

**Initial REMS Approval: 09/25/2012**  
**Most Recent Modification: 11/2015**

**RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

**Single Shared System for Mycophenolate**

## **I. GOALS**

The goal of the Mycophenolate REMS is to mitigate the risk of embryofetal toxicity associated with use of mycophenolate during pregnancy by:

1. Educating healthcare providers on the following:
  - The increased risks of first trimester pregnancy loss and congenital malformations associated with exposure to mycophenolate during pregnancy.
  - The need to counsel females of reproductive potential on the importance of pregnancy prevention and planning when taking mycophenolate.
  - The need to report pregnancies to the Mycophenolate Pregnancy Registry.
2. Informing females of reproductive potential who are prescribed mycophenolate about:
  - The increased risks of first trimester pregnancy loss and congenital malformations when taking mycophenolate during pregnancy.
  - The importance of pregnancy prevention and planning when taking mycophenolate.

## **II. REMS ELEMENTS**

### **A. Elements to Assure Safe Use**

#### **1. Training must be provided to healthcare providers who prescribe mycophenolate.**

- a) Training must be provided to healthcare providers that include information on the increased risks of embryofetal toxicity and congenital malformations associated with use of mycophenolate during pregnancy using the *Mycophenolate REMS Healthcare Provider Brochure*.
- b) In order to facilitate training, Mycophenolate Sponsors must:
  - i. Ensure healthcare providers can report that they have completed training via online (Mycophenolate REMS Program website), mail, email, or fax using the *Mycophenolate REMS Prescriber Training Confirmation Form*.
  - ii. Ensure a designee of a center (e.g., transplant center) can report via mail, email, or fax using the *Mycophenolate REMS Center Training Confirmation Form* that healthcare providers at the center have completed training through a centralized process administered at the center.
  - iii. Maintain a Mycophenolate REMS Call Center (1-800-617-8191) and a Mycophenolate REMS Program website that continues for the duration of the REMS.
  - iv. Ensure within 60 calendar days of the REMS modification, the Mycophenolate REMS materials listed below are available on the Mycophenolate REMS Program website and by calling the Mycophenolate REMS Call Center.
  - v. Maintain a list of all healthcare providers who have reported completing the Mycophenolate REMS training.

- vi. Monitor distribution and prescription data monthly to identify new mycophenolate prescribers who need to be trained.
- vii. Send a *Mycophenolate REMS Dear Healthcare Provider (DHCP) Letter* within 60 calendar days of the approval of the REMS modification. The intended audience must be all healthcare providers who prescribed mycophenolate at least three times in the 12 months prior to the date of the REMS modification approval (11/13/2015). The *Mycophenolate REMS DHCP Letter* must address the increased risks of embryofetal toxicity and congenital malformations associated with use of mycophenolate during pregnancy. Mycophenolate Sponsors must make the *Mycophenolate REMS DHCP Letter* available via a link from the Mycophenolate REMS Program website for one (1) year after the approval of the REMS modification.

Send a Mycophenolate REMS Dear Healthcare Provider Letter for Centers within 60 calendar days of the approval of the REMS modification to all transplant centers.

Email must be used as the primary method to disseminate the *Mycophenolate REMS Dear Healthcare Provider Letter* and the *Mycophenolate REMS Dear Healthcare Provider Letter for Centers*. If an email is marked as unopened, a second email must be sent within 7 calendar days of the date that the first email was sent. If the second email is marked as unopened, the Mycophenolate REMS letter must be mailed in a hard copy within 30 calendar days of the date that the second email was sent. If a healthcare provider's email address is not available or the email is undeliverable, the Mycophenolate REMS letter must be mailed in hard copy within 30 calendar days of the date that the first set of emails were sent.

c) The following materials are part of the Mycophenolate REMS and are appended:

- *Mycophenolate REMS Healthcare Provider Brochure*
- *Mycophenolate REMS Patient-Prescriber Acknowledgement Form*
- *Mycophenolate REMS Prescriber Training Confirmation Form*
- *Mycophenolate REMS Center Training Confirmation Form*
- *Mycophenolate REMS Dear Healthcare Provider Letter for Centers*
- *Mycophenolate REMS Dear Healthcare Provider Letter*
- *Mycophenolate REMS Obstetrician/Gynecologist Referral Template Letter for Contraception Counseling*
- *Mycophenolate REMS Obstetrician/Gynecologist Referral Template Letter for Preconception Counseling*
- *Mycophenolate REMS Patient Brochure: What You Need To Know About Mycophenolate*
- *Mycophenolate REMS Program Website*

**2. Mycophenolate Sponsors must maintain a centralized pregnancy registry (the Mycophenolate Pregnancy Registry) for females who become pregnant and consent to participate.**

The primary objectives of the Registry are to:

- Document maternal and fetal outcomes of each exposed pregnancy to further characterize the risk of mycophenolate fetal exposure.
- Determine mycophenolate exposure status for each reported pregnancy.
- Understand the circumstances that led to the fetal exposure (root cause analysis).
- Identify factors that affect the risk of adverse outcomes such as dose, timing of exposure, or maternal characteristics.

**III. Timetable for Submission of Assessments**

Mycophenolate NDA Sponsors must submit REMS assessments to the FDA at 6 months and 12 months from the date of initial approval of the Mycophenolate REMS (09/25/2012) and then annually, thereafter.

To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each submission will conclude no earlier than 60 calendar days before the submission date for that assessment. Mycophenolate NDA Sponsors must submit each assessment so that it will be received by the FDA on or before the due date.