

# Vonoprazan: A Novel Potassium-Competitive Acid Blocker in the Management of *H. pylori* Infection and Acid-Related Disorders

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## ABSTRACT

**Background:** Vonoprazan is a novel PCAB and the first in its class to receive US FDA approval for the treatment of *H. pylori* infection and gastric acid-related disorders. It binds directly to the proton pumps, blocking the exchange of potassium ions for hydrogen ions, thereby preventing the secretion of gastric acid. Vonoprazan represents a new class of medications designed to provide more consistent and reliable control of gastric acid secretion. **Materials and Methods:** This article searched databases like PubMed, Google Scholar, ScienceDirect, Web of Science and Medline using keywords such as "vonoprazan," "PCABs," and "*H. pylori* infection." Recent, high-quality research was prioritized during the screening process. **Results and Discussion:** Research studies showed that vonoprazan demonstrated superior acid suppression compared to traditional Proton Pump Inhibitors (PPIs) and was found to be highly effective in eradicating *Helicobacter pylori* infection. The drug was effective and associated with mild and manageable adverse events compared to those seen with PPIs. Vonoprazan is generally well-tolerated in patients with mild to moderate renal and hepatic impairment. It is primarily metabolized by the CYP3A4 enzyme, which results in fewer drug interactions. **Conclusion:** Vonoprazan is a safe and effective medication that provides faster, more potent and longer-lasting gastric acid suppression compared to conventional PPIs.

**Keywords:** Vonoprazan, Potassium-Competitive Acid Blocker, Proton Pump Inhibitors, Gastroesophageal Reflux Disease.

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## INTRODUCTION

Vonoprazan, the first-in-class Potassium-Competitive Acid Blocker (PCAB), demonstrates prolonged and potent acid suppression and is recognized for addressing the unmet needs of conventional Proton Pump Inhibitors (PPIs) (St Onge and Phillips, 2023; Oshima and Miwa, 2018). For the past three decades, PPIs have been a mainstay in the management of acid-related disorders. However, their slow-onset of action, inability to suppress nighttime acid breakthrough and the interindividual variations in drug exposure due to genetic polymorphic Cytochrome P450 (CYP)2C19 have led researchers to develop a more powerful anti-secretory drug (Echizen, 2015).

Takeda Pharmaceutical Company Limited developed Vonoprazan to overcome the limitations of PPIs and the hepatotoxicity of

other P-CABs (Otake *et al.*, 2016). It selectively and reversibly inhibits H<sup>+</sup>, K<sup>+</sup>-Adenosine Triphosphate (ATP) ase, is acid-stable, activates without an acidic environment, does not need an enteric coating for protection against gastric degradation, has a rapid onset of action and provides longer-lasting and superior acid suppression compared to conventional PPIs (St Onge and Phillips, 2023; Oshima and Miwa, 2018; Shirley, 2024). It is also non-inferior to PPIs in terms of safety and tolerability.

Vonoprazan is a pyrrole derivative, specifically 1-[5-(2-fluorophenyl)-1-(pyridin-3-ylsulfonyl)-1H-pyrrol-3-yl]-N-methylmethanamine fumarate (TAK-438) (Figure 1), with molecular weight of 461.5 g/mol. It was first marketed in Japan in February 2015 to treat acid-related disorders and *Helicobacter pylori* infection.<sup>2</sup> Later, in 2022, the U.S. Food and Drug Administration (FDA) approved two combination products containing vonoprazan for treating *H. pylori* infection, followed by its approval as a standalone treatment for healing and maintaining healed Erosive Esophagitis (EE) and relieving heartburn associated with Non-Erosive Reflux Disease (NERD)



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(Shirley, 2024). Vonoprazan is also approved in India by Drugs Controller General of India (DCGI) in May 2024.

## MATERIALS AND METHODS

This article comprehensively searched databases such as PubMed, Google Scholar, ScienceDirect, Web of Science and Medline for publications including vonoprazan relevant keywords. The search keywords included: “vonoprazan”, “PCABs”, “proton pump inhibitors”, “*H. pylori* infection”, “Gastroesophageal Reflux Disease”, “NSAID/LDA-related ulcers”, “tolerability”, “safety and efficacy”, etc. During the screening process, selection of recent and high-quality research was prioritized.

### Indications

Vonoprazan is the first P-CAB approved by the U.S. FDA in May 2022 to treat *H. pylori* infection in adults. Later, in November 2023, the FDA also approved vonoprazan for treating both erosive and non-erosive GERD.

### FDA-Approved Indications

#### Adjunct to *Helicobacter pylori* eradication

Vonoprazan has demonstrated a significantly higher *Helicobacter pylori* eradication rate than PPIs. It is recommended to use with amoxicillin and clarithromycin as triple therapy or with amoxicillin alone as dual therapy for the treatment of *H. pylori* infection in adults (Murakami *et al.*, 2016; Jung *et al.*, 2017; Maruyama *et al.*, 2017). Moreover, vonoprazan-based regimens were superior in treating clarithromycin-resistant *H. pylori* infection, which typically decreases the success rate of PPIs and they also showed a better eradication rate (Fallone, 2022). Therefore, to eliminate the *H. pylori* infection, vonoprazan-based triple and dual therapies provide effective substitutes for conventional PPI-triple therapy (Chey *et al.*, 2022).

#### Gastroesophageal Reflux Disease (GERD)

GERD is a common disorder with a prevalence of 10-20% in the Western World and 2.5-7.8 % in East Asia (Maradey-Romero and Fass, 2014). The two major phenotypes of GERD are NERD and EE (Maradey-Romero and Fass, 2014; Altomare, 2013). PPIs were considered as the gold standard in treating GERD (Maradey-Romero and Fass, 2014). However, several preclinical and clinical studies proved that vonoprazan has longer-lasting acid suppression than PPIs (Ashida *et al.*, 2015; Hori *et al.*, 2010).

#### Healing and maintenance of healed EE

Several published articles suggest that vonoprazan is a faster, more potent and longer-lasting gastric acid-suppressing agent, providing better heartburn relief and esophagitis healing than standard PPIs (Ashida *et al.*, 2015; Ashida *et al.*, 2015). It is also proven that vonoprazan is effective, well-tolerated and

non-inferior to PPIs for the long-term maintenance of healed EE (Ashida *et al.*, 2015).

### Symptomatic relief of heartburn associated with NERD

On July 18, 2024, the FDA approved vonoprazan for heartburn relief associated with NERD. Findings from clinical trials showed that vonoprazan is an effective therapy in alleviating the symptoms of heartburn in patients with NERD, with benefits appearing on the very first day of therapy (Fass *et al.*, 2022; Laine *et al.*, 2024). Additionally, vonoprazan provided rapid and sustained heartburn relief, with a greater number of 24 hr heartburn-free days and a higher percentage of days without daytime or nighttime heartburn, as well as reduced need for rescue antacid use (Kinoshita *et al.*, 2019; Miwa *et al.*, 2016).

### Off-Label Indications

#### Treatment of Gastric and Duodenal Ulcers

A randomized, double-blinded, multicenter study revealed that the safety and tolerability of vonoprazan 20 mg for treating Gastric Ulcers (GU) or Duodenal Ulcers (DU) were similar to those of lansoprazole 30 mg. The study also confirmed the non-inferiority of vonoprazan to lansoprazole for the healing of GU; however, it did not confirm the non-inferiority of vonoprazan to lansoprazole for the healing of DU (Miwa *et al.*, 2016).

#### Prevention of Gastric or Duodenal ulcers

An extensive range of chronic conditions, such as osteoarthritis and rheumatoid arthritis, are managed with Non-Steroidal Anti-inflammatory Drugs (NSAIDs) for pain and inflammation. Low-Dose Aspirin (LDA) is also frequently used in at-risk patients to lower the risk of ischemic or cerebrovascular events and to prevent clotting (Zhou *et al.*, 2013). The long-term use of NSAIDs and aspirin has raised concerns about associated gastric and duodenal mucosal injury and ulceration (Hunt and Yuan, 2011). The use of Proton Pump Inhibitors (PPIs) can prevent NSAID-induced peptic ulcers; however, some patients experience recurrence of the disease and alternative therapy has to be sought (Kawai *et al.*, 2022). A randomized, active-controlled, phase 3 study conducted in Japan reported that vonoprazan 10 mg and 20 mg were effective and well-tolerated for preventing NSAID-induced peptic ulcer recurrence (Mizokami *et al.*, 2017). Another study reported a greater preventive effect of vonoprazan 10 mg and 20 mg compared to lansoprazole 15 mg in preventing LDA-associated peptic ulcers (Kawai *et al.*, 2017). Therefore, vonoprazan 10 mg can be used as a daily clinical dose for the prevention of recurrence of NSAID/LDA-related ulcers.

## MECHANISM OF ACTION

The H<sup>+</sup>, K<sup>+</sup>-ATPase, commonly known as the proton pump, facilitates the final step in gastric acid production by transferring hydrogen ions across the canalicular membrane in exchange for luminal potassium ions (St Onge and Phillips, 2023). The movement of H<sup>+</sup> and K<sup>+</sup> ions and chloride ions creates an acidic gastric environment and maintains electrochemical balance across the membrane (St Onge and Phillips, 2023; Echizen, 2015). Vonoprazan, a basic compound, passively diffuses from the parietal cell cytoplasm into the acidic secretory canaliculi, where it accumulates in high concentrations (Otake *et al.*, 2106). In the highly acidic environment, the drug gets protonated, which decreases its membrane permeability and leads to its extended retention in the secretory canaliculi. It binds non-covalently to the H<sup>+</sup>, K<sup>+</sup>-ATPase enzyme, competitively and reversibly disrupting the binding of K<sup>+</sup> to the phosphorylated proton pump, blocking the entry of hydrogen ions into the stomach, thus inhibiting the secretion of gastric acid (Echizen, 2015; Otake *et al.*, 2106). Vonoprazan has a slow dissociation rate from H<sup>+</sup>, K<sup>+</sup>-ATPase, is acid-stable and consequently remains in the secretory canaliculi for a long duration, leading to prolonged acid suppression. Its half-life is about 7-8 hr, which supports prolonged acid control, often extending beyond 24 hr of effective acid suppression (Martinucci *et al.*, 2017). It also exhibits an efficacy of inhibition that is almost 350 times greater than PPIs (Echizen, 2015).

## Pharmacokinetics

### Absorption

Vonoprazan is rapidly absorbed after oral administration, reaching a peak plasma concentration (C<sub>max</sub>) of 37.8 ng/mL within 2 hr after a single dose and around 3 hr after multiple doses when steady state is achieved (t<sub>max</sub>). After the 12 hr dosing period, 273 ng\*hr/mL is the Area Under the Curve (AUC) from the time of administration (St Onge and Phillips, 2023). Vonoprazan can be taken with or without food, as it has time-independent pharmacokinetics and the half-life (t<sub>1/2</sub>) is 7 to 9 hr and remains consistent regardless of food intake (St Onge and Phillips, 2023; Oshima and Miwa, 2018). Moreover, P-CABs being acid-resistant do not require enteric-coated formulations (Martinucci *et al.*, 2017). They also dissolve quickly across various pH levels, leading

to a rapid onset of action and long-lasting suppression of gastric acid production (Otake *et al.*, 2016).

## Distribution

There are no available data on the plasma concentration-time after the injection of vonoprazan. However, the apparent oral volume of distribution after a single 20 mg dose of vonoprazan is 1001 L and at steady state, it is 782.7 L (Echizen, 2015; <https://pubchem.ncbi.nlm.nih.gov/compound/Vonoprazan>).

## Metabolism

Vonoprazan is primarily metabolized by CYP3A4 and to a certain extent by CYP2B6, CYP2C19, CYP2D6 and CYP2C9. Unlike PPIs, vonoprazan is not predominantly metabolized by CYP2C19; therefore, the CYP2C19 polymorphism does not influence its pharmacokinetics. However, drugs metabolized by CYP3A4 can affect vonoprazan's metabolism and vice versa, necessitating caution (Oshima and Miwa, 2018; Echizen, 2015; Otake *et al.*, 2016; Mulford *et al.*, 2021; Sugano, 2018).

## Excretion

Vonoprazan is primarily eliminated through the urinary system (67%) and in feces (31%), with only 8% and 1.4% of the oral dose excreted as unchanged drug via these routes, respectively (St Onge and Phillips, 2023; Echizen, 2015).

## DOSAGE AND ADMINISTRATION

### Available Dosage Forms and Strengths

Vonoprazan is administered orally, with or without food and is available in 10 mg and 20 mg tablets.

### Recommended Dosages

Healing of EE and relief of associated heartburn: Vonoprazan 20 mg once daily for eight weeks is the recommended oral dosage for adults (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>).

Maintenance of healed EE and relief of associated heartburn: The usual oral dosage for adults is 10 mg of vonoprazan once a day for up to six months (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>).

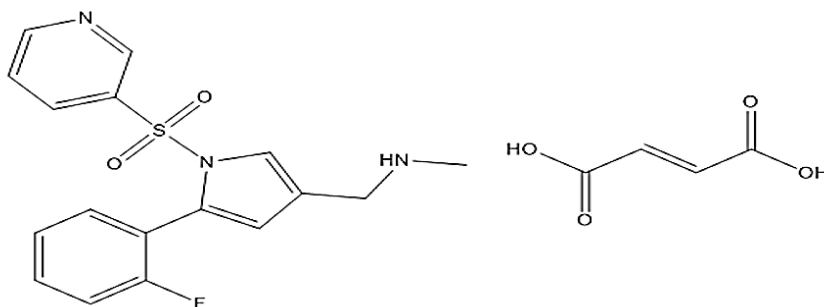


Figure 1: Chemical Structure of Vonoprazan (ChemDraw).

Relief of Heartburn Associated with NERD: The recommended adult dose is 10 mg of vonoprazan once daily per oral for 4 weeks (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>).

## Adjunct to *H. pylori* eradication

### Triple Therapy

For adults, an oral combination of 20 mg of vonoprazan, 1,000 mg of amoxicillin and 500 mg of clarithromycin is recommended to be taken twice a day, 12 hr apart, for 14 days (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>).

### Dual Therapy

The suggested oral dosage for adults is 20 mg of vonoprazan given twice a day (in the morning and evening) and 1,000 mg of amoxicillin taken three times a day (in the morning, mid-day and evening), for 14 days (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>).

## Specific Patient Population

### Hepatic and renal impairment

#### Healing of Erosive Esophagitis

Hepatic impairment	Classification	Recommended Dosage
	Child-Pugh Class A	20 mg once daily
	Child-Pugh Class B and C	10 mg once daily
Renal Impairment	Estimated Glomerular Filtration Rate (eGFR)	Recommended Dosage
	≥ 30 mL/min	20 mg once daily
	< 30 mL/min	Use not recommended
Maintenance of healed Erosive Esophagitis: No dosage adjustment is required.		

## Treatment of *H. pylori* infection

Hepatic impairment	Classification	Recommended Dosage
	Child-Pugh Class A	20 mg twice daily.
	Child-Pugh Class B and C	Use not recommended.
Renal Impairment	Estimated Glomerular Filtration Rate (eGFR).	Recommended Dosage.
	≥ 30 mL/min	20 mg twice daily.
	< 30 mL/min	Use not recommended.

## Elderly Patients

Clinical studies revealed similar safety and effectiveness between adult and elderly patients. However, changes in physiological function among the elderly cannot be ruled out, so vonoprazan should be administered with caution in this population (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>; <https://www.uptodate.com/contents/vonoprazan-drug-information>; Kusunoki *et al.*, 2019).

## Pediatric Patients

The safety and effectiveness of vonoprazan have not been established in patients under 18 years of age (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>).

## Pregnancy and lactation

There are no adequate data on vonoprazan use in pregnant and lactating women (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>).

## ADVERSE EFFECTS

The adverse effects associated with vonoprazan reported in adults are hypertension, peripheral edema, tachycardia, abdominal distention, abdominal pain, diarrhea, dry mouth, gastric polyps, intestinal polyps, urinary tract infection, increased liver enzymes and bone fracture. The incidence of dermatological reactions like Eczema, skin rash, urticaria and upper respiratory tract infections were ≤1% (St Onge and Phillips, 2023; Echizen, 2015; <https://dailymed.nlm.nih.gov/dailymed/lookup.cfm>; <https://www.uptodate.com/contents/vonoprazan-drug-information>). The adverse events identified during the post marketing were hematologic disorders (thrombocytopenia), hypersensitivity reaction (anaphylactic shock), hepatobiliary disorders (hepatic injury, jaundice, hepatic failure), dermatologic reactions (Stevens-Johnson Syndrome (SJS), Erythema multiforme, Toxic Epidermal Necrolysis (TEN)) and Endocrine and metabolic (hypomagnesemia, hypocalcemia, hypokalemia, vitamin B<sub>12</sub> deficiency) (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm>; <https://www.uptodate.com/contents/vonoprazan-drug-information>).

## DRUG INTERACTIONS

Vonoprazan alters the gastric acid level, which might decrease the absorption of medications like antiretroviral drugs, iron salts and ketoconazole/itraconazole that rely on an acidic environment, potentially reducing their effectiveness (St Onge and Phillips, 2023; <https://dailymed.nlm.nih.gov/dailymed/lookup.cfm>).

Vonoprazan is a weak CYP3A inhibitor and can elevate the levels of CYP3A4 substrates, which could heighten the risk of side effects associated with these drugs. Additionally, CYP3A4 inducers can decrease both the effectiveness and concentration of vonoprazan, so it is advisable to avoid using moderate to strong

inducers together with it (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>). Additionally, vonoprazan is a weak CYP2C19 inhibitor and might alter the plasma levels of medications metabolized by this enzyme (e.g., clopidogrel), either decreasing their active metabolites or increasing their exposure (e.g., citalopram, cilostazol). However, it is unlikely to result in clinically significant interactions with CYP2C19 (St Onge and Phillips, 2023; <https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>).

Vonoprazan's dosage is not modified based on drug interactions; however, depending on the medication, these interactions might require avoiding vonoprazan, careful monitoring, or adjusting the dose of the interacting drug (St Onge and Phillips, 2023).

## CONTRAINDICATIONS

Vonoprazan is contraindicated in patients who have a history of known hypersensitivity to vonoprazan or any of its ingredients. Vonoprazan may lower the level or effectiveness of rilpivirine by inhibiting its gastrointestinal absorption. Hence, vonoprazan is contraindicated with rilpivirine-containing products (<https://www.uptodate.com/contents/vonoprazan-drug-information>).

## Warning and precautions

Warnings and precautions for the use of vonoprazan include several important considerations to ensure safe and effective use. Prolonged treatment with vonoprazan may lead to hypomagnesemia, especially in patients taking the drug for extended periods or in combination with other medications like diuretics. Hence, monitoring of magnesium levels is recommended (<https://www.uptodate.com/contents/vonoprazan-drug-information>). Treatment with acid-suppressing drugs, including vonoprazan, may increase the risk of *Clostridium difficile* infection, leading to *Clostridioides difficile*-associated diarrhea. Patients should be monitored for persistent or worsening diarrhea (Yang *et al.*, 2022). It may also lead to osteoporosis-related bone fractures. Therefore, it is advisable to use vonoprazan for the shortest duration necessary (Otake *et al.*, 2016). Additionally, prolonged use of vonoprazan may reduce the absorption of vitamin B12 due to hypo- or achlorhydria, leading to potential vitamin B12 deficiency over time. If symptoms suggesting a deficiency appear, further examinations and monitoring are required (<https://www.uptodate.com/contents/vonoprazan-drug-information>). There have been reports of acute tubulointerstitial nephritis; if suspected, stop the medication and evaluate the patient (Yang *et al.*, 2022).<sup>32</sup> Patients with significant liver or renal impairment should use vonoprazan with caution, as dose adjustments or increased monitoring may be necessary. The safety profile of vonoprazan during pregnancy and lactation has not been fully established. Consequently, it should be administered only when

indicated and after a thorough evaluation of the potential risks and benefits by a healthcare provider.

## MONITORING

Monitoring for hypomagnesemia is essential, particularly in patients undergoing prolonged treatment or those concurrently using medications that may decrease magnesium levels, such as diuretics (<https://www.uptodate.com/contents/vonoprazan-drug-information>). Given that vonoprazan can impact electrolyte balance, periodic assessment of calcium and potassium levels is recommended, especially in individuals with conditions that increase the risk of electrolyte disturbances (<https://www.uptodate.com/contents/vonoprazan-drug-information>). Routine evaluation of renal and hepatic function is advised, particularly in patients with pre-existing conditions affecting these organs (<https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>; <https://www.uptodate.com/contents/vonoprazan-drug-information>). For patients undergoing long-term therapy, especially those at increased risk for osteoporosis, monitoring of bone density may be necessary to evaluate fracture risk (Otake *et al.*, 2016). Additionally, for patients on extended therapy who are at risk, monitoring for signs of vitamin B12 deficiency is recommended.

## CONCLUSION

Vonoprazan, a potassium-competitive acid blocker, has become a prominent alternative to conventional Proton Pump Inhibitors (PPIs) for treating acid-related conditions and eradicating *Helicobacter pylori*. It is the first U.S. FDA-approved P-CAB for the treatment of *H. pylori* infection. Vonoprazan is non-inferior to PPIs in terms of safety, tolerability and efficacy. Additionally, it possesses a rapid onset of action, a long-lasting acid inhibitory effect and prevents nocturnal acid breakthrough. Therefore, the drug may address the unmet needs of conventional therapies. However, future research should focus on the efficacy and safety of vonoprazan in specific patient populations, as well as on patient adherence and toxicity associated with vonoprazan.

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## CONFLICT OF INTEREST

The author declares that there are no conflicts of interest.

## ABBREVIATIONS

**ATP:** Adenosine Triphosphate; **AUC:** Area Under the Curve; **CYP-450:** Cytochrome P450; **DCGI:** Drugs Controller General of India; **DU:** Duodenal Ulcers; **EE:** Erosive Esophagitis; **FDA:** Food and Drug Administration; **GU:** Gastric Ulcers; **GERD:**

Gastroesophageal Reflux Disease; **LDA**: Low-Dose Aspirin; **NERD**: Non-Erosive Reflux Disease; **NSAID**: Non-Steroidal Anti-inflammatory Drugs; **PCAB**: Potassium-Competitive Acid Blocker; **PPI**: Proton Pump Inhibitors; **SJS**: Stevens-Johnson syndrome; **TEN**: Toxic Epidermal Necrolysis.

## REFERENCES

- Altomare, A., Guarino, M. P. L., Cocca, S., Emerenziani, S., & Cicala, M. (2013). Gastroesophageal reflux disease: Update on inflammation and symptom perception. *World Journal of Gastroenterology*, 19(39), 6523–6528. <https://doi.org/10.3748/wjg.v19.i39.6523>
- Ashida, K., Sakurai, Y., Hori, T., Kudou, K., Nishimura, A., Hiramatsu, N., Umegaki, E., & Iwakiri, K. (2016). Randomised clinical trial: Vonoprazan, a novel potassium-competitive acid blocker, vs. lansoprazole for the healing of erosive oesophagitis. *Alimentary Pharmacology and Therapeutics*, 43(2), 240–251. <https://doi.org/10.1111/apt.13461>
- Ashida, K., Sakurai, Y., Nishimura, A., Kudou, K., Hiramatsu, N., Umegaki, E., Iwakiri, K., & Chiba, T. (2015). Randomised clinical trial: A dose-ranging study of vonoprazan, a novel potassium-competitive acid blocker, vs. lansoprazole for the treatment of erosive oesophagitis. *Alimentary Pharmacology and Therapeutics*, 42(6), 685–695. <https://doi.org/10.1111/apt.13331>
- Chey, W. D., Mégraud, F., Laine, L., López, L. J., Hunt, B. J., & Howden, C. W. (2022). Vonoprazan triple and dual therapy for *Helicobacter pylori* infection in the United States and Europe: Randomized clinical trial. *Gastroenterology*, 163(3), 608–619. <https://doi.org/10.1053/j.gastro.2022.05.055>
- DailyMed. (n.d.). VOQUEZNA- vonoprazan fumarate tablet. <https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0cc52ac5-77ec-4d66-a770-762a1a960914>
- Echizen, H. (2016). The first-in-class potassium-competitive acid blocker, vonoprazan fumarate: Pharmacokinetic and pharmacodynamic considerations. *Clinical Pharmacokinetics*, 55(4), 409–418. <https://doi.org/10.1007/s40262-015-0326-7>
- Fallone, C. A. (2022). The current role of vonoprazan in *Helicobacter pylori* treatment. *Gastroenterology*, 163(3), 572–574. <https://doi.org/10.1053/j.gastro.2022.06.076>
- Fass, R., Vaezi, M. F., Sharma, P., Yadlapati, R., Hunt, B., Harris, T., Smith, N., Leifke, E., & Armstrong, D. (2022). S390 Efficacy and Safety of On-Demand Vonoprazan versus Placebo in the Treatment of Heartburn in Symptomatic Nonerosive Reflux Disease (NERD) Patients: A Phase 2 randomized controlled trial. *American Journal of Gastroenterology*, 117(10S), e272–e273. <https://doi.org/10.14309/01.ajg.0000858200.17525.4a>
- Hori, Y., Imanishi, A., Matsukawa, J., Tsukimi, Y., Nishida, H., Arikawa, Y., Hirase, K., Kajino, M., & Inatomi, N. (2010). 1-[5-(2-Fluorophenyl)-1-(pyridin-3-ylsulfonyl)-1H-pyrrol-3-yl]-N-methylmethanamine monofumarate (TAK-438), a novel and potent potassium-competitive acid blocker for the treatment of acid-related diseases. *The Journal of Pharmacology and Experimental Therapeutics*, 335(1), 231–238. <https://doi.org/10.1124/jpet.110.170274>
- Hunt, R. H., & Yuan, Y. (2011). Acid-NSAID/Aspirin interaction in peptic ulcer disease. *Digestive Diseases*, 29(5), 465–468. <https://doi.org/10.1159/000332211>
- Jung, Y. S., Kim, E. H., & Park, C. H. (2017). Systematic review with meta-analysis: The efficacy of vonoprazan-based triple therapy on *Helicobacter pylori* eradication. *Alimentary Pharmacology and Therapeutics*, 46(2), 106–114. <https://doi.org/10.1111/apt.14130>
- Kawai, T., Oda, K., Funao, N., Nishimura, A., Matsumoto, Y., Mizokami, Y., Ashida, K., & Sugano, K. (2018). Vonoprazan prevents low-dose aspirin-associated ulcer recurrence: Randomised phase 3 study. *Gut*, 67(6), 1033–1041. <https://doi.org/10.1136/gutjnl-2017-314852>
- Kawai, T., Suzuki, C., Honda, Y., & Fernandez, J. L. (2023). Long-term safety and effectiveness of vonoprazan for prevention of gastric and duodenal ulcer recurrence in patients on nonsteroidal anti-inflammatory drugs in Japan: A 12-month post-marketing surveillance study. *Expert Opinion on Drug Safety*, 22(5), 425–431. <https://doi.org/10.1080/14740338.2023.2136163>
- Kinoshita, Y., Sakurai, Y., Takabayashi, N., Kudou, K., Araki, T., Miyagi, T., Iwakiri, K., & Ashida, K. (2019). Efficacy and safety of vonoprazan in patients with nonerosive gastroesophageal reflux disease: A randomized, Placebo-Controlled, Phase 3 study. *Clinical and Translational Gastroenterology*, 10(11), Article e00101. <https://doi.org/10.14309/ctg.0000000000000101>
- Kusunoki, M., Yuki, M., Ishitobi, H., Kobayashi, Y., Nagaoka, M., Takahashi, Y., Fukuba, N., Komazawa, Y., Shizuku, T., & Kinoshita, Y. (2019). Effect of Age on Effectiveness of Vonoprazan in Triple Therapy for *Helicobacter pylori* Eradication. *Internal Medicine (Tokyo, Japan)*, 58(11), 1549–1555. <https://doi.org/10.2169/internalmedicine.2233-18>
- Laine, L., Spechler, S., Yadlapati, R., Schnoll-Sussman, F., Smith, N., Leifke, E., Harris, T., Hunt, B., Fass, R., & Katz, P. (2024). Vonoprazan is efficacious for treatment of heartburn in non-erosive reflux disease: A randomized trial. *Clinical Gastroenterology and Hepatology*, 22(11), 2211–2220.e10. <https://doi.org/10.1016/j.cgh.2024.05.004>
- Maradey-Romero, C., & Fass, R. (2014). New and future drug development for gastroesophageal reflux disease. *Journal of Neurogastroenterology and Motility*, 20(1), 6–16. <https://doi.org/10.5056/jnm.2014.20.1.6>
- Martinucci, I., Blandizzi, C., Bodini, G., Marabotto, E., Savarino, V., Marchi, S., De Bortoli, N., & Savarino, E. (2017). Vonoprazan fumarate for the management of acid-related diseases. *Expert Opinion on Pharmacotherapy*, 18(11), 1145–1152. <https://doi.org/10.1080/14656566.2017.1346087>
- Maruyama, M., Tanaka, N., Kubota, D., Miyajima, M., Kimura, T., Tokutake, K., Imai, R., Fujisawa, T., Mori, H., Matsuda, Y., Wada, S., Horiuchi, A., & Kiyosawa, K. (2017). Vonoprazan-based regimen is more useful than PPI-based one as a first-line *Helicobacter pylori* eradication: A randomized controlled trial. *Canadian Journal of Gastroenterology and Hepatology*, 2017, Article 4385161. <https://doi.org/10.1155/2017/4385161>
- Miwa, H., Uedo, N., Watari, J., Mori, Y., Sakurai, Y., Takanami, Y., Nishimura, A., Tatsumi, T., & Sakaki, N. (2017). Randomised clinical trial: Efficacy and safety of vonoprazan vs. lansoprazole in patients with gastric or duodenal ulcers – Results from two phase 3, non-inferiority randomised controlled trials. *Alimentary Pharmacology and Therapeutics*, 45(2), 240–252. <https://doi.org/10.1111/apt.13876>
- Mizokami, Y., Oda, K., Funao, N., Nishimura, A., Soen, S., Kawai, T., Ashida, K., & Sugano, K. (2018). Vonoprazan prevents ulcer recurrence during long-term NSAID therapy: Randomised, lansoprazole-controlled non-inferiority and single-blind extension study. *Gut*, 67(6), 1042–1051. <https://doi.org/10.1136/gutjnl-2017-314010>
- Mulford, D. J., Leifke, E., Hibberd, M., & Howden, C. W. (2022). The effect of food on the pharmacokinetics of the Potassium-Competitive acid blocker vonoprazan. *Clinical Pharmacology in Drug Development*, 11(2), 278–284. <https://doi.org/10.1002/cpdd.1009>
- Murakami, K., Sakurai, Y., Shiino, M., Funao, N., Nishimura, A., & Asaka, M. (2016). Vonoprazan, a novel potassium-competitive acid blocker, as a component of first-line and second-line triple therapy for *Helicobacter pylori* eradication: A phase III, randomised, double-blind study. *Gut*, 65(9), 1439–1446. <https://doi.org/10.1136/gutjnl-2015-311304>
- Oshima, T., & Miwa, H. (2018). Potent potassium-competitive acid blockers: A new era for the treatment of acid-related diseases. *Journal of Neurogastroenterology and Motility*, 24(3), 334–344. <https://doi.org/10.5056/jnm18029>
- Otake, K., Sakurai, Y., Nishida, H., Fukui, H., Tagawa, Y., Yamasaki, H., Karashima, M., Otsuka, K., & Inatomi, N. (2016). Characteristics of the novel Potassium-Competitive Acid Blocker Vonoprazan fumarate (TAK-438). *Advances in Therapy*, 33(7), 1140–1157. <https://doi.org/10.1007/s12325-016-0345-2>
- PubChem. (n.d.). Vonoprazan. PubChem. <https://pubchem.ncbi.nlm.nih.gov/compound/Vonoprazan>
- Shirley, M. (2024). Vonoprazan: A review in *Helicobacter pylori* infection. *Drugs*, 84(3), 319–327. <https://doi.org/10.1007/s40265-023-01991-5>
- St Onge, E., & Phillips, B. (2023). Vonoprazan: A new Potassium-Competitive acid blocker. *The Journal of Pharmacy Technology*, 39(3), 139–146. <https://doi.org/10.1177/87551225231166531>
- Sugano, K. (2018). Vonoprazan fumarate, a novel potassium-competitive acid blocker, in the management of gastroesophageal reflux disease: Safety and clinical evidence to date. *Therapeutic Advances in Gastroenterology*, 11, Article 1756283X17745776. <https://doi.org/10.1177/1756283X17745776>
- UpToDate. (n.d.). UpToDate. <https://www.uptodate.com/contents/vonoprazan-drug-information>
- Yang, M., Ren, C., & Yang, Z. (2023). Vonoprazan may induce *Clostridium difficile* infection and nephrotoxicity. *Gastroenterology*, 164(4), 699. <https://doi.org/10.1053/j.gastro.2022.10.004>
- Zhou, Y., Boudreau, D. M., & Freedman, A. N. (2014). Trends in the use of aspirin and nonsteroidal anti-inflammatory drugs in the general U.S. population. *Pharmacoepidemiology and Drug Safety*, 23(1), 43–50. <https://doi.org/10.1002/pds.3463>

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