IMPORTANT DRUG WARNING

Subject: ENTEREG® is indicated only for short-term use (no more than 15 doses) in hospitalized patients

Dear Healthcare Provider:

ENTEREG, a peripherally acting μ-opioid receptor antagonist, is indicated to accelerate the time to upper and lower gastrointestinal (GI) recovery following surgeries that include partial bowel resection with primary anastomosis. **Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., would like to inform/remind you that ENTEREG is indicated only for short-term use (no more than 15 doses) in hospitalized patients.**

The FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary to ensure that the benefits of ENTEREG outweigh the potential risk of:

- Myocardial Infarction observed with long-term use

The E.A.S.E.® ENTEREG REMS Program

In one long-term (12-month) clinical study of 0.5 mg alvimopan in patients treated with opioids for chronic pain, a numeric imbalance was seen in the incidence of ischemic cardiovascular events. As a result, the E.A.S.E. Program was developed to ensure that ENTEREG is administered only short-term in inpatient hospital settings and for no more than 15 doses.

ENTEREG is available only to hospitals that perform surgeries that include bowel resections and are enrolled in the E.A.S.E. ENTEREG REMS Program, and will not be dispensed for outpatient use.

www.enteregrems.com

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Dispensing by Certified Inpatient Hospitals

To become certified, your hospital pharmacy must be enrolled in the E.A.S.E.® ENTEREG REMS Program before you can prescribe ENTEREG. This program requires that an authorized representative designated by the hospital pharmacy attests that:

- The E.A.S.E. ENTEREG REMS Program Kit 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 administration of ENTEREG.
- The representative understands the risks and benefits of ENTEREG and has read the materials in the E.A.S.E. ENTEREG REMS Program Kit before ENTEREG is dispensed.
- 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.
- The certified hospital pharmacy will not dispense ENTEREG for outpatient use and will not transfer ENTEREG to any hospital pharmacy not enrolled with the E.A.S.E. ENTEREG REMS Program.

For more information on the program, contact your Merck account manager or visit www.ENTEREGREMS.com.

Adverse Event Reporting

To report suspected adverse reactions contact:

- Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. at 1-877-888-4231
- FDA at 1-800-FDA-1088 (1-800-332-1088) or at www.fda.gov/medwatch.

Please see accompanying complete Prescribing Information.

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