

## Potassium-Competitive Acid Blockers (P-CABS) as a New Breakthrough in the Treatment of Gastroesophageal Reflux Disease and Erosive Esophagitis : A Recent Literature Review

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### Article History

Received : 22 May 2025

Revised : 11 June 2025

Accepted : 11 June 2025

Published : 12 June 2025

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### Cite This Article:

Ayuni Putri, N. (2025).  
POTASSIUM-COMPETITIVE  
ACID BLOCKERS (P-CABS)  
SEBAGAI TEROBOSAN BARU  
DALAM TERAPI GERD DAN  
EROSIVE ESOPHAGITIS (EE) :  
TINJAUAN LITERATUR  
TERKINI. *Jurnal Kesehatan  
Dan Kedokteran*, 4(2), 01–06.

### DOI:

<https://doi.org/10.56127/juke.v4i2.2031>

**Abstract:** Gastroesophageal reflux disease (GERD) and erosive esophagitis (EE) are common gastrointestinal disorders typically managed with proton pump inhibitors (PPIs). Although effective, PPIs have certain limitations, prompting the development of a new class of acid-suppressing agents known as potassium-competitive acid blockers (P-CABs). These agents offer the potential for faster and possibly more effective treatment compared to PPIs. This literature review aims to evaluate the efficacy, safety, and potential cost-effectiveness of P-CABs versus PPIs in the treatment of GERD and EE, based on five recent clinical trials. This review includes randomized controlled clinical trials investigating four types of P-CABs: vonoprazan, linaprazan glurate, fexuprazan, and tegoprazan, based on five source articles. The findings indicate that all P-CABs demonstrate efficacy that is comparable to or greater than that of PPIs, with a faster onset of action, favorable safety profiles, and promising cost-effectiveness, particularly in severe cases of EE. These results suggest that P-CABs are a promising alternative therapy for GERD and EE, supported by strong clinical evidence across various treatment scenarios. This review offers a novel contribution by summarizing five recent clinical trials on four P-CAB agents. Addressing the lack of comparative evaluations on their efficacy, safety, and cost-effectiveness, especially in PPI-resistant GERD and EE cases, this review supports more informed clinical decision-making.

**Keywords:** Acid suppression, GERD therapy, P-CABs

## INTRODUCTION

Gastroesophageal Reflux Disease (GERD) is one of the most common gastrointestinal disorders encountered in clinical practice, characterized by the backflow of stomach contents into the esophagus, which can cause various symptoms such as heartburn, regurgitation, chest pain, and long-term complications. One common complication is Erosive Esophagitis (EE), a condition in which the esophageal mucosa is damaged due to continuous exposure to gastric acid. EE may lead to more severe symptoms, such as dysphagia, odynophagia, even gastrointestinal bleeding (Vakil et al., 2006; Chait, 2025).

The prevalence of GERD has increased significantly in recent decades, both in Western countries and in the Asian region. The rise in cases in Asia appears to be more prominent in younger age groups. A study in Japan reported that the highest prevalence of GERD occurs in individuals aged 20-29, likely influenced by changes in dietary patterns, increased consumption of high-fat foods, and sedentary lifestyles. In addition to causing physical symptoms, GERD also has a significant impact on the quality of life of patients. Chronic cough due to reflux, for example, has been shown to significantly reduce LCQ (Leicester Cough Questionnaire) scores, and improvement in these symptoms can only be achieved if the reflux is well-controlled (Kang et al., 2025). Long-term complications such as esophageal stricture and Barrett's esophagus have become important considerations in patient selection for clinical studies due to the severity of the clinical impact they cause.

Proton pump inhibitors (PPIs) have become the primary standard in the treatment of GERD and EE, thanks to their ability to effectively suppress gastric acid production through the irreversible inhibition of the proton pump ( $H^+$ ,  $K^+$ -ATPase) in gastric parietal cells. However, the increasing use of long-term PPIs has highlighted several limitations. The effects of PPIs are relatively slow and require consumption before meals to achieve optimal effectiveness. Moreover, not all patients show a satisfactory therapeutic response, particularly those with severe erosive esophagitis (LA grade C/D). Long-term use also raises concerns about side effects, such as hypergastrinemia, nutrient malabsorption, gastrointestinal infections, and histopathological changes in the gastric mucosa, which may potentially lead to further complications (Katz et al., 2013).

This condition has driven the search for alternative therapies that act more quickly, provide more consistent acid control, and have a better safety profile. Potassium-competitive acid blockers (P-CABs) have emerged as a solution to these challenges. Unlike PPIs, P-CABs work by competitively inhibiting the proton pump against potassium ions, are reversible, and provide faster acid suppression that is not affected by meal timing. This characteristic offers a clinical advantage in managing acid reflux, particularly in patients who do not show an optimal response to PPI therapy. Additionally, P-CABs demonstrate consistency in symptom control and have the potential to reduce the risk of recurrence (Kahrilas et al., 2008; Leowattana & Leowattana, 2022).

Gastroesophageal reflux disease (GERD) and erosive esophagitis (EE) are common gastrointestinal disorders typically managed with proton pump inhibitors (PPIs). Although PPIs are effective, their limitations such as delayed onset of action, ineffectiveness in some

patients (e.g., those with PPI-resistant GERD), and potential long-term side effects have created a need for better therapeutic alternatives. Potassium-competitive acid blockers (P-CABs) have emerged as a promising new class of drugs, offering a potentially faster and more effective approach compared to PPIs. However, there is a notable research gap due to the lack of comprehensive reviews directly comparing the efficacy, safety, and cost-effectiveness of various P-CABs with PPIs, particularly in difficult-to-treat cases of GERD and EE. Therefore, this study aims to evaluate and compare the efficacy, safety profiles, and potential cost-effectiveness of four types of P-CABs vonoprazan, linaprazan glurate, fexuprazan, and tegoprazan based on five recent randomized controlled trials, providing updated clinical evidence to support more informed therapeutic decision-making for GERD and EE.

## RESEARCH METHOD

This literature review analyzes five key articles consisting of recent randomized controlled clinical trial results published between 2024 and 2025. The included studies meet the inclusion criteria of assessing the efficacy and safety of P-CABs compared to PPIs in patients with GERD or EE. The evaluation is conducted narratively, focusing on several key clinical parameters, namely mucosal healing rates, speed of symptom improvement, side effect profiles, and the cost-efficiency of the therapy.

## RESULT AND DISCUSSION

### 1. Long-term Safety of Vonoprazan: The VISION Study

The VISION study, a Phase IV clinical trial conducted over five years, evaluated the long-term safety of vonoprazan as maintenance therapy in patients with erosive esophagitis (EE). In this study, patients who achieved healing of EE through an induction therapy with vonoprazan 20 mg or lansoprazole 30 mg for up to 8 weeks subsequently entered a maintenance phase with vonoprazan 10 mg or lansoprazole 15 mg for 260 weeks. The results showed no detection of malignant epithelial changes or gastric neuroendocrine tumors in either group. However, parietal cell hyperplasia and foveolar hyperplasia were more frequently observed in the vonoprazan group compared to the lansoprazole group (97.1% vs. 86.5% and 14.7% vs. 1.9%, respectively). Median serum gastrin levels were also higher in the vonoprazan group (625 pg/mL) than in the lansoprazole group (200 pg/mL). Nevertheless, the incidence of adverse events was similar between the two groups,

indicating an acceptable safety profile for long-term use of vonoprazan (Uemura et al., 2025).

## **2. Efficacy of Linaprazan Glurate in Healing Severe EE**

Sharma et al. (2025) conducted a dose-finding study to evaluate the efficacy of linaprazan glurate in healing erosive esophagitis (EE), particularly in patients with high-grade severity (LA grade C/D). In this study, linaprazan glurate demonstrated a higher rate of esophageal mucosal healing compared to lansoprazole after 4 weeks of treatment. The reported side effects were mild and well-tolerated, indicating that linaprazan glurate may serve as an effective and safe alternative for patients with severe EE who may not respond optimally to conventional PPI therapy.

## **3. Fexuprazan in the Management of GERD-Related Chronic Cough**

A randomized, double-blind, active-controlled clinical trial by Kang et al. (2025) evaluated the effectiveness of fexuprazan compared to esomeprazole in treating chronic cough associated with GERD. The study involved 161 participants who received either fexuprazan 40 mg or esomeprazole 40 mg once daily for eight weeks. The results showed that both groups experienced significant improvements in quality of life, as measured by changes in the Leicester Cough Questionnaire (LCQ) scores (fexuprazan:  $4.9 \pm 4.0$  vs. esomeprazole:  $5.3 \pm 3.8$ ;  $p = 0.558$ ). Additionally, changes in the numerical rating scale for cough severity and Reflux Disease Questionnaire (RDQ) scores were similar between the two groups. Reported adverse events were mostly mild and comparable across both groups, supporting the potential of fexuprazan as an alternative therapy for GERD-related chronic cough (Kang et al., 2025).

## **4. Tegoprazan as an On-Demand Therapy for GERD**

Another study by Kang et al. (2025) evaluated the effectiveness of tegoprazan as an on-demand therapy in GERD patients who had previously experienced symptom improvement with acid-suppressive treatment. In this study, participants were randomly assigned to receive either tegoprazan 50 mg or esomeprazole 20 mg for eight weeks. The results showed that patient satisfaction with on-demand therapy was similar between the two groups. However, a higher proportion of patients in the tegoprazan group experienced symptom relief within 30 minutes of medication intake compared to the esomeprazole

group (26.2% vs. 16.1%;  $p < 0.05$ ), indicating a faster onset of action with tegoprazan. No serious adverse events were reported in either group, confirming the safety and effectiveness of tegoprazan as an on-demand therapy for GERD (Kang et al., 2025).

### 5. Cost-Effectiveness Analysis of Vonoprazan in Severe EE

Jeyarajan et al. (2025) conducted a cost-effectiveness analysis comparing vonoprazan and lansoprazole in patients with severe erosive esophagitis (EE). The study found that vonoprazan was more cost-effective in this patient population, with an Incremental Cost-Effectiveness Ratio (ICER) per Quality-Adjusted Life Year (QALY) that remained within the threshold set by the National Institute for Health and Care Excellence (NICE). These findings indicate that vonoprazan is not only clinically effective but also offers greater economic value compared to lansoprazole in the management of severe EE (Jeyarajan et al., 2025).

## CONCLUSION

P-CABs show promising potential as a therapy in the management of GERD and EE, in terms of efficacy, safety profile, and patient convenience. This advantage is particularly relevant for patients who demonstrate suboptimal responses to PPI therapy, where agents such as vonoprazan, linaprazan, fexuprazan, and tegoprazan may be considered as first-line therapies. The authors believe that P-CABs have the potential to revolutionize the therapeutic approach to GERD and EE, and therefore, it is important for the medical community to begin considering the integration of these therapies into evidence-based clinical practice. However, further long-term studies are required to evaluate the safety of chronic use and its impact on healthcare economic aspects more comprehensively.

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