

**Initial REMS Approval: 05/29/2008**

**Last modified/revised: 06/2016**

**NDA 21-775 ENTEREG (alvimopan)**

**Cubist Pharmaceuticals LLC , a  
subsidiary of Merck Sharp &  
Dohme Corp.**

Weystrasse 20,  
6000 Lucerne 6, Switzerland  
Phone: 41 58 618 16 16

**Address for Merck Sharp & Dohme  
Corp., a subsidiary of Merck & Co.,  
Inc.**

1 Merck Drive  
P.O. Box 100  
Whitehouse Station, NJ  
08889-0100

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

### **I. GOAL**

The goal of the E.A.S.E. ENTEREG REMS Program is to mitigate the potential risk of myocardial infarction by:

- Ensuring that ENTEREG (alvimopan) is used only for short-term use (no more than 15 doses) in a hospital inpatient setting
- Informing healthcare providers about the potential risk of myocardial infarction observed with long-term use of ENTEREG.

### **II. REMS ELEMENTS**

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

1. Merck will ensure that ENTEREG will only be dispensed by hospital pharmacies that are specially certified.
  - a. To become certified to dispense ENTEREG, each hospital pharmacy must enroll in the E.A.S.E. ENTEREG REMS Program.
  - b. Each hospital pharmacy must designate an authorized representative to complete enrollment on behalf of the hospital pharmacy.
  - c. In order for the hospital pharmacy to be certified, the authorized representative must attest that:
    - i. The E.A.S.E. ENTEREG REMS Program Kit has been received by the hospital and education on the benefits and risks of ENTEREG has been provided to the healthcare practitioners who are responsible for ordering, dispensing, or administering ENTEREG.
    - ii. The representative understands the risks and benefits of ENTEREG and has read the materials in the E.A.S.E. ENTEREG REMS Program Kit
    - iii. The certified hospital pharmacy has pharmacy systems, order sets, protocols, and/or other measures in place to limit the use of ENTEREG to no more than 15 doses per patient for administration in the hospital inpatient setting only.
    - iv. The certified hospital pharmacy will not dispense ENTEREG for outpatient use and will not transfer ENTEREG to any hospital pharmacy not enrolled in the E.A.S.E. ENTEREG REMS Program.
  - d. The certified hospital pharmacy must train relevant staff (e.g., staff involved in prescribing, dispensing, or administering ENTEREG) on the

safe use of ENTEREG, as described in the E.A.S.E. ENTEREG REMS Program Kit materials.

- e. Merck will ensure that, as part of the hospital pharmacy enrollment process, E.A.S.E. ENTEREG REMS Program Kit contains the following materials:
- **E.A.S.E. ENTEREG REMS Program Overview**, which provides an overview of the E.A.S.E. program requirements and lists the materials included in the kit.
  - **Dear Healthcare Provider Letter**, which states that due to the potential risk of myocardial infarction observed with long-term use, ENTEREG is indicated only for short-term use (no more than 15 doses) in hospitalized patients, and provides details on how the E.A.S.E. ENTEREG REMS Program Kit can be accessed.
  - **Prescriber and Pharmacist Information Brochure**, which:
    - states that due to the potential risk of myocardial infarction observed with long-term use, ENTEREG is indicated only for short-term use (no more than 15 doses) in hospitalized patients
    - describes that enrollment in the E.A.S.E. program permits hospitals performing surgeries that include bowel resections to receive ENTEREG
    - describes the required pharmacy systems, order sets, protocols and/or other measures that must be in place to limit the use of ENTEREG to no more than 15 doses per hospitalized patient
  - **Hospital Pharmacy Enrollment Form**, which specifically describes how a hospital pharmacy will enroll into the E.A.S.E. ENTEREG REMS Program.
- f. Merck will ensure that all materials listed in or appended to the E.A.S.E. ENTEREG REMS Program are available to hospital pharmacies in hard copy and online through the E.A.S.E. ENTEREG REMS Program website, [www.ENTEREGREMS.COM](http://www.ENTEREGREMS.COM).

Merck will ensure that ENTEREG will only be dispensed in a hospital inpatient setting that performs bowel resection surgery

## **B. Implementation System**

The Implementation System includes the following:

1. Merck will ensure that ENTEREG is distributed only to certified hospital pharmacies;
2. Merck will maintain a database of all certified hospital pharmacies;
3. Merck will monitor distribution to determine whether or not the drug is only

- distributed to certified hospital pharmacies and will conduct audits to verify;
4. Merck will monitor dispensing of ENTEREG to ensure that it is dispensed only for inpatient use;
  5. Merck will monitor the duration of therapy to determine whether or not ENTEREG is being dispensed only to inpatients with evidence that the patient underwent bowel resection surgery and received no more than 15 doses;
  6. Based on monitoring and evaluation of the elements to assure safe use, Merck will take reasonable steps to work to improve implementation of these elements.

### **C. Timetable for Submission of Assessments**

Merck will submit REMS Assessments to FDA at 12 months following initial REMS approval (May 20, 2008), 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 assessment should conclude no earlier than 60 days before the submission date for that assessment. Merck will submit each assessment so that it will be received by the FDA on or before the due date.