



E.A.S.E.[®]
 ENTEREG Access Support & Education Program
 ENTEREG REMS Program

Prescriber and Pharmacist Information Brochure



ENTEREG[®] is a peripherally acting μ -opioid receptor antagonist indicated to accelerate the time to upper and lower gastrointestinal (GI) recovery following surgeries that include partial bowel resection with primary anastomosis. ENTEREG is approved for short-term use in the hospital in-patient setting.

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

Enrollment in the E.A.S.E. ENTEREG REMS Program

ENTEREG is available only to hospitals that perform surgeries that include a bowel resection and dispensed by pharmacies that are enrolled in the E.A.S.E. ENTEREG REMS Program. This program is designed to ensure that ENTEREG is used in accordance with the FDA-approved label and requires that an authorized representative designated by the hospital pharmacy attests that:

- 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 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.

How to Order

In order to receive ENTEREG, your hospital pharmacy must enroll in the E.A.S.E. ENTEREG REMS Program. Upon registration:

- ENTEREG can be ordered directly from wholesalers
- ENTEREG will be shipped directly to your inpatient hospital pharmacy by the distributor
- ENTEREG cannot be transferred from a certified to a non-certified hospital pharmacy

How supplied	Product code	Description
 Actual size ENTEREG 12 mg	NDC 67919-020-10	Blue, hard gelatin capsules printed with "ADL2698" on both the body and the cap of the capsule

Store at 25°C (77°F); excursions permitted to 15°C–30°C (59°F–86°F) [see USP Controlled Room Temperature].



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Important Safety Information for ENTEREG

**WARNING: POTENTIAL RISK OF MYOCARDIAL INFARCTION WITH LONG-TERM USE:
FOR SHORT-TERM HOSPITAL USE ONLY**

See full prescribing information for complete boxed warning.

- **Increased incidence of myocardial infarction was seen in a clinical trial of patients taking alvimopan for long-term use.**
- **ENTEREG is available only through a restricted program for short-term use (15 doses) called the ENTEREG Access Support and Education (E.A.S.E.) Program.**

ENTEREG Capsules are contraindicated in patients who have taken therapeutic doses of opioids for more than 7 consecutive days immediately prior to taking ENTEREG.

There were more reports of myocardial infarctions in patients treated with alvimopan 0.5 mg twice daily compared with placebo-treated patients in a 12-month study of patients treated with opioids for chronic non-cancer pain (alvimopan, n=538; placebo, n=267). In this study, the majority of myocardial infarctions occurred between 1 and 4 months after initiation of treatment. This imbalance has not been observed in other studies of alvimopan in patients treated with opioids for chronic pain nor in patients treated within the surgical setting, including patients undergoing surgeries that included bowel resection who received alvimopan 12 mg twice daily for up to 7 days (the indicated dose and patient population); (alvimopan 12 mg, n= 1,142; placebo, n= 1,120). A causal relationship with alvimopan has not been established.

ENTEREG should be administered with caution to patients receiving more than 3 doses of an opioid within the week prior to surgery. These patients may be more sensitive to Entereg and may experience GI side effects (eg, abdominal pain, nausea and vomiting, diarrhea).

ENTEREG is not recommended for use in patients with severe hepatic impairment, end-stage renal disease, complete gastrointestinal obstruction, or pancreatic or gastric anastomosis, or in patients who have had surgery for correction of complete bowel obstruction.

Overall, the incidence of adverse reactions in short-term surgical clinical trials was similar between patients receiving either ENTEREG or placebo. The most common adverse reaction (incidence $\geq 1.5\%$) occurring with a higher frequency than placebo among ENTEREG treated patients undergoing surgeries that included a bowel resection was dyspepsia (ENTEREG, 1.5%; placebo, 0.8%).



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Dosing and administration**For hospital use only**

The recommended adult dosage of ENTEREG is:

- 12 mg administered 30 minutes to 5 hours prior to surgery
- Followed by 12 mg twice daily beginning the day after surgery
- For a maximum of 7 days or until discharge

Patients should not receive more than 15 doses of ENTEREG.

Adverse Event Reporting

To report suspected adverse reactions, contact Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or 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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www.enteregrem.com
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