

Efficacy and Safety of Linaclotide as an Adjunct to Polyethylene Glycol in Bowel Preparation: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION**Support** - No specific financial support was received for this review.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2024120123**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 December 2024 and was last updated on 30 December 2024.**INTRODUCTION**

Review question / Objective To evaluate the efficacy and safety of linaclotide as an adjunct to polyethylene glycol (PEG) for bowel preparation prior to colonoscopy. The study examines primary outcomes such as adequate bowel preparation and Boston Bowel Preparation Scale (BBPS) scores and secondary outcomes including adverse events and patient tolerability.

Rationale High-volume polyethylene glycol (PEG) solutions are effective for bowel cleansing but often lead to poor patient adherence due to tolerability issues. Linaclotide, a guanylyl cyclase-2C agonist, has shown promise in improving bowel preparation efficacy and tolerability when used with PEG. This systematic review synthesizes existing evidence to assess its clinical benefits compared to PEG alone.

Condition being studied Colonoscopy bowel preparation for improved diagnostic and therapeutic outcomes in gastrointestinal procedures.

METHODS**Search strategy**

- 'Linaclotide' OR 'ASP-0456' OR 'ASP0456' OR 'MD-1100' OR 'Linzess'
- 'PEG' OR 'Goly*' OR 'Golytely' OR 'Polyethy*' OR 'Polyoxyethylenes' OR 'Polyoxyethylene' OR 'Polyglycol' OR 'Polyglycols' OR 'Glycol, Polyethylene' OR 'Glycols, Polyethylene'
- 'Cathartics' OR 'Bowel Evacuants' OR 'Purgatives' OR 'Bowel Preparation Solutions' OR 'Bowel prep*'
- #1 AND #2 AND #3.

Participant or population Adult patients (≥ 18 years) undergoing colonoscopy for diagnostic or therapeutic purposes.

Intervention Linaclotide combined with polyethylene glycol (PEG) for bowel preparation.

Comparator Polyethylene glycol (PEG) alone for bowel preparation.

Study designs to be included Randomized controlled trials (RCTs).

Eligibility criteria

Inclusion criteria:

Adult patients undergoing colonoscopy.

Studies comparing linaclotide plus PEG versus PEG alone.

Outcomes including bowel preparation quality (BBPS scores), adverse events, and patient tolerability.

Exclusion criteria:

Case reports, single-arm studies, guidelines, and non-comparative studies.

Studies focusing exclusively on chronic constipation.

Information sources PubMed, MEDLINE, Embase, Scopus, Cochrane databases, grey literature, and citation searching.

Main outcome(s) Primary outcomes:

Adequate bowel preparation rates.

Total Boston Bowel Preparation Scale (BBPS) scores.

Additional outcome(s) Adverse events (nausea, abdominal pain).

Patient willingness to repeat the procedure.

Polyp detection rates.

Data management Data extraction was performed using a predefined Excel template, managed collaboratively by two reviewers, with discrepancies resolved by a third reviewer.

Quality assessment / Risk of bias analysis The revised Cochrane Risk of Bias Tool (RoB 2.0) was used for RCTs. The certainty of evidence was assessed using the GRADE framework.

Strategy of data synthesis A random-effects meta-analysis was conducted using RevMan Web, with dichotomous outcomes expressed as risk ratios (RRs) and continuous outcomes as weighted mean differences (WMDs).

Subgroup analysis Subgroup analyses based on PEG volume (e.g., 2L PEG versus 3L PEG) and geographic region.

Sensitivity analysis Conducted by excluding studies with a high risk of bias to evaluate the robustness of findings.

Language restriction No language restrictions were applied.

Country(ies) involved United States, China, and other international contributors.

Keywords Linaclotide; Polyethylene Glycol; Colonoscopy; Bowel Preparation; Meta-analysis.

Dissemination plans Findings will be disseminated through publication in Journal.

Contributions of each author

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