



**ESPS PEER REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 9899

**Title:** Lubiprostone versus Senna in Postoperative Opioid-induced Constipation: A Double-Blind, Active-Comparator Trial

**Reviewer code:** 02526197

**Science editor:** Su-Xin Gou

**Date sent for review:** 2014-03-03 18:15

**Date reviewed:** 2014-04-06 12:10

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

This study addresses an important clinical issue. It investigated the efficacy of lubiprostone-based new therapy for opioid use-associated constipation in post-operative orthopedic patients, primarily in a geriatric population. It appears that the new drug did not show better efficacy than the conventional senna. My suggestions for revisions are as follows: 1) As noted by the authors, the sample size in this study was too small limiting the necessary power required to reach the above conclusion. This needs to be addressed, at least emphasized in the discussion. 2) The results were obtained from a specific patient population but the current title of the manuscript did not reflect this important information. 3) Constipation is common in non opioid user, non orthopedic, general geriatric population. Was there any such patient being included in this study? If so, then the authors need to determine whether those prior constipated patients were appropriate to be excluded or included.



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## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 9899

**Title:** Lubiprostone versus Senna in Postoperative Opioid-induced Constipation: A Double-Blind, Active-Comparator Trial

**Reviewer code:** 00227519

**Science editor:** Su-Xin Gou

**Date sent for review:** 2014-03-03 18:15

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

1. Was pre-operative opioid use an exclusion criterion? 2. Were the post-operative diet and ambulation protocols identical in both groups? 3. Was pre-operative constipation an exclusion criterion?

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 9899

**Title:** Lubiprostone versus Senna in Postoperative Opioid-induced Constipation: A Double-Blind, Active-Comparator Trial

**Reviewer code:** 02531237

**Science editor:** Su-Xin Gou

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**Date reviewed:** 2014-04-11 14:48

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

### COMMENTS TO AUTHORS

The study by Marciniak and colleague is a well designed and conducted double-blind case-control trial. They assessed the efficacy of Lubiprostone compared to senna on opioid-induced constipation. The results show that there was no statistically significant difference between the two treatment and that both regimens required additional laxative medications. The manuscript is clear, well written and results and discussion sections are sufficiently developed. However, there are few revision that should be considered: Major revision: 1) it is not clear if patients with chronic constipation were enrolled or not in the study. Please, state that clearly in Materials and Methods section. 2) due to the age of the patients enrolled it is highly probable that several medications were used by the subjects during the trial. These latter might influence the efficacy of the medications studied. The author should at least provide data that between the two groups there were no differences in terms of predisposing conditions. Moreover, this should be part of the Discussion. Minor revision: 3) Statistical section: lines from 274 to 289 might better fit in the Material and Methods sections. I kindly suggest removing them from the original section. 4) Although not statistically significant, the morphine equivalents daily dose in the two groups seems to be relevant from a clinical point of view (line 318, page 13). The author might consider adding a sentence about that in the discussion. Moreover, have the authors' data about a potential direct relation between opioid dose (daily or cumulative) and severity/onset of constipation? 5) can the author provide more information about



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the rescue laxative medications that part of the Study population received? 6) lubiprostone and senna have different manufacturing costs. The authors should take this into consideration in their costs/benefits analysis and discuss it in the manuscript. Therefore, according to their results, lubiprostone should not be recommended as a valid option for transitory constipation induced by opioid intake.



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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 9899

**Title:** Lubiprostone versus Senna in Postoperative Opioid-induced Constipation: A Double-Blind, Active-Comparator Trial

**Reviewer code:** 00009062

**Science editor:** Su-Xin Gou

**Date sent for review:** 2014-03-03 18:15

**Date reviewed:** 2014-04-11 15:39

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

The study compares the activity of senna and lubiprostone in the treatment of post-operative opioid induced constipation. The study is interesting but the text can be improved. Some suggestions: Line 4 and in the text delete "active comparator" Line 35 delete "measures". Add "treated with opioids" Line 46 add "(FIM)" Line 73-75: Change in : Constipation is frequent in post operative orthopedic patients treated with opioids" Line 76 Delete one of "comparing" add "opioid induced" before constipation Line 79-80 delete" in the CPac-Sym and Pac -Quol and However" Tables 3 and 4 (Gastrointestinal symptoms and Bowel Movements ) can be deleted. Line 345 Now table 3 Lines 362-375 are repetitive of figure 1 . Please delete what is repetitive. Line 389 Please summarize the data of the deleted table 3 in the text as median and 25-75 percentiles. Place the activity data on Rehabilitation (lines 375 386) before the adverse events (line 343) Line 432 add-SYM and -QOL questionnaires.



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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 9899

**Title:** Lubiprostone versus Senna in Postoperative Opioid-induced Constipation: A Double-Blind, Active-Comparator Trial

**Reviewer code:** 00467030

**Science editor:** Su-Xin Gou

**Date sent for review:** 2014-03-03 18:15

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

The authors intend to investigate lubiprostone versus Senna in postoperative opioid-induced constipation and they concluded individuals using either lubiprostone or senna showed improvement in symptoms of constipation and quality of life. Most participants in each of the treatment groups required additional medications to control symptoms, and also demonstrate that more than one medication may be required for control of constipation symptoms for the study population. These results would have potential benefits to the physicians who are interested in this area and valuable to be documented in the literatures.