursing Society (INS)
d. Oncology Nursing Society (ONS)
e. National Comprehensive Cancer Network (NCCN)
f. Society of Surgical Oncologists (SSO)

The following materials will be included in the communications:

a. A *Dear Healthcare Provider Letter* informing healthcare providers about the incidence, type, severity and management of immune-mediated adverse reactions caused by YERVOY
b. The *Immune-Mediated Adverse Reaction Management Guide*
c. The *Patient Wallet Card*
d. The *Nursing Immune-Mediated Adverse Reaction Symptom Checklist*

Communications via mail and electronic delivery will also target all known prescribers and infusion centers that have administered YERVOY.

2. No later than one week after first availability of YERVOY to healthcare providers, and every six months for three years thereafter, Bristol-Myers Squibb will send a communication via electronic delivery to the following non-oncology specialists who may be consulted during the care of patients receiving YERVOY: gastroenterologists, dermatologists, endocrinologists, emergency room physicians, hepatologists, and health-system pharmacists. Recipients will include members of the following organizations:
    a. American Association of Clinical Endocrinology (AACE)
    b. American Academy of Dermatology (AAD)
    c. American Association of Neurology (AAN)
    d. American Association for the Study of Liver Diseases (AASLD)
    e. American College of Emergency Physicians (ACEP)
    f. American Gastroenterological Association (AGA)
    g. American Society of Health-System Pharmacists (ASHP)
    h. Endo Society

The following materials will be included in the communications:
    a. A *Dear Healthcare Provider Letter* informing healthcare providers about the incidence, type, severity and management of immune-mediated adverse reactions caused by YERVOY
    b. The *Immune-Mediated Adverse Reaction Management Guide*

3. No later than 1 week after first availability of YERVOY to healthcare providers, Bristol-Myers Squibb will communicate to the leadership of the headquarters of the above professional societies and the American Academy of Family Physicians (AAFP) and Society of General Internal Medicine (SGIM). This communication

will include the communication materials described a-b, above. The letter will request that these societies disseminate this information to their membership.

The *Dear Healthcare Provider Letter*, the *Immune-Mediated Adverse Reaction Management Guide*, the *Patient Wallet Card*, and the *Nursing Immune-Mediated Adverse Reaction Symptom Checklist* are part of the REMS and are appended.

4. Bristol-Myers Squibb will ensure that all communication materials listed above are available in print format and electronic format beginning at least 1 week prior to first availability of YERVOY to healthcare providers and continuing for seven years after initial approval of the REMS via a REMS-dedicated webpage (appended).
5. At least 1 week prior to first availability of YERVOY to healthcare providers and continuing for seven years following approval of the REMS, Bristol-Myers Squibb will ensure that hard copies of the *Nursing Immune-Mediated Adverse Reaction Symptom Checklist*, *Immune-Mediated Adverse Reaction Management Guide* and the *Patient Wallet Card* are available to oncology related specialists.
6. At least 1 week prior to first availability of YERVOY to healthcare providers and continuing for seven years following approval of the REMS, Bristol-Myers Squibb will ensure that hard copies of the *Nursing Immune-Mediated Adverse Reaction Symptom Checklist* and the *Patient Wallet Card* are available to cancer treatment infusion centers.
7. Within 48 hours of receiving notification of a new YERVOY prescriber/purchaser, Bristol-Myers Squibb will attempt to contact the new prescriber/purchaser via phone to communicate the risks of YERVOY and provide printed REMS materials listed in 1. a-d above within 1 week.
8. Beginning with the June 2011 American Society of Clinical Oncology (ASCO) meeting in Chicago, Illinois and continuing for seven years following approval of the REMS, the communication package including all the materials listed in 1. a-d will be available annually at the Bristol-Myers Squibb booth.

B. Timetable for Submission of Assessments

Bristol-Myers Squibb Company will submit REMS Assessments to FDA 18 months, 3 years, and 7 years from the date of the approval of the REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for the assessment. Bristol-Myers Squibb will submit each assessment so that it will be received by the FDA on or before the due date.