NDA 21-775 Entereg (alvimopan)

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

To reduce the risk of myocardial infarction observed with longer use, Entereg (alvimopan) will be used only for short-term use (not to exceed 15 doses) in inpatient settings.

II. REMS ELEMENTS

A. Communication Plan

Adolor will implement a communication plan to healthcare providers to support implementation of this REMS.

Adolor will provide educational materials for distribution to healthcare professionals involved in the prescribing, dispensing, or administration of Entereg. This includes surgeons who perform bowel resection surgery, hospitalists, anesthesiologists, nurse anesthetists, pharmacists, nurses, and physicians assistants.

Healthcare Professional Education

- **Dear Hospital Pharmacist Letter**

The Dear Hospital Pharmacist Letter, to be distributed on product launch, will state that Entereg can be used for no more than 15 doses in inpatients, and that Entereg is not available for outpatient use. Additionally, the letter will provide a description of and directions on how to enroll in the E.A.S.E. program, the program that incorporates elements for safe use as shown in the appended Dear Hospital Pharmacist Letter.

- **Entereg Access Support and Education (E.A.S.E.) educational materials**

Adolor will use the E.A.S.E. educational materials (available in printed form as part of the E.A.S.E. Program Kit Folder [a print-based registration package], and on-line as part of the web-based registration system), to educate all hospital-based healthcare professionals that are involved in the prescribing, dispensing, or administration of Entereg.

The E.A.S.E. printed materials include:

- E.A.S.E. Program Overview
- E.A.S.E. Hospital Brochure
- E.A.S.E. Kit Folder
- Program Overview

- Registration Form
- Hospital Brochure
- Prescribing Information Brochure

Additional educational materials include:

- Dear Hospital Pharmacist Letter
- Professional Labeling

The educational materials will prominently feature the safety-related message that because of the risk of myocardial infarction observed with longer use, Entereg can be used for no more than 15 doses in inpatients, and Entereg cannot be prescribed for outpatients as shown in the appended printed material and web shots.

B. Elements to Assure Safe Use

1. Drug Dispensed Only in Hospitals

Entereg will be dispensed to patients only in hospitals. The hospital will not dispense Entereg for outpatient use.

2. Drug Dispensed in Specially Certified Hospitals

Entereg will be dispensed only in hospitals that perform bowel resection surgery and that are specially certified by enrollment in the E.A.S.E. program. The specially certified hospital will not transfer Entereg to any hospital not registered with the E.A.S.E. Program. To register in the E.A.S.E. program, responsible hospital personnel must attest that:

- E.A.S.E. educational materials have been received by the hospital and distributed to healthcare professionals who are responsible for the ordering, prescribing, dispensing, or administering of Entereg;
- The hospital has systems, order sets, protocols, or other measures in place to ensure that Entereg is dispensed only to patients with evidence of safe use conditions. Please see the appended Hospital Registration form.

Entereg will be distributed to registered hospitals via a drop-ship program through which Adolor retains direct control over who purchases Entereg. Hospitals that are registered in the E.A.S.E. Program may purchase Entereg utilizing the drop-ship program. The registered hospitals may order Entereg through their usual wholesalers; the wholesalers transmit the order through Adolor's distributor. This distributor sends Entereg only to registered hospitals. Please see the appended Drop Shipment Procedure.

3. Drug Dispensed Only to Patients with Evidence of Safe-Use Conditions

Entereg will be dispensed only to patients in hospitals performing bowel resections; each patient will receive no more than 15 doses of the drug.

C. Implementation System

The Implementation System includes the following:

- Adolor will maintain a database of all specially certified hospitals;
- Adolor will monitor distribution to determine whether the drug is only drop-shipped to certified hospitals and will conduct audits to verify;
- Adolor will monitor dispensing of Entereg to ensure that it is dispensed only for inpatient use;
- Adolor will monitor the duration of therapy to determine whether Entereg is being dispensed to patients with evidence that the patient is hospitalized for bowel resection surgery and has received no more than 15 doses;
- Based on monitoring and evaluation of the elements to assure safe use, Adolor will take reasonable steps to work to improve implementation of these elements.

D. Timetable for Submissions of Assessments

REMS Assessments (see III below for content) will be submitted to FDA quarterly for the first 18 months following approval, then annually (from approval date) thereafter.

III. INFORMATION NEEDED FOR ASSESSMENTS

REMS Assessments will include the following:

- An assessment of use data establishing the circumstances of use of Entereg:
  - the extent of outpatient use;
  - the extent of inpatient use;
  - the extent of use > 15 doses within hospitals;
  - the extent of use in bowel resection procedures;
  - the extent of use in non-bowel resection procedures;
  - the extent of use for other (not associated with bowel resection or non-bowel resection procedures) reasons;
  - the extent of use by specially certified hospitals; and
  - the extent of use by hospitals that are not specially certified.
- A description of the investigation of use deviations and corrective actions taken.

- An assessment of healthcare professional understanding regarding the safe use of Entereg; i.e., the results of surveys administered to hospital pharmacists and surgeons 12 and 18 months following the launch of Entereg, and every 12 months thereafter if sufficient understanding is not displayed. Please see the appended Survey Program.
- A narrative summary and analysis of myocardial infarctions reported with use of Entereg.
- Based on the information provided, an assessment and conclusion of whether the REMS is meeting its goals, and whether modifications to the REMS are needed.

Dear Hospital Pharmacist Letter

GlaxoSmithKline
Three Franklin Plaza
1600 Vine Street
Philadelphia, PA 19102

adolor CORPORATION
700 Pennsylvania Drive
Exton, PA 19341-1127

May 1, 2008

Dear Hospital Pharmacist:

Adolor and GlaxoSmithKline are pleased to introduce you to ENTEREG® (alvimopan) and the ENTEREG Access Support & Education (E.A.S.E.™) Program.

ENTEREG, a peripherally acting μ-opioid receptor antagonist, is indicated to accelerate the time to upper and lower gastrointestinal (GI) recovery following partial large or small bowel resection with primary anastomosis.

ENTEREG is approved for short-term use in the hospital setting. Enrollment in the E.A.S.E. Program permits hospitals performing bowel resection surgeries to receive ENTEREG. It is important that you understand this program in order to help your pharmacy order, stock, and dispense ENTEREG.

Efficacy in clinical trials in the management of postoperative ileus following bowel resection

ENTEREG:

- Accelerated time to upper and lower GI recovery
- Reduced the length of hospital stay

In clinical trials, ENTEREG did not reverse opioid analgesia.

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

In one long-term (12-month) clinical study of 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. See Important Safety Information.

ENTEREG is available only to hospitals that perform bowel resections and are enrolled in the E.A.S.E. Program. This program is designed to ensure that ENTEREG is used in accordance with the FDA-approved label and requires that:

- The E.A.S.E. Program Educational Materials have been received by the hospital and provided to the healthcare practitioners who are responsible for the ordering, dispensing, or administration of ENTEREG
- The hospital has systems, order sets, protocols, or other measures in place to limit the use of ENTEREG to no more than 15 doses per patient for administration in the hospital only
- The hospital will not dispense ENTEREG for outpatient use and will not transfer ENTEREG to any hospital not registered with the E.A.S.E. Program

For more information on the program, contact your Adolor/GlaxoSmithKline account manager or visit www.entereg.com.

Ordering Information

After hospitals have enrolled in the E.A.S.E. Program, ENTEREG can be ordered from wholesalers and will be shipped directly to your inpatient hospital pharmacy by the distributor. ENTEREG cannot be transferred from an enrolled to a nonenrolled hospital.

GlaxoSmithKline
Three Franklin Plaza
1600 Vine Street
Philadelphia, PA 19102

adolor CORPORATION
700 Pennsylvania Drive
Exton, PA 19341-1127

Dosing With ENTEREG

ENTEREG is for hospital use only. The recommended adult dose 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.

Important Safety Information

ENTEREG® (alvimopan) is 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 pain. 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, including studies of patients undergoing bowel resection surgery who received alvimopan 12 mg twice daily for up to 7 days. A causal relationship with alvimopan has not been established.

Overall, the incidence of adverse reactions in short-term surgical clinical trials was similar between patients receiving either ENTEREG or placebo. Most common adverse reactions (incidence ≥3% and ≥1% placebo) in patients undergoing bowel resection were anemia, dyspepsia, hypokalemia, back pain, and urinary retention.

Adverse Event Reporting

Healthcare professionals should report all suspected adverse events associated with the use of ENTEREG. Please contact Adolor Corporation at 700 Pennsylvania Drive, Exton, PA 19341 or 1-866-4ADOLOR (1-866-423-6567), or the GSK Response Center at 1-888-825-5249.

Alternatively, this information may be reported to the FDA MedWatch Reporting System by phone at 1-800-FDA-1088 (1-800-332-1088) or by mail using Form 3500 at www.fda.gov/medwatch.

If you have any questions, please contact Adolor Corporation at 1-866-4ADOLOR (1-866-423-6567) or visit www.entereg.com.

Please see accompanying complete Prescribing Information.

Sincerely,

(Signature)

Eric Mortensen, MD, PhD
Group Director, Gastroenterology
and Urology
GlaxoSmithKline
2301 Renaissance Blvd.
King of Prussia, PA 19406

(Signature)

David Jackson, MD
Senior Vice President and
Chief Medical Officer
Adolor Corporation
700 Pennsylvania Drive
Exton, PA 19341

Source: ENTEREG [prescribing information]. Exton, PA: Adolor Corporation; 2008.

E.A.S.E. Program Kit Folder

E.A.S.E. Program Overview

Welcome to the ENTEREG Access Support & Education Program

Adolor and GlaxoSmithKline are pleased to introduce you to ENTEREG and the E.A.S.E. Program. Enrollment in the E.A.S.E. Program permits hospitals performing bowel resection surgeries to receive ENTEREG. It is important that you understand this program in order to help your pharmacy order, stock, and dispense ENTEREG. Information about the E.A.S.E. Program to help educate healthcare professionals at your hospital is available from your Adolor/GlaxoSmithKline account manager. It can also be downloaded in PDF form at www.entereg.com.

ENTEREG, a peripherally acting μ-opioid receptor antagonist, is indicated to accelerate the time to upper and lower gastrointestinal (GI) recovery following partial large or small bowel resection with primary anastomosis. ENTEREG is approved for short-term use in the hospital setting. ENTEREG is available only to hospitals that perform bowel resections and are enrolled in the E.A.S.E. Program.

In one long-term (12-month) clinical study of 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. See Important Safety Information.

The E.A.S.E. Program requires that:

- The E.A.S.E. Program Educational Materials have been received by the hospital and provided to the healthcare practitioners who are responsible for the ordering, dispensing, or administration of ENTEREG
- The hospital has systems, order sets, protocols, or other measures in place to limit the use of ENTEREG to no more than 15 doses per patient for administration in the hospital only
- The hospital will not dispense ENTEREG for outpatient use and will not transfer ENTEREG to any hospital not registered with the E.A.S.E. Program

The enclosed E.A.S.E. Program kit contains all materials necessary to register your inpatient hospital pharmacy:

- Registration Form
- Ordering Information
- Hospital Brochure
- Complete Prescribing Information for ENTEREG® (alvimopan)

In addition, these pieces are available on the Web site for ENTEREG at www.entereg.com.

Important Safety Information

ENTEREG is 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 pain. 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, including studies of patients undergoing bowel resection surgery who received alvimopan 12 mg twice daily for up to 7 days. A causal relationship with alvimopan has not been established.

Overall, the incidence of adverse reactions in short-term surgical clinical trials was similar between patients receiving either ENTEREG or placebo. Most common adverse reactions (incidence ≥3% and ≥1% placebo) in patients undergoing bowel resection were anemia, dyspepsia, hypokalemia, back pain, and urinary retention.

Adverse Event Reporting

Healthcare professionals should report all suspected adverse events associated with the use of ENTEREG. Please contact Adolor Corporation at 700 Pennsylvania Drive, Exton, PA 19341 or 1-866-4ADOLOR (1-866-423-6567), or the GSK Response Center at 1-888-825-5249.

Alternatively, this information may be reported to the FDA MedWatch Reporting System by phone at 1-800-FDA-1088 (1-800-332-1088) or by mail using Form 3500 at www.fda.gov/medwatch.

Please see enclosed complete Prescribing Information.

If you have any questions, please contact Adolor Corporation at 1-866-4ADOLOR (1-866-423-6567) or visit www.entereg.com.

Hospital Registration Form

Approved for hospital use only

ENTEREG® (alvimopan) | E.A.S.E.™
ENTEREG Access Support & Education Program

HOSPITAL REGISTRATION FORM

Enrollment in the E.A.S.E. Program permits hospitals performing bowel resection surgeries to receive ENTEREG for short-term, in-hospital use.

In one long-term (12-month) clinical study of 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. See Important Safety Information.

This hospital acknowledges that:

1. The E.A.S.E. Program Educational Materials have been received by the hospital and provided to the healthcare practitioners who are responsible for the ordering, dispensing, or administration of ENTEREG
2. The hospital has systems, order sets, protocols, or other measures in place to limit the use of ENTEREG to no more than 15 doses per patient for administration in the hospital only
3. The hospital will not dispense ENTEREG for outpatient use and will not transfer ENTEREG to any hospital not registered with the E.A.S.E. Program

Hospital Name _____

DEA # _____

Hospital Identification Number _____

First Name _____ Middle Name _____ Last Name _____

Title _____

E-mail Address _____

Office Phone _____ Fax _____

Hospital Ship-to Address _____

City _____ State _____ ZIP Code _____

I confirm that the information above is correct

I understand that this information will be used to enable Adolor to identify hospitals at which bowel resections are performed that are eligible to receive shipments of ENTEREG. I also understand that this information may be shared with others working with Adolor, other hospitals enrolled in the E.A.S.E. Program, and may be shared with government agencies.

Signature _____ Date _____

To submit via fax: Sign and fax to 1-800-278-1365

After verification of eligibility, a confirmation will be provided to you.

If you have any questions, please contact Adolor Corporation at 1-866-4ADOLOR (1-866-423-6567) or visit www.entereg.com.

E.A.S.E.

Hospital Brochure

Approved for hospital use only

ENTEREG® (alvimopan) | E.A.S.E.™
ENTEREG Access Support & Education Program

ENTEREG, now available to enrolled hospitals

ENTEREG is a peripherally acting μ-opioid receptor antagonist indicated to accelerate the time to upper and lower gastrointestinal (GI) recovery following partial large or small bowel resection with primary anastomosis. ENTEREG is approved for short-term use in the hospital setting.

In one long-term (12-month) clinical study of 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.
See Important Safety Information.

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

ENTEREG is available only to hospitals that perform bowel resections and are enrolled in the E.A.S.E. Program. This program is designed to ensure that ENTEREG is used in accordance with the FDA-approved label and requires that:

- The E.A.S.E. Program Educational Materials have been received by the hospital and provided to the healthcare practitioners who are responsible for the ordering, dispensing, or administration of ENTEREG
- The hospital has systems, order sets, protocols, or other measures in place to limit the use of ENTEREG to no more than 15 doses per patient for administration in the hospital only
- The hospital will not dispense ENTEREG for outpatient use and will not transfer ENTEREG to any hospital not registered with the E.A.S.E. Program

For more information on the program, contact your Adolor/GlaxoSmithKline account manager or visit www.entereg.com.

How to Order

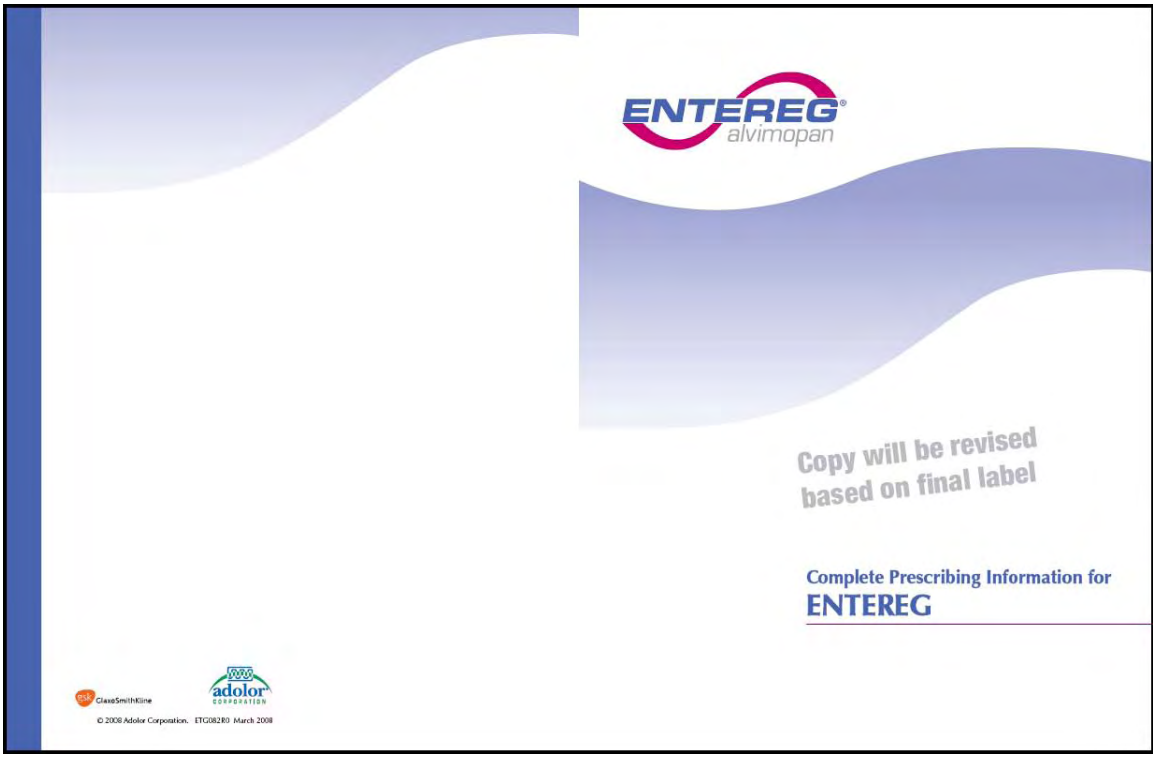
In order to receive ENTEREG, your hospital must enroll in the E.A.S.E. Program. Upon enrollment:

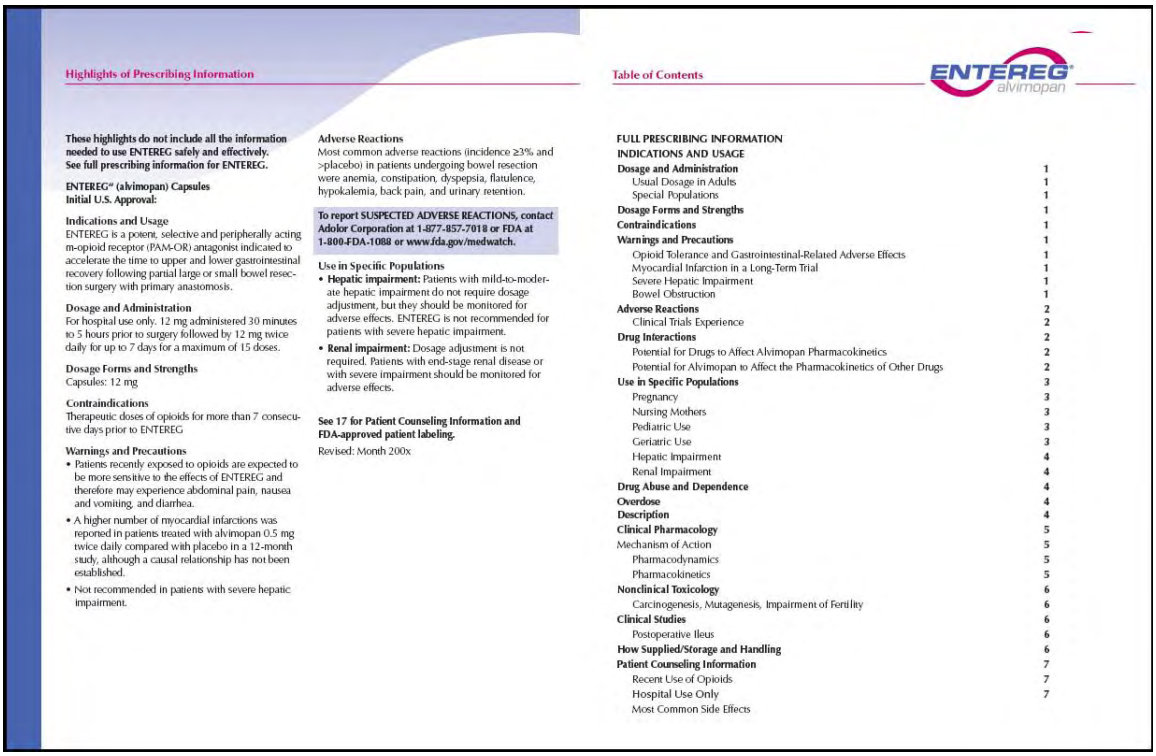
- ENTEREG can be ordered directly from wholesalers
- ENTEREG will be shipped directly to your inpatient hospital pharmacy by the distributor
- ENTEREG cannot be transferred from an enrolled to a nonenrolled hospital

How supplied	Product code	Description
	NDC 112227-010-30	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].

Prescribing Information Brochure





Highlights of Prescribing Information

These highlights do not include all the information needed to use ENTEREG safely and effectively. See full prescribing information for ENTEREG.

ENTEREG® (alvimopan) Capsules
Initial U.S. Approval:

Indications and Usage
ENTEREG is a potent, selective and peripherally acting m-opioid receptor (PAM-OR) antagonist indicated to accelerate the time to upper and lower gastrointestinal recovery following partial large or small bowel resection surgery with primary anastomosis.

Dosage and Administration
For hospital use only. 12 mg administered 30 minutes to 5 hours prior to surgery followed by 12 mg twice daily for up to 7 days for a maximum of 15 doses.

Dosage Forms and Strengths
Capsules: 12 mg

Contraindications
Therapeutic doses of opioids for more than 7 consecutive days prior to ENTEREG

Warnings and Precautions
- Patients recently exposed to opioids are expected to be more sensitive to the effects of ENTEREG and therefore may experience abdominal pain, nausea and vomiting, and diarrhea.
- A higher number of myocardial infarctions was reported in patients treated with alvimopan 0.5 mg twice daily compared with placebo in a 12-month study, although a causal relationship has not been established.
- Not recommended in patients with severe hepatic impairment.

Adverse Reactions
Most common adverse reactions (incidence ≥3% and >placebo) in patients undergoing bowel resection were anemia, constipation, dyspepsia, flatulence, hypokalemia, back pain, and urinary retention.

To report SUSPECTED ADVERSE REACTIONS, contact Adolor Corporation at 1-877-857-7018 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Use in Specific Populations
- **Hepatic impairment:** Patients with mild-to-moderate hepatic impairment do not require dosage adjustment, but they should be monitored for adverse effects. ENTEREG is not recommended for patients with severe hepatic impairment.
- **Renal impairment:** Dosage adjustment is not required. Patients with end-stage renal disease or with severe impairment should be monitored for adverse effects.

See 17 for Patient Counseling Information and FDA-approved patient labeling.

Revised: Month 200x

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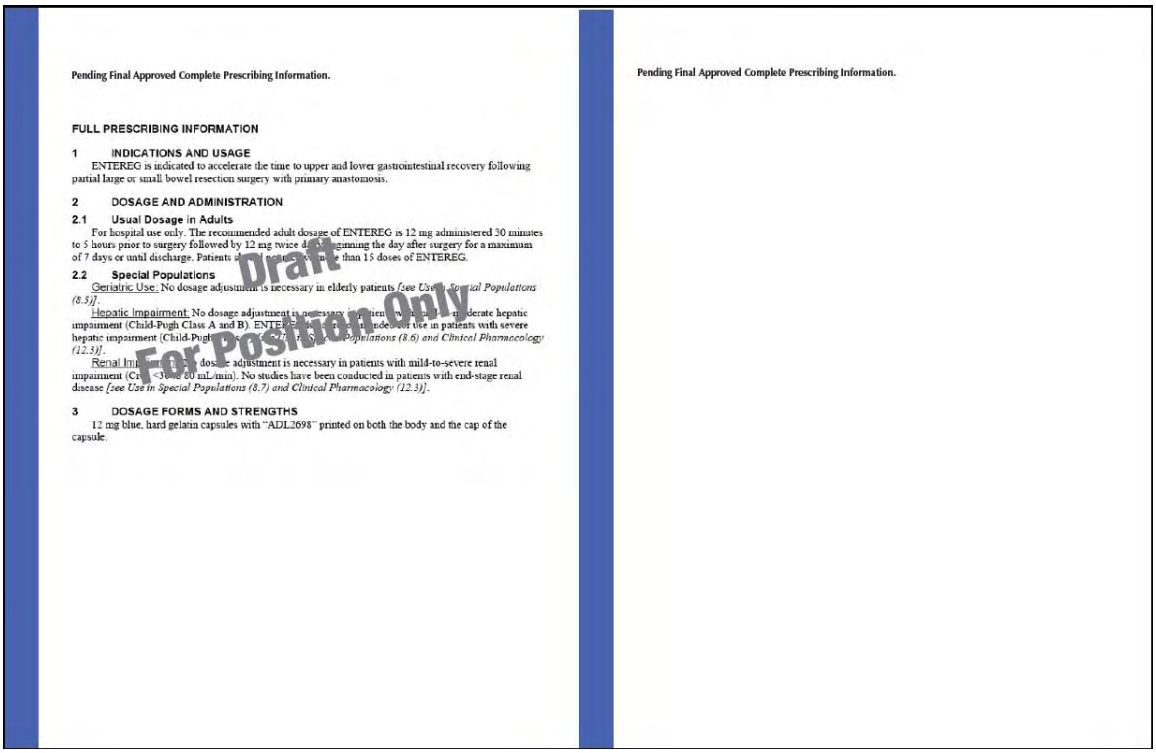
ENTEREG® alvimopan



Pending Final Approved Complete Prescribing Information.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ENTEREG is indicated to accelerate the time to upper and lower gastrointestinal recovery following partial large or small bowel resection surgery with primary anastomosis.

2 DOSAGE AND ADMINISTRATION

2.1 Usual Dosage in Adults

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.

2.2 Special Populations

Geriatric Use: No dosage adjustment is necessary in elderly patients *[see Use in Special Populations (8.5)]*.

Hepatic Impairment: No dosage adjustment is necessary in patients with mild to moderate hepatic impairment (Child-Pugh Class A and B). ENTEREG is contraindicated for use in patients with severe hepatic impairment (Child-Pugh Class C) *[see Use in Special Populations (8.6) and Clinical Pharmacology (12.3)]*.

Renal Impairment: No dosage adjustment is necessary in patients with mild-to-severe renal impairment (CrCl <30 to 80 mL/min). No studies have been conducted in patients with end-stage renal disease *[see Use in Special Populations (8.7) and Clinical Pharmacology (12.3)]*.

3 DOSAGE FORMS AND STRENGTHS

12 mg blue, hard gelatin capsules with "ADL2698" printed on both the body and the cap of the capsule.

Pending Final Approved Complete Prescribing Information.

Web Site Sample Screens

Important Safety Information | Prescribing Information

NEW ENTEREG® alvimopan

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The E.A.S.E. Program

Important Safety Information

ENTEREG is contraindicated in patients who have taken therapeutic doses of opioids for more than 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 with opioids for chronic pain. 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, including studies of patients undergoing bowel resection surgery who received alvimopan 12 mg twice daily for up to 7 days. A causal relationship with alvimopan has not been established.

Overall, the incidence of adverse reactions in short-term surgical clinical trials was similar between patients receiving either ENTEREG or placebo. Most common adverse reactions (incidence ≥3% and ≥1% placebo) in patients undergoing bowel resection were anemia, dyspepsia, hypokalemia, back pain, and urinary retention.

Adverse event reporting

Healthcare professionals should report all suspected adverse events associated with the use of ENTEREG. Please contact Adolor Corporation at 700 Pennsylvania Drive, Exton, PA 19341 or 1-866-4ADOLOR (1-866-423-6567).

Alternatively, this information may be reported to the FDA MedWatch Reporting System by phone at 1-800-FDA-1088 (1-800-332-1088) or by mail using Form 3500 at www.fda.gov/medwatch .

Please see complete prescribing information

If you have any questions, please contact Adolor Corporation at 1-866-4ADOLOR (1-866-423-6567).

Home : Prescribing Information : Important Safety Information : The E.A.S.E. Program

adolor CORPORATION gsk GlaxoSmithKline

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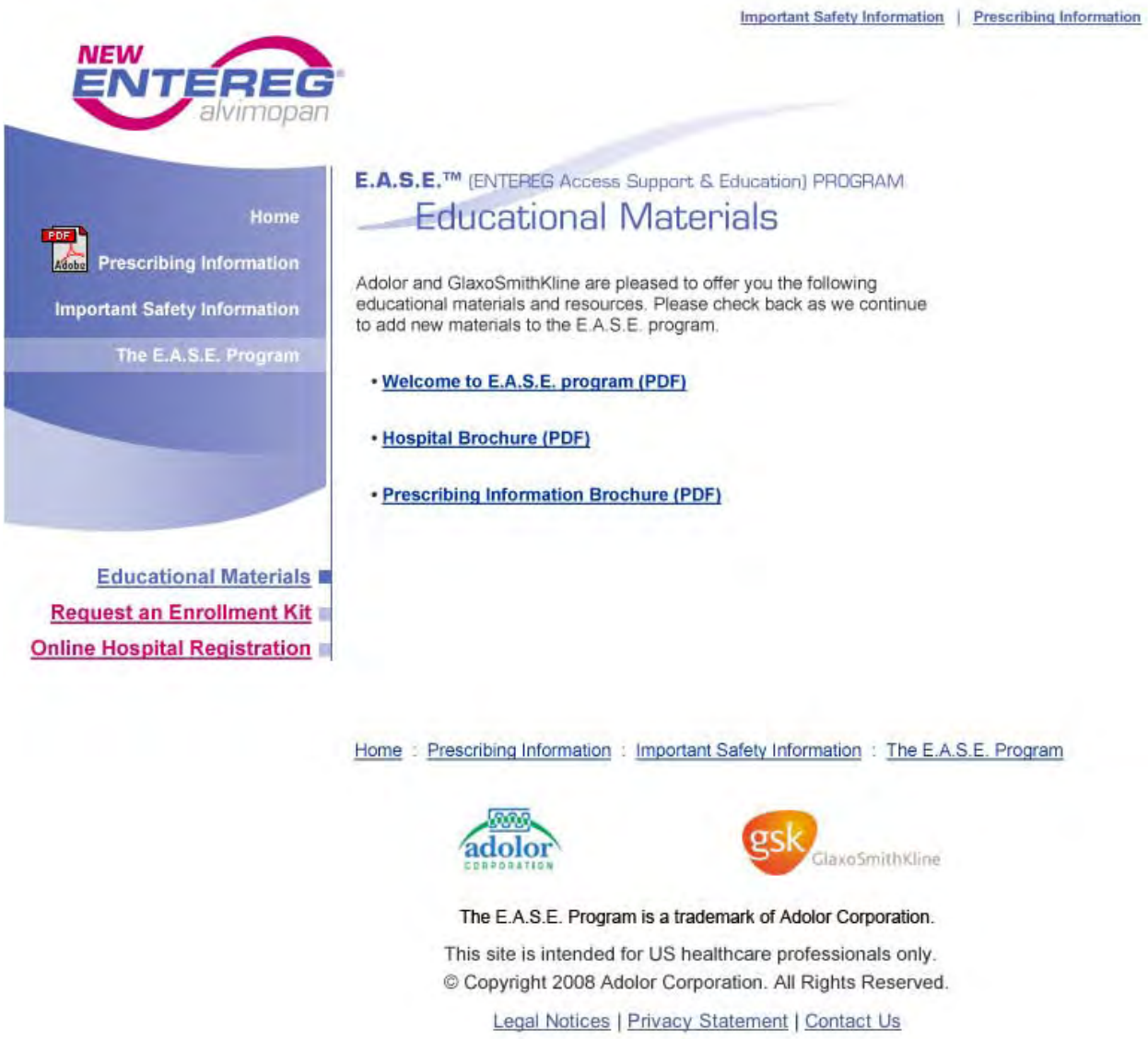
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E.A.S.E.™ (ENTEREG Access Support & Education) PROGRAM
Educational Materials
Adolor and GlaxoSmithKline are pleased to offer you the following educational materials and resources. Please check back as we continue to add new materials to the E.A.S.E. program.
• Welcome to E.A.S.E. program (PDF)
• Hospital Brochure (PDF)
• Prescribing Information Brochure (PDF)
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gsk GlaxoSmithKline
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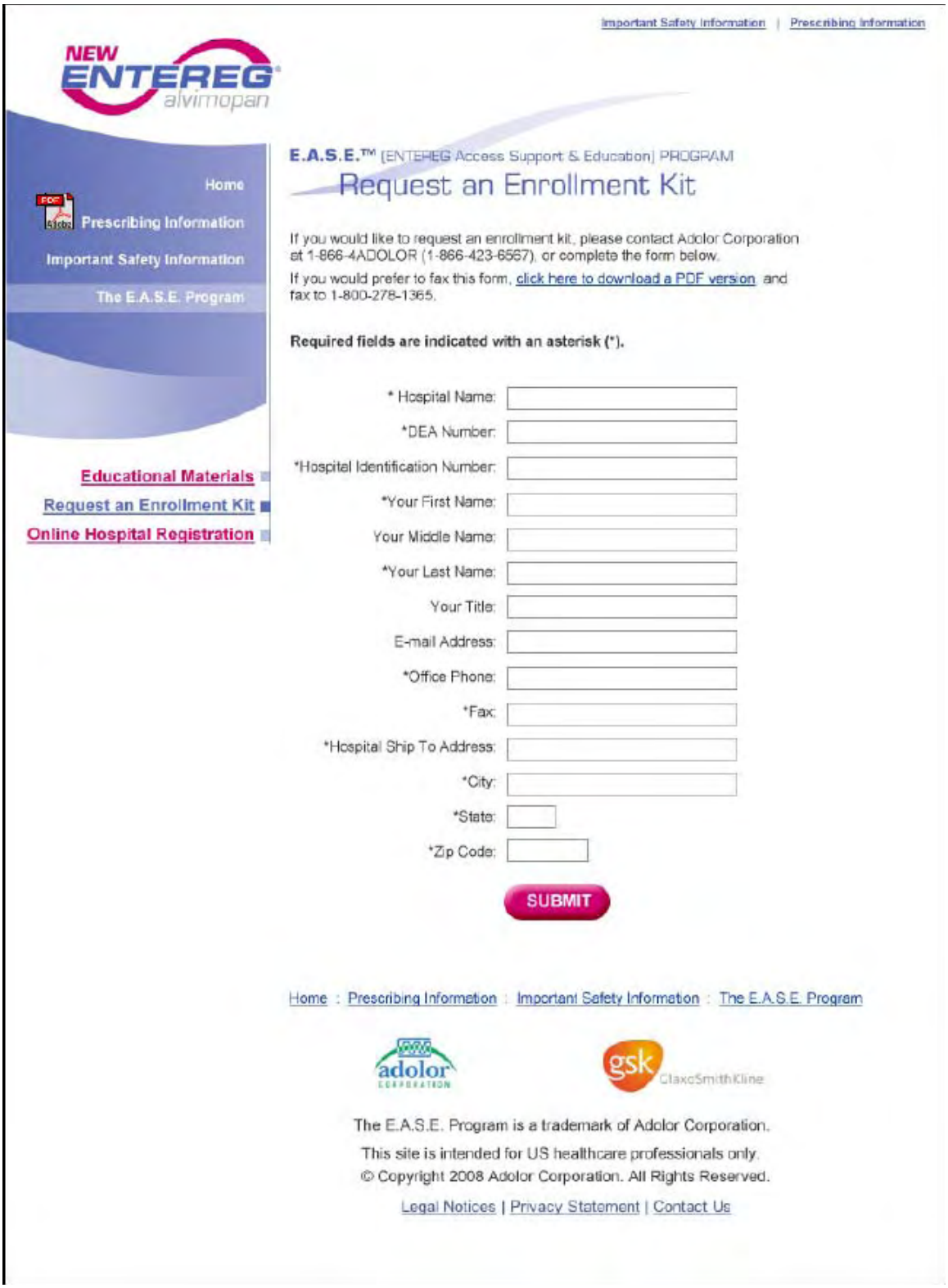

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Online Hospital Registration

E.A.S.E.™ (ENTEREG Access Support & Education) PROGRAM

Request an Enrollment Kit

If you would like to request an enrollment kit, please contact Adolor Corporation at 1-866-4ADOLOR (1-866-423-6567), or complete the form below.

If you would prefer to fax this form, click here to download a PDF version and fax to 1-800-278-1365.

Required fields are indicated with an asterisk (*).

* Hospital Name:
*DEA Number:
*Hospital Identification Number:
*Your First Name:
Your Middle Name:
*Your Last Name:
Your Title:
E-mail Address:
*Office Phone:
*Fax:
*Hospital Ship To Address:
*City:
*State:
*Zip Code:

SUBMIT

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adolor CORPORATION

gsk GlaxoSmithKline

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Welcome to the E.A.S.E.™ (ENTEREG Access Support and Education) Program

Adolor and GlaxoSmithKline are pleased to introduce you to ENTEREG and the E.A.S.E. Program. Enrollment in the E.A.S.E. Program permits hospitals performing bowel resection surgeries to receive ENTEREG. It is important that you understand this program in order to help your pharmacy order, stock and dispense ENTEREG.

ENTEREG, a peripherally acting μ-opioid receptor antagonist, is indicated to accelerate the time to upper and lower gastrointestinal (GI) recovery following partial large or small bowel resection with primary anastomosis. ENTEREG is approved for short-term use in the hospital setting. ENTEREG is available only to hospitals that perform bowel resections and are enrolled in the E.A.S.E. Program.

In one long-term (12-month) clinical study of 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. See Important Safety Information.

This program requires that:

1. The E.A.S.E. Program Educational Materials have been received by the hospital and provided to the healthcare practitioners who are responsible for the ordering, dispensing, or administering of ENTEREG.
2. The hospital has systems, order sets, protocols, or other measures in place to limit the use of ENTEREG to no more than 15 doses per patient for administration in the hospital only.
3. The hospital will not dispense ENTEREG for outpatient use and will not transfer ENTEREG to any hospital not registered with the E.A.S.E. Program.

The E.A.S.E. Program kit contains all materials necessary to register your inpatient hospital pharmacy.

- Registration form
- Ordering information
- Hospital Brochure
- Complete Prescribing Information for ENTEREG (alvimopan)

Important Safety Information

ENTEREG is 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 with opioids for chronic pain. 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, including studies of patients undergoing bowel resection surgery who received alvimopan 12 mg twice daily for up to 7 days. A causal relationship with alvimopan has not been established.

Overall, the incidence of adverse reactions in short-term surgical clinical trials was similar between patients receiving either ENTEREG or placebo. Most common adverse reactions (incidence ≥3% and ≥1% placebo) in patients undergoing bowel resection were anemia, dyspepsia, hypokalemia, back pain, and urinary retention.

Adverse event reporting

Healthcare professionals should report all suspected adverse events associated with the use of ENTEREG. Please contact Adolor Corporation at 700 Pennsylvania Drive, Exton, PA 19341 or 1-866-4ADOLOR (1-866-423-6567).

Alternatively, this information may be reported to the FDA MedWatch Reporting System by phone at 1-800-FDA-1088 (1-800-332-1088) or by mail using Form 3500 at www.fda.gov/medwatch.

Please see complete prescribing information.

If you have any questions, please contact Adolor Corporation at 1-866-4ADOLOR (1-866-423-6567).

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NEW ENTEREG alvimopan

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Educational Materials
Request an Enrollment Kit
Online Hospital Registration

E.A.S.E.™ (ENTEREG Access Support & Education) PROGRAM

Online Hospital Registration

Enrollment in the E.A.S.E. Program permits hospitals performing bowel resection surgeries to receive ENTEREG for short-term, in-hospital use.

In one long-term (12-month) clinical study of 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. See Important Safety Information.

This hospital acknowledges that:

1. The **E.A.S.E.** Program Educational Materials have been received by the Hospital and provided to the healthcare practitioners who are responsible for the ordering, dispensing or administering of ENTEREG.
2. The hospital has systems, order sets, protocols or other measures in place to limit the use of ENTEREG to no more than 15 doses per patient for administration in the hospital only.
3. The hospital will not dispense ENTEREG for outpatient use and will not transfer ENTEREG to any hospital not registered with the E.A.S.E. Program.

Required fields are indicated with an asterisk (*).

* Hospital Name:	
*DEA Number:	
*Hospital Identification Number:	
*Your First Name:	
Your Middle Name:	
*Your Last Name:	
*Your Title:	
*E-mail Address:	
*Office Phone:	
*Fax:	
*Hospital Ship To Address:	
*City:	
*State:	
*Zip Code:	

I confirm that the information above is correct

I understand that this information will be used to enable Adolor to identify hospitals, at which bowel resections are performed, that are eligible to receive shipments of ENTEREG. I also understand that this information may be shared with others working with Adolor, other hospitals enrolled in the E.A.S.E. program, and may be shared with government agencies.

*Your Signature:	
*Date:	

For electronic submission: Your e-signature and the date of signing are required to complete your hospital submission. Please type your name and date in the spaces provided. Your signature certifies that you have read and agree with the Hospital Registration Form. A confirmation will be e-mailed to you after verification of eligibility.

SUBMIT

To submit via fax: Simply print out, sign, and fax to 1-800-278-1365. After verification of eligibility, a confirmation will be provided to you.

If you have any questions, please contact Adolor Corporation at 1-866-4ADOLOR (1-866-423-6567).

Approved for hospital use only
E.A.S.E.™
ENTEREG Access Support & Education Program

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Drop Shipment Procedure

ENTEREG® (alvimopan)
RiskMAP
PROCEDURE FOR DIRECT SHIPMENT TO REGISTERED HOSPITALS

1.0 Objective

To describe the procedure utilized to restrict distribution of Entereg® (alvimopan) to hospitals that are registered with Adolor in accordance with the hospital registration procedure as set forth in the Procedure for Registration of Hospitals (Registered Hospital).

2.0 Action

2.1 Adolor maintains and updates a list of Registered Hospitals eligible to receive and dispense Entereg® based on the registration of these hospitals in accordance with the Procedure for Registration of Hospitals.

2.2 The Adolor's Contracted Distribution Designee (Distributor) updates their order management system to block shipments of Entereg® to wholesalers and any other customer.

2.3 Adolor provides the list of Registered Hospitals to the Distributor.

2.4 Hospitals place orders for Entereg® through their normal procurement channels (i.e. Wholesalers).

2.5 Wholesalers transmit the hospital orders to the Distributor either electronically or manually. Wholesalers are not eligible to carry inventory of or distribute Entereg®.

2.6 The Distributor receives the order and verifies ordering hospital against the current list of Registered Hospitals.

2.6.1 Orders from Registered Hospitals are transferred to the distributor's warehouse for fulfillment pursuant to section 2.7.

2.6.2 Orders from ineligible hospitals are rejected and reported to Adolor for notification of rejection to the wholesaler and the hospital.

2.7 Orders from Registered Hospitals that are transmitted to the Distributor's warehouse for fulfillment are prepared for direct shipment to the eligible recipient as follows:

2.7.1 The number of units ordered are picked from the Distributor's inventory of Entereg®.

2.7.2 The units are packaged in an appropriate shipping container addressed to the Registered Hospital's name and address (and pharmacy as appropriate).

2.7.3 The shipping container is sealed and staged to the outbound staging area for pick up by an authorized delivery service for delivery per customer request.

2.8 Via the invoice, the Distributor notifies the Wholesaler through which, the order was placed, that the shipment to the Registered Hospital has been made.

Survey Program

Survey Instrument to Assess the Risk Management Plan Education

Objective

To assess the effectiveness of the communication of the Key RiskMAP Messages to HCPs who are critical to the proper utilization of the Product in accordance with the goal of the RiskMAP as follows:

Overview

Sponsor commits to assessing the effectiveness of the communication of the Key RiskMAP messages and educational efforts through an unbiased survey. This survey will assess the level of understanding of the Key RiskMAP Messages. Respondents will include a representative sample of HCPs responsible for the ordering and/or dispensing of the Product in the Registered Hospitals.

Key elements of the research are as follows:

1. In administering the surveys, Sponsor will engage a third-party market research provider (Surveyor), such as National Analysts Worldwide, to conduct the surveys.

2. The representative sample will include general and colorectal surgeons and hospital pharmacists potentially engaged in the ordering and/or dispensing of the Product in Registered Hospitals.

3. The representative sample will be achieved through a random sampling of:
    a. Surgeons who practice at Registered Hospitals that have either:
        i. used the Product, or
        ii. probably / definitely will use, but have not yet used the Product
    b. Hospital pharmacists who practice at Registered Hospitals that have either:
        i. stocked and dispensed the Product, or
        ii. probably / definitely will dispense, but have not yet dispensed the Product

4. Sample sizes will result in data that is statistically significant.

5. Surveys will be administered at 12 and 18 months post-launch, with a target of achieving 80% participant accuracy rate on pre-selected questions related to the Key RiskMAP Messages. Sponsor will continue surveys at 12 month intervals thereafter should the 80% accuracy rate not be achieved.
    a. The survey will also contain questions not related to the Key RiskMAP Messages. Only those questions directly related to the Key RiskMAP Messages will be used to calculate the accuracy rate.
        i. These non-RiskMAP questions are provided to strengthen the survey in providing a frame of reference for the survey participants for the questions that follow. In particular, question 1 is a filter question to determine if a survey participant has heard of the Product. If the participant has not heard of the Product, the survey terminates and in all other cases it continues. Question 2 is meant to provide additional information regarding intended usage / dispensing of the Product. In addition, the information from questions 1 and 2 will be helpful in performing additional analysis of the core RiskMAP message questions, as they provide essential information in understanding the profile of the participants as related to the Product, as well as to provide an understanding of awareness of (question 1), usage / dispensing of (question1), and intended usage / dispensing of the Product (question 2).
    b. The accuracy rate can be calculated in any one of several ways for various diagnostic purposes. The Sponsor proposes it be based upon the percentage of surgeons and pharmacists who correctly answer all pre-selected Key RiskMAP Message-related questions.
        i. The Sponsor will tally the 80% success score by all respondents combined (surgeons, pharmacists); 80% of all respondents to the surgeon survey (General and Colorectal); 80% of all respondents to the pharmacists survey (hospital pharmacists involved in ordering product) and 80% of respondents from Wave 1 and 80% of respondents from Wave 2.

6. To maximize response rate, the surveys will be conducted via internet and/or telephone, with proper controls in place to ensure a uniform survey experience for both venues of participation.

7. To minimize sampling bias:
   a. All general and colorectal surgeons and hospital pharmacists potentially engaged in the ordering and/or dispensing of the Product in Registered Hospitals will be eligible for participation. This includes surgeons performing a high or low volume of bowel resection surgeries or pharmacists representing hospitals where a high or low volume of bowel resection surgeries occur.
   b. Multiple efforts will be made to re-contact potential respondents to minimize non-response bias.

8. Prior to the first wave of the research, the third-party market research vendor will conduct pretests. The pretest will serve to hone the questions to be utilized in the quantitative study, and to ensure that none of the questions induce bias. The Sponsor will submit the data collected via these survey pretests prior to the first wave of research.

9. Sponsor has submitted concise specialty-specific surveys which include screening questions, questions that will measure the knowledge of the Key RiskMAP messages, and other questions not directly related to Key RiskMAP messages, but deemed relevant for tracking.

Study Design & Methodology

The Sponsor has submitted Study Design and Methodology for surveying HCPs in Registered Hospitals to evaluate the success of the education program for the Product.

The survey will be comprised of:

A limited number of screening questions to assess whether a respondent is qualified to participate based on:

- Physician specialty
- Awareness of the Product
- Experience prescribing (surgeons), or dispensing (pharmacists)
- A participant's intent to prescribe (surgeons), or dispense (pharmacists) in the future

Survey questions designed to assess the knowledge of Key RiskMAP Messages:

- Entereg® (alvimopan) 12-mg Capsules are to be administered for a maximum of 15 doses.
- Entereg® (alvimopan) 12-mg Capsules are only to be administered within the registered acute-care hospital setting (not to be prescribed at discharge).
- The proper utilization of Entereg® (alvimopan) 12-mg Capsules is for short-term use (not to exceed 15 doses), due to results from one long-term (12-month) clinical study of alvimopan in patients treated with opioids for chronic pain, where a numeric imbalance was seen in the incidence of ischemic cardiovascular events.

The surgeon and pharmacist respondents will be recruited by third-party vendors using contact information maintained in representative market research lists. These lists will be used to create target lists that will include contact information for surgeons and pharmacists who practice at Registered Hospitals. These target lists will include high and low volume Product users (as well as potential users), and high and low volume

bowel resection performers. All will be given the opportunity to participate. Multiple efforts will be made to re-contact potential respondents to minimize non-response bias.

How the surveys will be administered

A third-party vendor will send blinded (as to Sponsor) invitations via phone, fax, and/or email to surgeons and pharmacists who reside at Registered Hospitals. They will be invited to participate via telephone or in an online web based application. This dual approach is the most effective way to reach the target audience, maximizing the rate of participation in this study, and ensuring that the most robust and defensible sample is obtained.

Frequency

The Sponsor recommends two waves of research, fielded at 12 and 18 months post-launch and then annually thereafter if education is deemed not successful (i.e., <80% accuracy rate based upon pre-selected questions related to the Key RiskMAP Messages).

Sample Designs & Size

The Sponsor is proposing the following sample sizes per wave:

PROJECTED SAMPLE SIZES PER WAVE

	Colorectal Surgeons & General Surgeons performing Bowel Resection surgeries	Hospital Pharmacists at hospitals that perform Bowel Resection surgeries
12 months post-launch	150	150
18 months post-launch	150	150

These sample sizes are based on the confidence intervals in the following table:

TABLE OF CONFIDENCE INTERVALS BY SAMPLE SIZE AND % ANSWERED CORRECTLY
- 95% Confidence Level -

	PERCENT CORRECT				
Sample Size	50%	60%	70%	80%	90%
50	14%	14%	13%	11%	8%
75	11%	11%	10%	9%	7%
100	10%	10%	9%	8%	6%
125	9%	9%	8%	7%	5%
150	8%	8%	7%	6%	5%

Confidence with Selected Sample Sizes

The recommended sample size of 150 establishes a confidence interval of ±6 percentage points at the 95% confidence level if 80% of the respondents answered correctly. It is important to note that this confidence interval should be applied to the accuracy rate on a per question basis.

A respondent will be considered to have adequate knowledge of the Key RiskMAP messages if they accurately answer the two pre-selected survey questions correctly (Knowledgeable Respondents). The response rate will be calculated based on the number of Knowledgeable Respondents divided by the total number of Respondents.

Assumptions

The ability to meet the aforementioned sample sizes is dependant upon assumptions, including but not limited to, the number of Registered Hospitals and the HCPs affiliated therewith, overall response rate for participation, and completion rate which will depend upon pre-determined survey eligibility (awareness of the Product and potential to use or dispense the Product).

The above sample sizes assume a total universe of approximately 2600 hospitals and 15,000 surgeons (general and colorectal) that perform bowel resections. The sample sizes are based upon the rationale that all surgeons who perform bowel resections and pharmacists at Registered Hospitals where bowel resections are performed will be invited to participate. For the purposes of this sampling design exercise, it is estimated that 50% of hospitals will have registered during the twelve months post launch, a 5% response rate can be achieved with these specialties, and a subset of this sample will be eligible to complete the survey based upon pre-determined survey requirements. It is important to note that a different frequency of reporting requires reevaluation of sample size.

Regarding participation eligibility, the Sponsor proposes:

1. Every qualifying surgeon and pharmacist affiliated with the Registered Hospitals who perform bowel resections will be invited to participate, since those surgeons and pharmacists all have potential responsibility for using or dispensing the Product.
2. Respondents who answered the RiskMAP questions in Wave 1 will not be eligible to participate in Wave 2.
3. Upon conclusion of the survey, a reinforcement of the RiskMAP information will be provided to participants who answered the questions correctly and a redirection will be provided to physicians who answered incorrectly. In this manner, the survey itself can be used as a means of education reinforcement for the Key RiskMAP messages.

Survey Controls for Bias

Sampling Bias

Surveyor will be instructed to randomly sample the participants in each universe (of surgeons and pharmacists) which, based upon the projected sample sizes, is expected to engage an appropriate cross-section of HCPs from both recently enrolled and tenured registrant hospitals. Screening questions will be designed to encourage participation by all levels of the Product users/dispensers, including surgeons that have not used but probably / definitely will use the Product in the future, and Pharmacists who have not dispensed but probably / definitely will dispense in the future.

The survey will include as participants any surgeon who has ever used the Product without reference to volume of the Product use or number of bowel procedures performed. Likewise, any pharmacist employed in a pharmacy at a Registered Hospital that stocks the Product or who has dispensed the Product will be included as an eligible participant.

Individual Target HCPs may be affiliated with more than one Registered Hospital and in such cases, will only be included once in the universe. If a Target HCP is affiliated with multiple hospitals, they will be included in the universe so long as at least one of the hospitals is a Registered Hospital.

Also, multiple attempts will be made to recruit respondents from each of the Registered Hospitals, thus minimizing non-response bias.

Questionnaire Bias

Surveyor will ensure that survey bias is minimized through the application of careful research methods, including but not limited to, randomization of questions and response lists within questions, carefully constructed non-leading questions, and a pretest which will serve to hone the questions to be utilized in the quantitative study, and to ensure that none of the questions induce bias.

Survey Pretests

Prior to the first wave of the research, the third-party market research vendor will conduct pre-tests. In these pretests approximately 8 qualifying physicians will be interviewed by a trained moderator, employing the appropriate use information and questioning sequences to be employed in the quantitative study. The pretest will serve to hone the questions to be utilized in the quantitative study, and to ensure that none of the questions induce bias. The Sponsor will submit the data collected via these survey pretests prior to the first wave of research.

Survey Instruments

Surgeon Survey

- **Screen for General & Colorectal Surgeons at Registered Hospitals. Record physician specialty.**
- **Questions shaded in GREEN indicate pre-selected questions to evaluate awareness of the Key RiskMAP Messages (involved in calculation of accuracy rate).**
- **Appropriate programming language will be enabled and thoroughly tested.**
- **Respondents will be prevented from altering their previous responses.**
- **Response lists will be randomized.**

Screener

1. Which of the following products have you heard of and/or ever used?

[NOTE: Multiple products used by bowel resection surgeons will be provided in question response lists to reduce the tendency of respondents to falsely indicate they have heard of or used any one product in order to collect honoraria for participation].

Product *Randomize list*	Yes (heard of)	No (haven't heard of)	Unsure if I have ever heard of	I have used this product at least once
Amitiza (lubiprostone)				
Azactam (aztreonam)				
Emend (aprepitant)				
Entereg (alvimopan)		*[If selected, terminate and tally]*	*[If selected, terminate and tally]*	
Relistor (methylnaltrexone)				
Reglan (metoclopramide)				
Zofran (ondansetron)				

[SHOW QUESTION 2 FOR THOSE WHO HAVE NOT USED SELECT PRODUCTS]

2. For each of the products you have not yet used, what are you likely to do in the future?

[Show all products from question above for which the respondent did not select "I have used this product at least once"]

Product *Randomize list*	Definitely will use	Probably will use	Don't know / Unsure	Probably will not use	Definitely will not use
Product 1					
Product 2					
Product 3					
Entereg (alvimopan)	*If selected, continue*	*If selected, continue*	*If selected, terminate and tally*	*If selected, terminate and tally*	*If selected, terminate and tally*
Product 4					

For the next several questions you will be asked about the product Entereg® (alvimopan).

3. What is the indication for the use of Entereg? Please be as specific as possible.

_____

_____

4. What is the maximum number of doses of Entereg that should be administered to a patient? *(Record one response)*

Randomize List

[ ]	Maximum of 15 doses (1 pre-op dose, then post surgery BID for a maximum of 7 days).....	1
[ ]	Maximum of 29 doses (1 pre-op dose, then post surgery BID for a maximum of 14 days)	2
[ ]	Maximum of 5 doses (1 pre-op dose, then post surgery BID for a maximum of 2 days)	3
[ ]	There is no limit to number of doses	4
[ ]	Don't know / unsure	5

5. Where should Entereg be administered? ... *(Record one response)*

Randomize List

[ ]	Only in the inpatient setting.....	1
[ ]	Only in the outpatient setting.....	2
[ ]	In both inpatient and outpatient settings	3
[ ]	Don't know / unsure	4

6. The reason Entereg should be limited to short term in-patient administration is: In a long-term (12-month) clinical study for another indication, a numeric imbalance was seen in the incidence of ….

(Record one response)

Randomize List

[ ]	Ischemic colitis	1
[ ]	Ischemic cardiovascular adverse events	2
[ ]	Abnormal liver function test results	3
[ ]	Don't know / unsure	4

[SHOW TO PHYSICIANS WHO ANSWERED Q4 AND OR Q5 INCORRECTLY] Thank you for participating in this study. Please note that you answered incorrectly to the following question(s). The correct information regarding appropriate use of the Product as presented in the Product labeling is as follows. Please be mindful of this information when using this medication: [INSERT QUESTION(S) HIGHLIGHTING CORRECTED RESP0NSE]
[SHOW TO PHYSICIANS WHO ANSWERED Q4 AND Q5 CORRECTLY] Thank you for participating in this study. Please note that you answered correctly to the following questions regarding appropriate use of the Product as presented in the Product labeling. Please continue to be mindful of this information: [INSERT QUESTION(S) HIGHLIGHTING CORRECT RESP0NSE]

END

Hospital Pharmacist Survey

- **Screen for Hospital Pharmacists at Registered Hospitals who have a role in the dispensing of medication.**
- **Questions shaded in GREEN indicate pre-selected questions to evaluate awareness of the Key RiskMAP Messages (involved in calculation of accuracy rate).**
- **Appropriate programming language will be enabled and thoroughly tested.**
- **Respondents will be prevented from altering their previous responses.**
- **Response lists will be randomized.**

1. Which of the following products have you heard of and/or ever dispensed?

[NOTE: Multiple products used by bowel resection surgeons will be provided in question response lists to reduce the tendency of respondents to falsely indicate they have heard of or used any one product in order to collect honoraria for participation].

Product *Randomize list*	Yes (heard of)	No (haven't heard of)	Unsure if I have ever heard of	I have dispensed this product at least once
Amitiza (lubiprostone)				
Azactam (aztreonam)				
Emend (aprepitant)				
Entereg (alvimopan)		*[If selected, terminate and tally]*	*[If selected, terminate and tally]*	
Relistor (methylnaltrexone)				
Reglan (metoclopramide)				
Zofran (ondansetron)				

[SHOW QUESTION 2 FOR THOSE WHO HAVE NOT DISPENSED SELECT PRODUCTS]

2. For each of the products you have not yet dispensed, what are you likely to do in the future?

[Show all products from question above for which the respondent did not select "I have dispensed this product at least once"]

Product *Randomize list*	Definitely will dispense	Probably will dispense	Don't know / Unsure	Probably will not dispense	Definitely will not dispense
Product 1					
Product 2					
Product 3					
Entereg (alvimopan)	*If selected, continue*	*If selected, continue*	*If selected, terminate and tally*	*If selected, terminate and tally*	*If selected, terminate and tally*
Product 4					

For the next several questions you will be asked about the product Entereg® (alvimopan).

3. What is the indication for the use of Entereg? Please be as specific as possible.

_____

_____

4. What is the maximum number of doses of Entereg that should be administered to a patient? *(Record one response)*

Randomize List

[ ] Maximum of 15 doses (1 pre-op dose, then post surgery BID for a maximum of 7 days)..... 1

[ ] Maximum of 29 doses (1 pre-op dose, then post surgery BID for a maximum of 14 days) 2

[ ] Maximum of 5 doses (1 pre-op dose, then post surgery BID for a maximum of 2 days) 3

[ ] There is no limit to number of doses..... 4

[ ] Don't know / unsure 5

5. Where should Entereg be administered? ... *(Record one response)*

Randomize List

[ ] Only in the inpatient setting..... 1

[ ] Only in the outpatient setting 2

[ ] In both inpatient and outpatient settings 3

[ ] Don't know / unsure 4

6. The reason Entereg should be limited to short term in-patient administration is: In a long-term (12-month) clinical study for another indication, a numeric imbalance was seen in the incidence of ….

(Record one response)

Randomize List

[ ] Ischemic colitis 1

[ ] Ischemic cardiovascular adverse events 2

[ ] Abnormal liver function test results 3

[ ] Don't know / unsure 4

[SHOW TO PHARMACISTS WHO ANSWERED Q4 AND OR Q5 INCORRECTLY] Thank you for participating in this study. Please note that you answered incorrectly to the following question(s). The correct information regarding appropriate use of the Product as presented in the Product labeling is as follows. Please be mindful of this information when using this medication: [INSERT QUESTION(S) HIGHLIGHTING CORRECTED RESP0NSE]
[SHOW TO PHARMACISTS WHO ANSWERED Q4 AND Q5 CORRECTLY] Thank you for participating in this study. Please note that you answered correctly to the following questions regarding appropriate use of the Product as presented in the Product labeling. Please continue to be mindful of this information: [INSERT QUESTION(S) HIGHLIGHTING CORRECT RESP0NSE]

END