

ENTEREG[®]: Health Economic Analysis Using the Nationally Representative Premier Perspective[™] Database¹

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

This retrospective health economic analysis included adult patients in the Premier Perspective Database undergoing partial large or small bowel resection surgery with primary anastomosis who were discharged from January 1 to December 31, 2009.

Eligible patients were derived from all hospitals in the updated Premier Perspective Database (including the Care Science Database).

About the Premier Perspective Database²

The Premier Perspective Database is the largest inpatient database in the United States and is developed and maintained by Premier, Inc., for quality and utilization benchmarking. The Premier Perspective Database captures complete billing and coding history during a patient's hospital visit and contains more than 45 million inpatient discharges from more than 500 acute care hospitals across the nation.

The hospitals in the database represent all geographic areas of the U.S. and include a broad range of bed sizes, teaching and nonteaching hospitals, and urban and rural facilities. The patient-level data are validated and HIPAA compliant and represent both the clinical and financial aspects of hospital operations.

WARNING: FOR SHORT-TERM HOSPITAL USE ONLY

ENTEREG is available only for short-term (15 doses) use in hospitalized patients. Only hospitals that have registered in and met all of the requirements for the ENTEREG Access Support & Education (E.A.S.E.[™]) Program may use ENTEREG.

Premier Perspective is a trademark of Premier, Inc.

Please see accompanying full Prescribing Information for ENTEREG.



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Study population and methods

- This was a retrospective hospital claims database analysis in which several prespecified endpoints were assessed, including length of stay (LOS) and total hospital costs
- The LOS and cost analyses were performed on a modified intent-to-treat (MITT) population. The MITT population received ≥ 3 and ≤ 15 doses of ENTEREG during the index hospitalization and received parenteral opioid on ≥ 1 postoperative day
- Patients were matched using 2 matching techniques (1:1 match)
 - **Exact matching**, in which patients were matched by category of index bowel resection procedure and surgeon type (general, colorectal, or other)
 - **Propensity score matching**, derived using a statistical model that incorporated all baseline measures (eg, age, gender, procedure-related diagnosis, comorbidities, and cardiovascular disease risk factors)
- Analyses
 - **Mean postoperative LOS** for bowel resection patients who received ENTEREG vs matched controls (patients who did not receive ENTEREG). LOS was defined as the time period from the calendar day of surgery until the calendar day of discharge
 - **Estimated mean total hospital cost** for bowel resection patients who received ENTEREG vs matched controls (patients who did not receive ENTEREG)
 - **Mean cost per day of operation and each postoperative day** were calculated using unmatched control patients from the Premier Perspective Database. These costs were then applied to the matched cohorts of patients treated with ENTEREG and patients not treated with ENTEREG. The cost of ENTEREG was then added to the total cost for each patient who received ENTEREG based on the number of doses received

Limitations of retrospective claims database analyses

- This is a retrospective economic analysis, and results may vary for individual hospitals
- Similar to other cost-accounting systems, the Premier Perspective Database could be subject to coding and administrative errors

Important Safety Information

- 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 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 in 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

Inclusion criteria

- **Patients met all inclusion criteria**

- Adults ≥ 18 years at discharge
- Medical claim with ICD-9-CM procedure codes for a primary procedure involving partial large or small bowel resection and primary anastomosis, including
 - Multiple segmental resection
 - Cecectomy
 - Hemicolectomy
 - Transverse colon resection
 - Sigmoidectomy
 - Partial excision of large intestine
 - Resection of rectum
 - Anterior resection of rectum/ Rectorectostomy
 - Small bowel resection/ Resection, small intestine
 - Closure of stoma
- Discharged within the study dates (1/1/2009 through 12/31/2009)
- Surgery at a participating Premier Perspective hospital

Exclusion criteria

- **Exclusion criteria included**

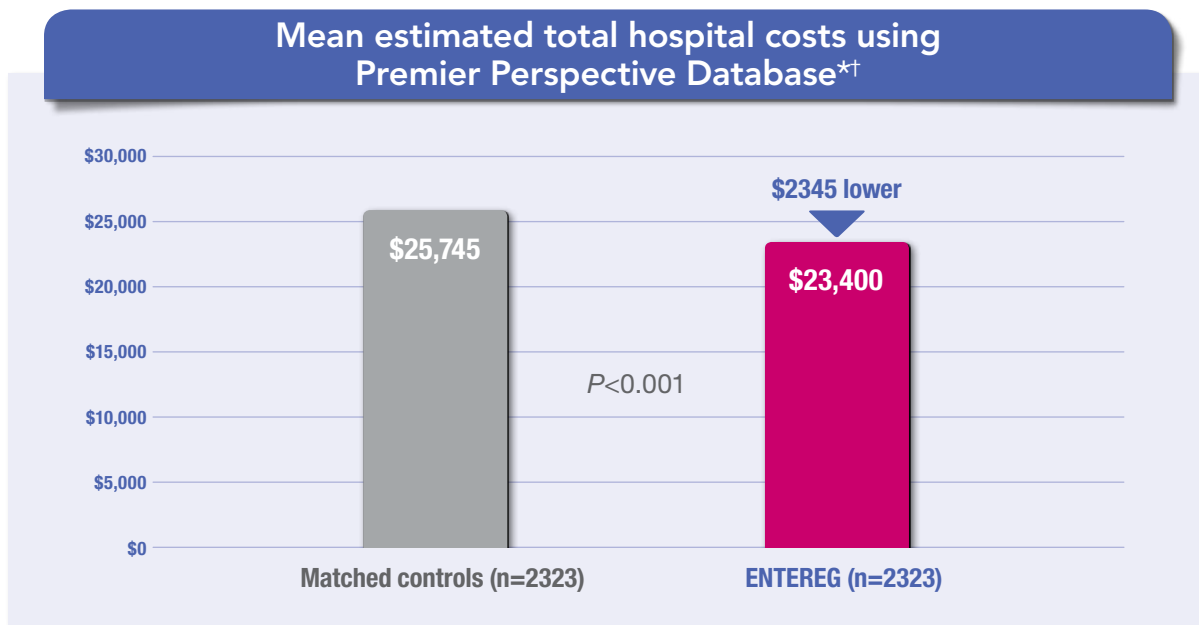
- A trauma diagnosis
- A bowel resection performed on more than 1 day during the index hospitalization
- An excluded non-bowel resection surgical code (as an additional procedure within the index hospitalization)

Please see accompanying full Prescribing Information, including Boxed Warning regarding short-term hospital use only and the ENTEREG Access Support & Education (E.A.S.E.™) Program.



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Patients receiving ENTEREG averaged \$2345 lower estimated total hospital costs than matched controls



^{*}Hospitalization cost includes the day of surgery up to and including the day of discharge.
[†]Costs were reported in 2009 dollars.

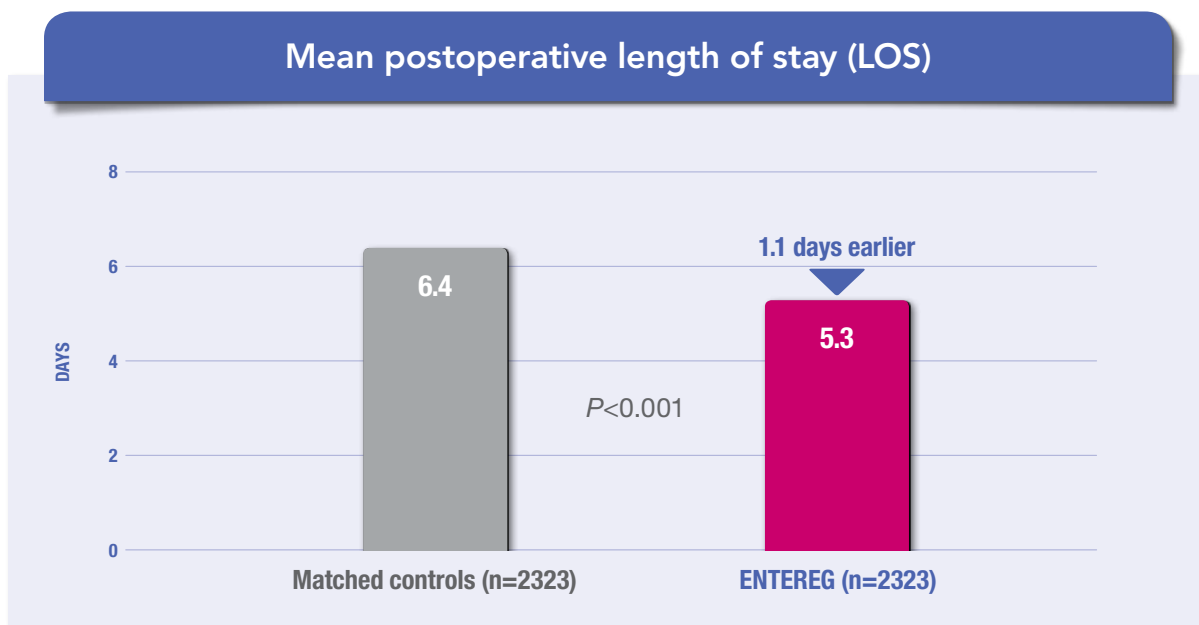
Cost of ENTEREG

- At the time this analysis was performed, the listed wholesale acquisition cost (WAC) of ENTEREG per dose was \$66.25[‡]
- In this study, the mean number of doses of ENTEREG received per patient in the active group was 8.5

[‡]Source: Wolters Kluwer Health Inc, December 2009. Wholesale acquisition cost is the listed price to wholesalers and warehousing chains, not including prompt pay, stocking or distribution allowances, or other discounts, rebates, refunds, or charge backs. Listed price may not represent prices charged to other customers, including specialty distributors.

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Patients receiving ENTEREG were discharged from the hospital a mean of 1.1 days earlier than the control group



- LOS was defined as the time period (in days) from the calendar day of surgery until the calendar day of discharge
- In the 4 pivotal North American Phase 3 clinical trials, ENTEREG reduced the mean time to discharge order written (DOW) by approximately 13 to 21 hours compared with patients receiving placebo. Time to DOW was defined as the time from the end of surgery to the time that the discharge order was written³

Important Safety Information

- ENTEREG is not recommended for use in patients with severe hepatic impairment, end-stage renal disease, or in patients undergoing surgery for correction of complete bowel obstruction
- 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)

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Study conclusions

- Patients receiving ENTEREG averaged **\$2345** lower estimated total hospital costs than matched controls
- Patients receiving ENTEREG were discharged from the hospital a mean of **1.1 days** earlier than the matched control group
- See study design and limitations on pages 2 and 3

Important Safety Information

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- ENTEREG Capsules are contraindicated in patients who have taken therapeutic doses of opioids for more than 7 consecutive days immediately prior to taking ENTEREG
- Most common adverse reactions in patients treated with ENTEREG (incidence $\geq 3\%$ with ENTEREG and at least 1% greater than placebo) undergoing bowel resection were anemia, dyspepsia, hypokalemia, back pain, and urinary retention
- ENTEREG is available only to hospitals that enroll in the E.A.S.E. Program. To enroll in the E.A.S.E. Program, the hospital must acknowledge that:
 - Hospital staff who prescribe, dispense, or administer ENTEREG have been provided the educational materials on the need to limit use of ENTEREG to short-term, inpatient use
 - Patients will not receive more than 15 doses of ENTEREG
 - ENTEREG will not be dispensed to patients after they have been discharged from the hospital

For more information on the E.A.S.E. Program, contact Adolor Corporation (a wholly owned subsidiary of Cubist Pharmaceuticals) at 1.866.4ADOLOR (1.866.423.6567) or visit www.entereg.com.

Please see accompanying full Prescribing Information for ENTEREG.

References: 1. Data on file. Adolor Corporation. 2. Premier, Inc. Perspective Rx database. <http://www.premierinc.com/quality-safety/tools-services/prs/services/perspectiverx.jsp>. Accessed September 14, 2010. 3. ENTEREG [package insert]. Exton, PA: Adolor Corporation; 2009.

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