

Drug Class Update: Antacids for *Helicobacter pylori*

Date of Review: October 2024

Date of Last Review: October 2020

Dates of Literature Search: 08/01/2020 - 05/01/2024

Current Status of PDL Class:

See **Appendix 1**.

Generic Name: vonoprazan

Brand Name: Voquezna® (Phathom)

Purpose for Class Update: The purpose of this update is to review new evidence related to benefits and harms of antacids used for the treatment of *Helicobacter pylori* (*H. pylori*) infections. The evidence for efficacy and safety of vonoprazan (VOQUEZNA) in the treatment of *H. pylori* will be presented and evaluated.

Plain Language Summary:

- Antacid medicines are used to treat many stomach conditions, including those caused by a germ called *Helicobacter pylori*, or *H. pylori*. Antacids are used with antibiotics to treat *H. pylori* infections.
- The Canadian Agency for Drugs and Technology in Health identified evidence that medicines for *H. pylori* are most beneficial when taken for 10 to 14 days.
- The Food and Drug Administration recently approved a new antacid medicine for the treatment of *H. pylori*. This medicine is called vonoprazan. Vonoprazan was found to be similar to other medicines used to treat *H. pylori* for curing the infection.
- Based on this information, we do not recommend any changes to the antacids for *H. pylori* preferred drug list for the Oregon Health Plan fee-for-service program.

Research Questions:

1. What is the comparative effectiveness of antacids (e.g., eradication rates) used for the treatment of *H. pylori*?
2. What is the comparative safety of *H. pylori* treatments?
3. What is the evidence for the safety and efficacy of vonoprazan when used as part of a regimen to treat *H. pylori*?
4. Are there subpopulations in which treatment for *H. pylori* may be more effective or cause more harm?

Conclusions:

- New evidence in this review came from one systematic review, 5 Food and Drug Administration (FDA) Safety alerts and one new drug evaluation.

- A publication by the Canadian Agency for Drugs and Technology in Health (CADTH) reviewed evidence for different durations of therapy used to treat *H. pylori*. Higher eradication rates were demonstrated in those treated for 10-14 days compared to 7 days. Current guidelines recommend 14 days of therapy for *H. pylori* treatment.¹
- In May of 2022 vonoprazan was approved as part of dual (vonoprazan/amoxicillin) and triple therapy (vonoprazan/amoxicillin/clarithromycin) for the treatment of *H. pylori* in adults. There is low quality of evidence based on one non-inferiority study demonstrating that eradication rates after 14 days of therapy for vonoprazan dual therapy (open-label) and vonoprazan triple therapy (double-blind) were non-inferior to the combination of lansoprazole/amoxicillin/clarithromycin.² Adverse reactions associated with vonoprazan dual and triple therapy were diarrhea, dysgeusia, vulvovaginal candidiasis and abdominal pain.

Recommendations:

- No changes to the preferred drug (PDL) list are recommended.
- Maintain vonoprazan dual and triple therapy combinations as nonpreferred on the PDL for the treatment of *H. pylori*. Vonoprazan monotherapy requires a prior authorization (PA) as outlined in the PPI PA.
- After review of costs in executive session, TALICIA was made preferred.

Summary of Prior Reviews and Current Policy

- In October of 2020 the antacids for *H. pylori* were reviewed and no changes were made to the PDL.
- There is a prior authorization (PA) Criteria in place for *H. pylori* that allows for 2 weeks of treatment.
- Preferred *H. pylori* treatments are: bismuth/metronidazole/clarithromycin capsules (generic and brand) and lansoprazole/amoxicillin/clarithromycin combination pack.
- Non-preferred products are subject to the general non-preferred products PA criteria.

Background:

Antacids are a common component of *H. pylori* treatment. *H. pylori* is associated with peptic ulcer disease (PUD), gastric adenocarcinoma, and gastric mucosa-associated lymphoid tissue (MALT) lymphoma.^{3,4} The incidence of *H. pylori* is lower in the United States (U.S.) compared to Central and South America and Asia.³ Patients at highest risk of infection should be tested for *H. pylori* and include individuals with the following conditions: active PUD, known history of PUD (unless documented cure), post-gastric cancer removal, dyspepsia requiring endoscopy, gastric MALT lymphoma, gastrointestinal reflux disease (GERD) requiring long-term proton pump inhibitor (PPI) therapy, and unexplained iron-deficiency anemia or idiopathic thrombocytopenic purpura.^{3,4} Symptoms of *H. pylori* are nonspecific and can present as gastritis and nausea.³

Diagnostic tests for *H. pylori* include invasive (endoscopic) and noninvasive (nonendoscopic) assessments.⁴ Urease tests (e.g., urea breath tests [UBTs]) are commonly used and are accurate to approximately 95% sensitivity.⁴ Patients that test positive for *H. pylori* should be treated with an approved regimen. *H. pylori* serology testing is not recommended as it does not test for active infection.³

The treatment of *H. pylori* usually includes treatment with a PPI or bismuth and 2 antibiotics (**Table 1**).³ First-line treatment regimens often include clarithromycin, amoxicillin (or metronidazole) and a PPI.³ Resistance has caused eradication rates to drop to less than 80%, primarily thought to be due to clarithromycin, metronidazole and levofloxacin resistance.² The US has a 4-16% resistance rate to clarithromycin when used for primary treatment.⁴ This is in

contrast to areas of high resistance, like Western Pacific Regions with 30-38% clarithromycin resistance when used for primary therapy.⁴ In areas with less than 15% clarithromycin resistance, clarithromycin triple therapy (e.g., PPI, clarithromycin 500 mg and amoxicillin 1 gm) is recommended by the American College of Gastroenterology Clinical Guideline.³ Bismuth quadruple therapy is also recommended first-line and is the preferred option in areas with high levels of clarithromycin resistance.⁵ Bismuth quadruple therapy (e.g., PPI, bismuth 300 mg, metronidazole 250 mg or 500 mg and tetracycline 500 mg) requires taking components of the treatment regimen four times daily which can be burdensome to patients. Treatment durations are commonly 14 days, due to clarithromycin resistance, with 10-day regimens also available.⁴ Increasing the treatment duration to 14 days has been associated with a 10% increase in eradication rates.⁴ Any previous antibiotic exposure, allergies, pregnancy status (e.g., tetracycline is contraindicated), and potential drug interactions should be considered when selecting treatment regimens.

Table 1. Medications for *H. pylori* Treatment

FDA Approved Combination Products	Brand Name	Dose	FDA Approved Duration
Bismuth 140mg/metronidazole 125 mg tetracycline 125 mg ^{6*}	PYLERA	3 capsules 4 times a day	10 days
Lansoprazole 30 mg/amoxicillin 1 g/ clarithromycin 500 mg ⁷	Not applicable	Lansoprazole capsule, 2 amoxicillin capsules and 1 clarithromycin tablet twice daily	10-14 days
Omeprazole 10 mg/amoxicillin 250 mg/rifabutin 12.5 mg ⁸	TALICIA	4 capsules three times daily	14 days
Vonoprazan 20 mg/amoxicillin 500 mg ⁹	VOQUEZNA DUAL PAK	Vonoprazan capsules twice daily and 2 amoxicillin capsules three times daily	14 days
Vonoprazan 20 mg/amoxicillin 500 mg/clarithromycin 500mg ⁹	VOQUEZNA TRIPLE PAK	Vonoprazan capsules twice daily and 2 amoxicillin capsules twice daily and clarithromycin tablet twice daily	14 days
Key: * Give with omeprazole 20 mg twice daily			

Eradication rates are the standard outcome assessment for determining efficacy of *H. pylori* treatment. Re-testing to determine eradication of *H. pylori* should be done at least 1 month after finishing treatment and is recommended to verify successful eradication.⁴ To ensure accurate testing (e.g., false negative results) no antibiotics or bismuth medications should be given within the last one month and no PPIs should be used within the last 1-2 weeks.⁴

In first quarter of 2024 there was no utilization for *H. pylori* antacid combination products.

Methods:

A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 3**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs), the Scottish Intercollegiate Guidelines Network (SIGN), and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for

quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews:

CADTH – Duration of Therapy for *Helicobacter pylori* Infection

A 2023 CADTH review evaluated patients with *H. pylori* infection to compare eradication rates of treatments used for different durations.¹ Regimens lasting 7 days were compared to 8-14 days of treatment. Antibiotics included in the review were: amoxicillin, clarithromycin, levofloxacin, moxifloxacin, and tetracycline. A systematic review and 8 guidelines were identified for inclusion.¹ Most of the included studies were treatments with PPI triple therapy lasting 7 days compared to the same therapies given for 14 days. The 14-day regimens were associated with higher eradication rates compared to 7 days of treatment. The evidence was considered low quality.¹ Eradication rates were found to be higher for those patients treated with 10 day regimens compared to 7 day regimens in 2 randomized controlled trials. Guidelines published from 2020-2023 recommend 14 days of therapy.¹ European guidelines strongly recommend triple therapy first-line based on moderate quality of evidence. The Italian Society of Gastroenterology and Italian Society of Digestive Endoscopy recommend bismuth-based quadruple therapy (concomitant or sequential) or standard triple-therapy in areas with proven low levels of clarithromycin resistance (moderate quality evidence; strong recommendation). Guidelines for treating those residing in Korea, strongly recommend triple-therapy (standard dose PPI, amoxicillin 1 g, and clarithromycin 500 mg, all given twice daily) first-line based on moderate quality evidence.¹ Limitations to these recommendations are that they are based on resistance patterns in specific geographical areas (e.g., Europe and Korea), which limits applicability to the US.; however, clarithromycin and metronidazole resistance rates are similar between Europe and the US.⁴

After review, 12 systematic reviews were excluded due to poor quality (e.g., indirect network-meta analyses or failure to meet AMSTAR criteria), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), outcome studied (e.g., non-clinical), or low external validity.¹⁰⁻²¹

New Guidelines:

None identified.

After review, 1 guideline was excluded due to poor external validity.²²

New Formulations or Indications:

None identified.

New FDA Safety Alerts:

Table 2. Description of new FDA Safety Alerts

Generic Name	Brand Name	Month / Year of Change	Location of Change (Boxed Warning, Warnings, CI)	Addition or Change and Mitigation Principles (if applicable)
bismuth/metronidazole/tetracycline ⁶	PYLERA	December 2021	Contraindication	Contraindicated in patients with Cockayne syndrome. Severe irreversible hepatotoxicity/acute liver failure with fatal outcomes have been reported after initiation of metronidazole in patients with Cockayne syndrome.
bismuth/metronidazole/tetracycline ⁶	PYLERA	March 2021	Warnings and Precautions	QT prolongation has been reported with metronidazole, more commonly when administered with drugs with the potential for prolonging the QT interval.
omeprazole/amoxicillin/rifabutin ⁸	TALICIA	October 2021	Warnings and Precautions	Risk of Severe Cutaneous Adverse Reactions (SCARs) such as drug reaction with eosinophilia and systemic symptoms (DRESS) have been associated with all the components included in TALICIA.
omeprazole/amoxicillin/rifabutin ⁸	TALICIA	March 2022	Warnings and Precautions	Severe cutaneous adverse reactions (SCAR), such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been associated with all the components included in TALICIA.
omeprazole/amoxicillin/rifabutin ⁸	TALICIA	July 2023	Adverse Reactions	Risk of erectile dysfunction reported in postmarketing experience.

NEW DRUG EVALUATION:

Clinical Efficacy:

Vonoprazan is a potassium-competitive acid blocker (PCAB) that is used in combination with amoxicillin or clarithromycin for the treatment of *H. pylori* infection in adult patients.⁹ Vonoprazan increases gastric pH allowing for maximal effect of antibiotics. The mechanism by which this is accomplished by vonoprazan is by enhancing the replication of *H. pylori* and increasing the stability and effectiveness of antimicrobials.⁹ Vonoprazan is available in a Dual Pak as which contains vonoprazan 20 mg, to be taken twice daily, and amoxicillin 500 mg, dosed as 2 capsules three times a day for 14 days.⁹ A Triple Pak is also available that contains vonoprazan 20 mg, amoxicillin 1,000 mg and clarithromycin 500 mg all to be taken twice a day for 14 days.⁹ Vonoprazan was approved in several countries before seeking approval in the U.S. Vonoprazan is also approved for the treatment of erosive esophagitis, for which the evidence is presented and analyzed in a separate review.

Initial clinical studies of vonoprazan for the treatment of *H. pylori* were primarily conducted in Japan and China. Studies found vonoprazan regimens to be noninferior to lansoprazole containing therapies.^{23,24} One open-label trial found vonoprazan dual therapy to be noninferior to rabeprazole dual therapy and a second trial demonstrated that vonoprazan dual therapy was inferior to bismuth quadruple therapy.^{13,25} Antibiotic resistance patterns are vary amongst different geographic regions and differences in Asian and Western populations may influence efficacy of *H. pylori* treatments. Therefore, only published evidence including US populations will be included (**Table 5**).

One study was used for FDA approval of vonoprazan for treatment of *H. pylori* (**Table 5**).² Eligible adult patients were treatment naïve and had a positive *H. pylori* infection as determined by a 13C urea breath test (¹³C-UBT) and biopsy as well as at least one clinical condition (e.g., dyspepsia, recent/new diagnosis of nonbleeding peptic ulcer, history of peptic ulcer not previously treated for *H. pylori* infection or requirement for long-term NSAID treatment at a stable dose). Biopsies taken during screening were cultured and tested for antimicrobial susceptibility. Patients (n=1046) were randomized to open-label dual therapy with vonoprazan and amoxicillin or double-blind triple therapy with vonoprazan/amoxicillin/clarithromycin versus lansoprazole/amoxicillin/clarithromycin for a total of 14 days. PPI and antibiotic use were not permitted in the 2 weeks before the study or 30 days after the last dose. Patients were a mean age of 51 years old with dyspepsia (98%) being the most common clinical condition.²

The primary outcome was noninferiority in eradication rates of *H. pylori* in patients without clarithromycin- and amoxicillin-resistant strains determined by a ¹³C-UBT at week 6 (2 weeks of treatment and 4 weeks after finishing treatment regimen). Patients who remained *H. pylori* positive had a repeat endoscopy with repeat antimicrobial susceptibility testing for clarithromycin, metronidazole, and amoxicillin. Eradication of clarithromycin-resistant *H. pylori* infections was an important secondary outcome. The primary and secondary outcomes were analyzed in the full analysis set and repeated on the per protocol population.

Patients included in the full analysis set were tested at 4 weeks after treatment for presence of *H. pylori*. Eradication rates for vonoprazan dual and triple therapy were noninferior to lansoprazole triple therapy for nonresistant strains, difference of 5.9% and -0.3%, respectively (**Table 5**).² Dual and triple therapy with vonoprazan were superior to lansoprazole triple therapy for the eradication of *H. pylori* in patients with clarithromycin resistant infections, difference of 33.9% and 37.7%, respectively (**Table 5**).²

Limitations to the evidence include a small percentage of patients with comorbid PUD, which is a common risk factor for *H. pylori*, probably due to the exclusion of evidence of bleeding which is often associated with PUD . The comparison for vonoprazan dual therapy was open label, leading to a high risk of performance bias. It is recommended that the per protocol population is used preferentially for non-inferiority studies to more accurately detect treatment differences. The study of vonoprazan relied on the full analysis set for the primary endpoint.

Clinical Safety:

Common adverse events occurring in 2% or more of patients prescribed vonoprazan dual or triple packs were diarrhea, dysgeusia, vulvovaginal candidiasis and abdominal pain (**Table 3**).⁹ Severe adverse reactions were rare in all treatment groups.² Severe cutaneous reactions, *Clostridioides difficile*-associated diarrhea, QT prolongation and hepatotoxicity are potential risks of therapy.⁹ Contraindications to treatment are known hypersensitivity to any of the components and use in patients with renal or hepatic impairment. Vonoprazan should not be used in pregnant women or in patients with myasthenia gravis.

Table 3. Adverse Reactions with Vonoprazan Dual and Triple Pack Occurring in 2% or more of Patients⁹

Adverse Reactions	Vonoprazan Dual Pak (n=348)	Vonoprazan Triple Pak (n=346)	Lansoprazole Triple Pak (n=345)
Diarrhea	18 (5.2%)	14 (4%)	33 (9.6%)
Dysgeusia	2 (0.6%)	16 (4.6%)	21 (6.1%)
Vulvovaginal candidiasis (men and women combined)	7 (2.0%)	11 (3.2%)	5 (1.4%)
Abdominal pain	9 (2.6%)	8 (2.3%)	10 (2.9%)
Headache	5 (1.4%)	9 (2.6%)	5 (1.4%)
Hypertension	4 (1.1%)	7 (2.0%)	3 (0.9%)
Nasopharyngitis	7 (2.0%)	1 (0.3%)	3 (0.9%)

Vonoprazan is a CYP3A4 and CYP2C19 inhibitor and use with drugs primarily metabolized by these enzymes may cause clinically significant drug interactions.⁹ Vonoprazan labeling should be consulted before concomitant use with other drugs that are strong to moderate inducers or substrates of CYP3A4 or CYP2C19. Additionally, drugs that require gastric pH for absorption may have safety and/or effectiveness altered if given with vonoprazan.⁹ Due to the clarithromycin component in the Triple Pak, vonoprazan Triple Pak should not be used with pimozide, lomitapide, lovastatin, simvastatin, ergot alkaloids, colchicine in renal or hepatic impairment, or in patients with a history of jaundice/hepatic dysfunction.⁹ The use of vonoprazan Dual or Triple packs are contraindicated in those taking rilpivirine-containing products.

Comparative Endpoints:

Clinically Meaningful Endpoints:

- 1) Eradication of *H. pylori*
- 2) Serious adverse events
- 3) Study withdrawal due to an adverse event

Primary Study Endpoint:

- 1) Eradication of *H. pylori*

Table 4. Pharmacology and Pharmacokinetic Properties.⁹

Parameter	
Mechanism of Action	Inhibits the hydrogen-potassium-ATPase enzyme system in gastric parietal cells which blocks the final step of acid production
Oral Bioavailability	Time to peak absorption: 1 to 3 hours
Distribution and Protein Binding	Volume of distribution: 782 to 1,270 L (dose dependent: 20 mg twice daily vs. 10 mg once daily) Protein binding ranges from 85 to 88%
Elimination	67% of dose recovered in urine and 31% of dose recovered in feces (as unchanged drug)
Half-Life	6.8 to 7.9 hours depending on daily dose (20 mg twice daily vs. 20 mg once a day)
Metabolism	Metabolized to inactive metabolites via multiple pathways including CYP3A4/5, CYP2B6, CYP2C9, CYP2C19, and CYP2D6

Abbreviations: ATP = adenosine triphosphate mg = milligram; L = Liter

Table 5. Comparative Evidence Table.

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/ NNT	Safety Outcomes	ARR/ NNH	Risk of Bias/ Applicability
1. Chey, et al ² DB/OL, MC, NI, phase 3 RCT	1. Vonoprazan 20 mg orally 2 times a day/ 1 g amoxicillin 3 times a day* 2. Vonoprazan 20 mg orally 2 times a day/ amoxicillin 1 g/ clarithromycin 500 mg twice a day† Vs. 3. Lansoprazole 30 mg/ 1 g amoxicillin/ clarithromycin 500 mg twice a day Duration of therapy: 14 days	Demographics: -Mean age: 51 y -Male Gender: 26.1% -Hispanic: 26% -Race White: 90% Black: 7% -Dyspepsia: 98% -PPI use: 11% -Clarithromycin resistant: 22% -Amoxicillin resistant: 1.2% -Metronidazole resistant: 69% -PUD: 2.1% Key Inclusion Criteria: -Adults 18 y and older -Treatment-naïve - <i>H. pylori</i> infection confirmed with a positive ¹³ C-urea breath test (UBT) -At least one of the following: ▪ Dyspepsia ▪ A recent/new diagnosis of nonbleeding peptic ulcer ▪ History of peptic ulcer not previously treated for <i>H. pylori</i> infection ▪ Requirement for long-term NSAIDs at a stable dose Key Exclusion Criteria: -Previously treated with regimen to eradicate <i>H. pylori</i> -Adults with active gastric or duodenal ulcer with evidence of current or recent bleeding -Gastric cancer -Colchicine use -Zollinger-Ellison syndrome -Systemic lupus erythematosus -Allergy to PPIs, clarithromycin and/or amoxicillin.	FAS: 1. 324 2. 338 3. 330 PP: 1. 265 2. 280 3. 277 Attrition: 1. 59 (18%) 2. 58 (21%) 3. 53 (19%)	Primary Endpoint: Non-inferiority in eradication rates in patients without clarithromycin- and amoxicillin-resistant strains 1. 208 (78.5%) 2. 222 (84.7%) 3. 201 (78.8%) 1 vs. 3: Difference -0.3% 95% CI -0.74 to 6.8 P<0.007 for NI (NI margin = 10%) 2 vs. 3: Difference 5.9% 95% CI -0.8 to 12.6 P<0.001 for NI (NI margin = 10%) Secondary Endpoints: Superiority in eradication rates in patients without clarithromycin-resistant infection and in all patients (FAS): 1. 39 (69.6%) 2. 48 (65.8%) 3. 23 (31.9%) 1 vs. 3: Difference 37.7% (95% CI 20.5 to 52.6) P<0.001 2 vs. 3: Difference 33.9% (95% CI 17.7 to 48.1) P<0.001	NA NA NA	SAE: 1. 5 (1.4%) 2. 6 (1.7%) 3. 3 (0.9%) AEs leading to treatment discontinuation: 1. 3 (0.9%) 2. 8 (2.3%) 3. 4 (1.2%) 95% CI and p-values NR	NA for all	Risk of Bias (low/high/unclear): Selection Bias: Low. Randomization 1:1:1 via a central, password-protected, web-based randomization system. Baseline characteristics were similar between groups. Performance Bias: High. Dual therapy was open label. No details beyond having a double-blind design for the triple therapy comparisons were provided. Detection Bias: Low. All <i>H. pylori</i> tests were objectively assessed by ¹³ C-UBT analysis and verified by breath test and biopsy to determine eradication. Attrition Bias: High. Attrition rates were above 10% in all groups. Analysis of the ITT population was used for the primary endpoint. Handling of missing data was not described. Reporting Bias: Low. Study was conducted as described in the methods. All prespecified endpoints were reported as planned. Other Bias: High. The study was funded by the manufacturer. Data was analyzed by statisticians employed by sponsor. Interpretation of data was also done by sponsor. Applicability: Patients: The results are most applicable to patients who are treatment naïve, middle-aged white females, which is minimally representative of overall Medicaid enrollees. Intervention: Vonoprazan doses determined by prior approval in other countries. Comparator: Lansoprazole 30 mg triple therapy is an appropriate comparator as it is commonly used for the treatment of <i>H. pylori</i> . Outcomes: Eradication rates is an appropriate outcome for the treatment of <i>H. pylori</i> . Setting: 107 sites in the United States and 43 sites in Europe (Poland, Czech Republic, Hungary, Bulgaria, and United Kingdom). Forty-one percent of patients in each treatment group were from the US.

Abbreviations: AC = active comparator; AEs = adverse events; ALT = alanine aminotransferase; ARR = absolute risk reduction; AST = aspartate aminotransferase; CI = confidence interval; DB = double blind; EE = erosive esophagitis; FAS = full analysis set; IRT = interactive response technology; ITT = intention to treat; LA = Los Angeles; MC = multi-center; N = number of subjects; NA = not applicable; NI = non-inferiority; NNH = number needed to harm; NNT = number needed to treat; NR = not reported; OL = open-label; PP = per protocol; PPI = proton pump inhibitor; PUD = peptic ulcer disease; RCT = randomized controlled trial; SAEs = serious adverse events; TEAE = treatment emergent adverse events; ULN = upper limit of normal; y = years

Key: * Open-label comparison, † double-blind comparison

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Appendix 1: Current Preferred Drug List

Generic	Brand	Form	PDL
bismuth/metronid/tetracycline	BISMUTH-METRONIDAZOLE-TETRACYC	CAPSULE	Y
bismuth/metronid/tetracycline	PYLERA	CAPSULE	Y
lansoprazole/amoxicillin/clarith	LANSOPRAZOL-AMOXICIL-CLARITHRO	COMBO. PKG	Y
omeprazole/amoxicillin/rifabutin	TALICIA	CAP IR DR	N
vonoprazan/amoxicillin	VOQUEZNA DUAL PAK	COMBO. PKG	N
vonoprazan/amoxicillin/clarith	VOQUEZNA TRIPLE PAK	COMBO. PKG	N

Appendix 2: Medline Search StrategyDatabase(s): **Ovid MEDLINE(R) ALL** 1946 to May 06, 2024

Search Strategy:

#	Searches	Results
1	omeprazole.mp. or Omeprazole/	12401
2	Amoxicillin/ or amoxicillin.mp.	25084
3	rifabutin.mp. or Rifabutin/	2802
4	bismuth.mp.	16196
5	metronidazole.mp.	22880
6	Tetracycline/ or tetracycline.mp.	50313
7	lansoprazole.mp.	3245
8	clarithromycin.mp.	12538
9	vonoprazan.mp.	564
10	Helicobacter pylori.mp.	51260
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	168374
12	limit 11 to (english language and humans and yr="2020 -Current")	11601
13	limit 12 to (clinical trial, phase iii or guideline or meta analysis or practice guideline or "systematic review")	685
14	(1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9) and 10	8829
15	limit 14 to (english language and humans and yr="2020 -Current")	822
16	limit 15 to (clinical trial, phase iii or guideline or meta analysis or practice guideline or "systematic review")	92

Appendix 3: Key Inclusion Criteria

Population	Patients with <i>H. pylori</i> infection
Intervention	Antacid containing regimens with antibiotics
Comparator	Placebo or other antacid containing regimens
Outcomes	Eradication rates
Setting	Outpatient