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Pharmacovigilance of Vonoprazan: A Review of Safety and Adverse Event Profiles

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ABSTRACT

Vonoprazan is a novel potassium-competitive acid blocker (P-CAB) used to treat acid-related disorders, including gastroesophageal reflux disease (GERD) and Helicobacter pylori eradication therapy. Compared to traditional proton pump inhibitors (PPIs), vonoprazan exhibits a faster onset of action and sustained acid suppression. This pharmacovigilance review evaluates its safety profile based on post-marketing surveillance and clinical studies.

Data from the Japanese Adverse Drug Event Report (JADER) database and systematic reviews indicate that vonoprazan has a generally comparable safety profile to PPIs. Common adverse events include diarrhea, liver function abnormalities, and rash. However, vonoprazan has been associated with an increased risk of hemorrhagic enterocolitis, necessitating further investigation. Unlike PPIs, it does not show a significant correlation with interstitial lung disease. Meta-analyses suggest no significant increase in overall adverse events compared to PPIs, with some studies reporting fewer gastrointestinal side effects. Despite its favorable tolerability, long-term safety data remain limited. Continuous pharmacovigilance efforts and real-world studies are crucial to identifying rare but serious adverse effects. Future research should focus on elucidating the mechanisms underlying vonoprazan-associated risks and optimizing its safe clinical use.

Keywords: Vonoprazan, Pharmacovigilance, Adverse Drug Reactions, Potassium-Competitive Acid Blocker, Proton Pump Inhibitors, Gastroesophagel Reflux Disease

1. INTRODUCTION:

Vonoprazan is a potassium-competitive acid blocker which, unlike conventional PPIs, reversibly inhibits the enzyme H+/K+ ATPase independently of acid pH[1,2]. In Japan, vonoprazan was marketed in 2015 for the treatment of erosive oesophagitis, treatment of gastric and duodenal ulcers, eradication of Helicobacter pylori, and prevention of the recurrence of low-dose aspirin or nonsteroidal anti-inflammatory drug-related gastric and duodenal ulcer[3]. To efficacy and safety of vonoprazan have been demonstrated in patients with erosive oesophagitis[4], and also when administered as maintenance treatment in patients with healed

erosive oesophagitis refractory to conventional PPIs[5]. Furthermore, vonoprazan has demonstrated non-inferiority to the conventional PPI lansoprazole in patients with erosive oesophagitis[6]. Since long-term maintenance treatment is recommended for patients with erosive oesophagitis[7], it is imperative to establish the long-term safety of the therapeutic agent. As vonoprazan has been shown to have a more potent acid inhibitory effect than conventional PPIs both in vivo and in vitro[8], greater concern has been raised about side effects than with conventional PPIs[9]. A number of side effects have been reported with strong inhibitors of gastric acid secretion, including PPIs, but the most problematic is their potential association with

neoplastic lesions such as gastric cancer and gastric neuroendocrine tumours (NET). [9]the strong inhibition of gastric acid secretion causes hypergastrinemia, and gastrin is known to have a proliferative effect on the mucosa of the digestive tract [10], including the gastric mucosa[11]. Findings from several observational studies suggest that long-term use of PPIs is associated with an increased risk of developing gastric cancer[12]; therefore, additional well-designed prospective studies are warranted to confirm the potential role of PPIs in gastric cancer development according to gastric histology at baseline[13]. Vonoprazan is a potent inhibitor of gastric acid secretion, resulting in increased gastrin levels compared with conventional PPIs. Hypergastrinemia is thought to be one of the pathogenic causes of hyperplastic polyps[14], but there have been no prospective studies of vonoprazan-induced hypergastrinemia. In addition, endoscopic findings show that long-term treatment with PPIs is associated with a high incidence of lesions such as fundic gland polyps[15], hyperplastic polyps[16], cobblestone mucosa[17], multiple white fat elevated lesions[18], and black spots[19].Although the safety and efficacy of vonoprazan as maintenance therapy have been previously reported in a 52-week study[8], studies that examine the longer-term safety of vonoprazan maintenance treatment are needed. the objective of the Vonoprazan study In patients with erosive oesophagitis to evaluate long-term safety (VISION) is to evaluate the long-term safety and efficacy of vonoprazan 10 mg or 20 mg in patients receiving maintenance treatment for recurrent/reactivated erosive oesophagitis, compared with lansoprazole. Patients in the ongoing VISION trial will receive treatment for up to 5 years, but as vonoprazan is being used more frequently in clinical practice, we are reporting the results of the prespecified 3-year interim analysis to provide information on the long-term safety of vonoprazan that may be of reassurance to practitioners. the objective of the Vonoprazan study In patients with erosive oesophagitis to evaluate long-term safety (VISION) is to evaluate the long-term safety and efcacy of vonoprazan 10 mg or 20 mg in patients receiving maintenance treatment for recurrent/reactivated erosive oesophagitis, compared with lansoprazole. Patients in the ongoing VISION trial will receive treatment for up to 5 years, but as vonoprazan is being used more frequently in clinical practice, we are reporting the results of the prespecifed 3-year interim analysis to provide information on the long-term safety of vonoprazan that may be of reassurance to practitioners.

Proton pump inhibitors (PPIs) have often been used for acid related diseases including gastroesophageal reflux disease (GERD), gastric and duodenal ulcers, non-steroidal anti-inflammatory drug (NSAID)-associated ulcers, and Helicobacter pylori eradication therapy. Conventional PPIs with a benzimidazole structure irreversibly inhibit hydrogen potassium (H+, K+)-ATPases, which produce acid in gastric parietal cells and more strongly block acid secretion compared to histamine H2 receptor antagonists.[20]Although PPIs have been used for more than a quarter-century as a first-line treatment for these diseases, it has become clear that there are some issues in need of improvement (Table 1).[21] First, it takes several days to show maximal effect.[22]Reflux symptoms of GERD are not sufficiently relieved after the first dose of PPIs in two-thirds of patients because of its slow onset of the action,[23] and one-half of

patients still have symptoms even after 3 days of treatment.[23] Second, the effects of PPIs are influenced by cytochrome P450 (CYP) 2C19 polymorphism.[24] Third, its effects at night are not satisfactory.[25]Finally, although it requires an acidic environment for activation, PPIs are unstable in acidic conditions,[26] so enteric coating is needed

To overcome the aforementioned unmet needs, alternative formulations of conventional PPIs and new H+, K+-ATPase inhibitors have been established. With these efforts, vonoprazan (TAK-438), a potassium-competitive acid blocker (P-CAB), was developed. It was found to have satisfactory effects and a good safety profile in clinical studies of gastric and duodenal ulcers, reflux esophagitis, NSAID-associated ulcers, and H. pylori eradication. Vonoprazan (Takecab) was released to the market in Japan in February 2015. In this review, we summarize the effects of P-CABs, mainly using vonoprazan data. Alternative Formulation of Conventional Proton Pump Inhibitors Immediate-release omeprazole and dexlansoprazole modified release (MR), which improve nocturnal acid breakthrough (NAB), have been introduced as alternative formulations of PPIs in some countries.[27]Dexlansoprazole MR is the R-enantiomer of lanso prazole and is a PPI with dual delayed-release formulation.18 The dual release system in the duodenum and small intestine achieved 2 peak concentrations within 2 hours and 5 hours after administration.[29] Percentage time 24-hour intragastric pH above 4 of dexlansoprazole MR 60 mg and lansoprazole 30 mg once daily for 5 days administration was 71% and 60%, respectively ($P < 0.01$).20 However, these drugs only have small advantages for the control of acid secretion compared to conventional PPIs.[28]

1.2 WHY IS PHARMACOVIGILANCE IMPORTANT?

Pharmacovigilance is critically important, especially when evaluating drugs like Vonoprazan, a relatively new potassium-competitive acid blocker (P-CAB), because it ensures the ongoing monitoring of drug safety after it has been approved for use.

1. Ensures Patient Safety
2. Detects Rare and Delayed Adverse Events
3. Monitors Drug Interactions and Off-label Use
4. Improves Clinical Guidelines
5. Supports Regulatory Actions

1.3 BRIEF OVERVIEW OF ADVERSE EVENTS

AEs were reported in 89.6% of patients in the vonoprazan group and 95.5% of patients in the lansoprazole group (Table 1). AEs were mostly mild or moderate in severity, and the majority of AEs were not considered to be related to the vonoprazan or lansoprazole. During the maintenance phase up to week 156, 10 patients (7.4%) in the vonoprazan group and none in the lansoprazole group discontinued treatment because of an AE. No deaths were reported. The most commonly reported AEs, occurring in>5% of the study population, were in the system organ classes ‘gastrointestinal disorders’ and ‘infections and infestation[30]

Table 1: Overview of TEAEs in the Maintenance Phase up to Week 156

TEAEs	VPZ (N = 135)	LPZ (N = 67)
Overview of TEAEs, n (%)		
All TEAEs	121 (89.6%)	64 (95.5%)
Related to study drug	54 (40.0%)	31 (46.3%)
Serious TEAEs	39 (28.9%)	18 (26.9%)
- Related to study drug	3 (2.2%)	0 (0.0%)

TEAEs leading to death	0 (0.0%)	0 (0.0%)
TEAEs occurring in >5% of patients in any group, n (%)		
Gastrointestinal disorders	84 (62.2%)	54 (80.6%)
- Gastric polyps	48 (35.6%)	27 (40.3%)
- Gastric mucosal lesion	21 (15.6%)	11 (16.4%)
- Gastritis erosive	11 (8.1%)	8 (11.9%)
- Large intestine polyp	13 (9.6%)	9 (13.4%)
- Diarrhoea	9 (6.7%)	4 (6.0%)
- Gastrointestinal mucosal disorder	6 (4.4%)	6 (9.0%)
- Constipation	7 (5.2%)	2 (3.0%)
- Dyspepsia	2 (1.5%)	4 (6.0%)
Infections and infestations	80 (59.3%)	38 (56.7%)
- Nasopharyngitis	44 (32.6%)	26 (38.8%)
- Bronchitis	11 (8.1%)	7 (10.4%)
- Influenza	12 (8.9%)	1 (1.5%)
- Cystitis	8 (5.9%)	2 (3.0%)
- Gastroenteritis	7 (5.2%)	3 (4.5%)
- Pharyngitis	4 (3.0%)	5 (7.5%)
- Herpes zoster	2 (1.5%)	5 (7.5%)
- Tonsillitis	1 (0.7%)	4 (6.0%)
Musculoskeletal and connective tissue disorders	33 (24.4%)	16 (23.9%)
- Back pain	7 (5.2%)	3 (4.5%)
Skin and subcutaneous tissue disorders	14 (10.4%)	14 (20.9%)
- Eczema	7 (5.2%)	6 (9.0%)
Eye disorders	8 (5.9%)	6 (9.0%)
- Cataract	2 (1.5%)	5 (7.5%)
Vascular and nervous system disorders		
- Hypertension	12 (8.9%)	3 (4.5%)
- Dizziness	1 (0.7%)	4 (6.0%)

TEAE = treatment-emergent adverse event; LPZ = lansoprazole; VPZ = vonoprazan.

Among AEs with incidences of <5%, one case of gastric cancer, i.e., foveolar-type adenoma, was reported. Out of the 10 patients who discontinued due to an AE, the most common AEs were in the system organ classes gastrointestinal disorders', 'neoplasms benign, malignant and unspecifed (including cysts and polyps)' and 'infections and infestations.' The study drug was withdrawn in two patients because of treatment-related AEs. One patient experienced a mild treatment-related AE (gastric mucosal lesion) and a moderate serious AE (SAE) (acute cholangitis). After the SAE, the study drug was withdrawn in view of future interruptions in the study procedures. A second patient experienced two treatment-related SAEs

of mild intensity: abnormal hepatic function and leukopenia, and two mild SAEs not related to the treatment: tinnitus and loss of consciousness. Te
study drug was withdrawn due to the treatment-related SAEs and patient's anxiety regarding these SAEs. In the remaining eight patients, the study drug was withdrawn due to non-treatment related AEs. Te study drug was discontinued in four patients experiencing SAEs: suspected cancer of the tail of the pancreas in frst patient, duodenal obstruction because of uncinate pancreas cancer in the second patient, right lung cancer in the third patient, and myelodysplastic syndrome in the fourth patient. Study drug was also discontinued in two patients experiencing mild AEs: abnormal hepatic function in one and generalised pain in the second patient, and one
patient experiencing moderate AE of early colon cancer. In one patient the drug was withdrawn because of an SAE a malignant tumour – presumed to have existed before study participation (Table:2) and therefore this patient was removed from the group of patients discontinuing study
due to AEs.[30]

Table 2: Patient Disposition

Table representation of patient disposition from study on Vonoprazan vs Lansoprazole:

Phase	Vonoprazan	Lansoprazole
Signed informed consent	n = 302	
Excluded	n = 94 (Did not meet eligibility = 86, Voluntary withdrawal = 6, Other = 2)	
Entered healing phase	n = 139	n = 69
Discontinued during healing phase	n = 2 (Major protocol deviation = 1, Lost to follow-up = 1)	n = 1 (Major protocol deviation = 1)
Completed healing phase	n = 137	n = 68
Not eligible for maintenance phase	n = 2	n = 1
Entered 260-week maintenance phase	n = 135	n = 67
Discontinued during maintenance phase	n = 26 (Voluntary withdrawal = 13, Adverse event = 9, Other = 4)	n = 9 (Voluntary withdrawal = 6, Lost to follow-up = 1, Other = 2)
Received drug for >1008 days (included in 3-year interim analysis)	n = 109	n = 58

2. METHODOLOGY

VISION is a 5-year, randomized, open-label, parallel-group, multicenter, phase 4 study conducted across 33 specialized medical institutions (university hospitals, general hospitals, and clinics; Additional in Japan that are experienced in conducting clinical trials in gastroesophageal reflux disease or reflux esophagitis. The study design comprises a 4 to 8-week healing phase followed by a 260-week maintenance phase [40].Patients with endoscopically confirmed erosive esophagitis (LA Classification Grades A–D) at the

start of treatment (week 0) were randomized in a 2:1 ratio to receive either vonoprazan 20 mg or lansoprazole 30 mg once daily for a healing phase of either 4 weeks (for patients with confirmed endoscopic healing of erosive esophagitis at week 4) or 8 weeks (for patients with no confirmed endoscopic healing of erosive esophagitis at week 4). Patients with endoscopically confirmed healed erosive esophagitis at week 4 or 8 of the healing phase then entered a 260-week maintenance phase. Healed erosive esophagitis was defined as the absence of an endoscopic mucosal break (Grade 0 according to severity classification of erosive esophagitis). During the maintenance phase, patients in the vonoprazan group were administered a starting dose of vonoprazan 10 mg once daily, and patients in the lansoprazole group were administered a starting dose of lansoprazole 15 mg once daily, for up to 260 weeks (thus a total of up to 268 weeks of treatment). Vonoprazan and lansoprazole doses were increased to 20 mg and 30 mg, respectively, if initial doses were insufficient for maintenance treatment of erosive esophagitis. Patients were randomized and allocated to treatment via a web registration system and were administered the study drugs by the principal investigator or investigator. During the healing phase, visits were planned at weeks 0 and 4, and also at week 8 for patients with no endoscopic healing of erosive esophagitis at week 4. the maintenance phase, an initial visit took place on initiation of maintenance treatment followed by visits every 12 weeks up to week 108 and visits every 24 weeks up to week 228, with a final visit at week 260.For a uniform evaluation process of endoscopic images, a standard operating procedure for the evaluation was established. A start-up meeting at each site and two seminars for all investigators were held to thoroughly inform the standard operating procedures. the delegated investigator at each study site conducted and evaluated the endoscopy. Throughout the study period, the same investigator was preferred to conduct and evaluate the endoscopy as far as possible for each patient. Is study is being and has been conducted in accordance with the Declaration of Helsinki Ethical Guidelines for Clinical Research, Clinical Trials Act (since 1 April 2018), and all applicable laws and regulations, including, without limitation, data privacy laws and conflict of interest guidelines. Before the enactment of the Clinical Trials Act, this study was conducted in accordance with the Ethical Guidelines on Biomedical Research Involving Human Subjects (the Ministry of Education, Culture, Sports, Science and Technology [MEXT] and the Minis-try of Health, Labour and Welfare [MHLW], 22 December 2014; this guideline has since been renamed the Ethical Guidelines for Life Science and Medical Research
Involving Human Subjects). Owing to the enforcement of the Clinical Trials Act in Japan on 1 April 2018, VISION was classified as a ‘Specified Clinical Trial’ on 21 November 2018. the transformation review was conducted at ‘Certified Review Board of National Center for Global Health and Medicine’ (CRB3180021) certified by MHLW, and after that the study was approved and registered under the trial ID jRCTs031180040. Prior to this classification, the study was reviewed by the Ethical Review
Boards of each study site, and informed written consent was obtained from all study participants. All authors have checked the study data and reviewed and approved the final manuscript. the study has been registered with ClinicalTrials.gov (NCT02679508, registration date 10/02/2016), JapicCTI-163153, and the Japan Registry of
Clinical Trials (jRCTs031180040)

2.1 Data Selection

A literature search was performed via PubMed from January 2010 to December 2022 using the search terms vonoprazan, Voquezna, TAK-438, potassium-competitive acid blocker, H pylori, and gastrointestinal. All relevant English-language studies assessing the pharmacokinetics, pharmacology, efficacy, safety, or tolerability of vonoprazan were evaluated. Information was also obtained from the

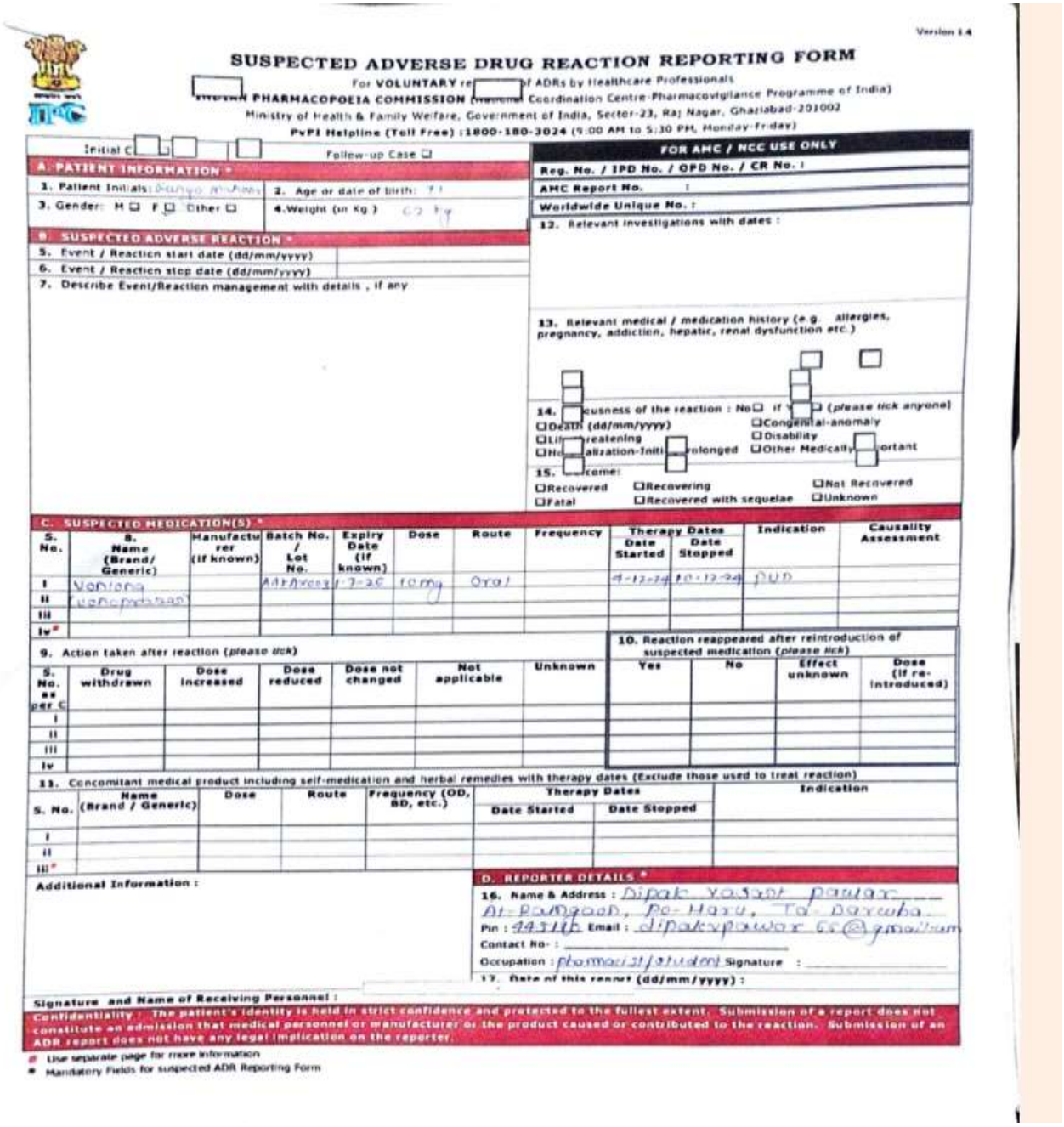
FDA-approved package insert. References from previously published manuscripts were also examined to identify additional source Pharmacology Following food consumption, parietal cell receptors actively transport hydrogen ions across the canalicular membrane which are exchanged for luminal potassium ions. Hydrogen potassium adenosine triphosphatase (HK-ATPase) transfers equal amounts of hydrogen and potassium along with passive movement of chloride ions to promote an acidic gastric environment as well as maintain electrochemical neutrality across the membrane. The final step in gastric acid production is through the HK-ATPase, which is commonly referred to as a proton pump.5Both vonoprazan and PPIs block this final step in acid production. However, PPIs work through irreversible covalent binding to the alpha subunit of HK-ATPase whereas vonoprazan selectively and reversibly competes with luminal potassium ions required for hydrogen exchange.[31]The positively charged side chain enables strong hydrogen bonding and charge interaction with the potassium-binding site. Vonoprazan competes with potassium's binding site to prevent potassium from binding and thereby inhibiting gastric acid secretion.[32]Hepatotoxicity, a problem with other P-CABs which are no longer available, is less of a concern with vonoprazan due to the absence of an imidazopyridine ring in its
chemical structure.8 Furthermore, due to the relatively high pKa value of vonoprazan (9.06), it does not require an acidic environment to bind to the enzyme and accumulates in gastric parietal cells to achieve longer-lasting gastric acid suppression. Unlike the PPIs, vonoprazan is acid stable and
does not require an acidic environment for activation nor does it require enteric coating to protect from gastric degradation.[33]Pharmacokinetics Vonoprazan is rapidly absorbed with peak plasma concentration (Cmax) of 37.8 ng/mL being reached after 2 hours with a single dose and an average of 3 hours after reaching steady state with repeated dosing (tmax). The area under the curve (AUC) from administration to the end of the 12-hour dosing interval is 273 ng*hr/mL.4 Both AUC and Cmax increase dose proportionally with drug accumulation complete by the third day of treatment and little to no accumulation in plasma after repeated doses.[34]Meals high in fat have
been shown to increase Cmax by 5%, AUC by 15%, and tmax to 5 hours; however, these differences are not considered clinically significant. Thus, vonoprazan can be administered regardless of food intake. The half-life (t1/2) is 7 to 9 hours regardless of a meal.Vonoprazan displays time-independent pharmacokinetics with steady state being reached by day 3 or 4.8 The volume of distribution (Vd) is 782.7 L with plasma protein binding of 85% to 88% and unlikely to be saturated even at drug concentrations above therapeutic range.[35] As previously stated, it has a relatively high pKa (9.06) resulting in near instant protonation and accumulation in gastric parietal cells within an acidic environment providing an explanation for its rapid onset, long-lasting duration of action (24 hours following a single dose and with repeated steady-state dosing), and elevated intragastric
pH following drug discontinuation (~24 to 48 hours after the last dose).[36] When compared to the acid-reducing capabilities of a PPI, one study comparing vonoprazan to lansoprazole showed that the proportion of a 24-hour period with intragastric pH > 4 was 3-fold higher in the vonopra-
zan group after a single dose and 2-fold higher after 1 week.13Vonoprazan is metabolized via cytochrome P450 (CYP) through CYP3A4/5, CYP2B6, CYP2C19, CYP2C9, and CYP2D6 with none of its metabolites being pharmacologically active. It has also been shown to inhibit p-glycoprotein
(p-gp); however, unlikely to have any clinically significant impact on p-gp inhibition.[35]In regards to CYP2C19 polymorphisms, there have been no confirmed differences in the pharmacokinetics of vonoprazan based on metabolizer status.[34]Vonoprazan is predominantly excreted via the urinary tract (67%), whereas, 31% is excreted in feces. Both routes have a minimal amount of unchanged drug at

approximately 8% and 1.4%, respectively

2.2 PHARMACOVIGILANCE ASSESSMENT OF VONOPRAZAN THROUGH SUSPECTED ADR REPORTING AND PRESCRIPTION AUDITS

This study aims to evaluate the safety and rational use of vonoprazan, a potassium-competitive acid blocker, by analyzing data collected through suspected adverse drug reaction (ADR) reporting forms and prescription audits. The objective is to identify potential adverse effects, assess prescription trends, and promote the safe and effective use of vonoprazan in clinical practice. This pharmacovigilance approach supports early detection of drug-related problems and enhances patient safety

In support of this pharmacovigilance assessment, the Suspected Adverse Drug Reaction (ADR) Reporting Form and the Prescription Audit Template will be attached below. Additionally, relevant literature and reference documents in PDF format will be provided to ensure a comprehensive understanding of the methodology and background information related to vonoprazan safety evaluation.



Version 1.4

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of ADRs by Healthcare Professionals

PHARMACOPOEIA COMMISSION (National Coordination Centre-Pharmacovigilance Programme of India)

Ministry of Health & Family Welfare, Government of India, Sector-23, Raj Nagar, Ghaziabad-201002

PvPI Helpline (Toll Free) :1800-180-3024 (9:00 AM to 5:30 PM, Monday-Friday)

Initial C ☐ Follow-up Case ☐

FOR AMC / NCC USE ONLY

Reg. No. / IPD No. / OFD No. / CR No. :

AMC Report No. :

Worldwide Unique No. :

A. PATIENT INFORMATION *

1. Patient Initials: Dhanya Krishna 2. Age or date of birth: 21

3. Gender: M ☐ F ☐ Other ☐ 4.Weight (in Kg) 62 kg

B. SUSPECTED ADVERSE REACTION *

5. Event / Reaction start date (dd/mm/yyyy)

6. Event / Reaction stop date (dd/mm/yyyy)

7. Describe Event/Reaction management with details , if any

12. Relevant investigations with dates :

13. Relevant medical / medication history (e.g. allergies, pregnancy, addiction, hepatic, renal dysfunction etc.)

14. Seriousness of the reaction : No ☐ If Yes ☐ (please tick anyone)
☐Death (dd/mm/yyyy) ☐Congenital-anomaly
☐Life-threatening ☐Disability
☐Hospitalization-Initial or prolonged ☐Other Medically Important

15. Outcome:
☐Recovered ☐Recovering ☐Not Recovered
☐Fatal ☐Recovered with sequelae ☐Unknown

C. SUSPECTED MEDICATION(S) *

S. No.	B. Name (Brand/ Generic)	Manufacturer (if known)	Batch No. / Lot No.	Expiry Date (if known)	Dose	Route	Frequency	Therapy Dates Date Started	Therapy Dates Date Stopped	Indication	Causality Assessment
I	Voniora		AAPA0031	7-26	10mg	Oral		9-12-24	10-12-24	PUD	
II	Pantoprazole										
III											
Iv*											

9. Action taken after reaction (please tick)

S. No. as per C	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown
I						
II						
III						
Iv						

10. Reaction reappeared after reintroduction of suspected medication (please tick)

Yes	No	Effect unknown	Dose (if re-introduced)

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S. No.	Name (Brand / Generic)	Dose	Route	Frequency (OD, BD, etc.)	Therapy Dates Date Started	Therapy Dates Date Stopped	Indication
I							
II							
III*							

Additional Information :

D. REPORTER DETAILS *

16. Name & Address : Dipak Vasant Pawar
At-Pimpach, Po-Hasu, Ta-Darwha
Pin : 443116 Email : dipakvpawar66@gmail.com
Contact No- :
Occupation : pharmacist/student Signature :

17. Date of this report (dd/mm/yyyy) :

Signature and Name of Receiving Personnel :

Confidentiality : The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

Use separate page for more information

* Mandatory Fields for suspected ADR Reporting Form

Prescription Audit for Vonoprazan

1. **Prescription Detail**
   - Patient Name ..Ganga Mahanor.....
   - Prescriber Name..Dr. Pankaj.....
   - Date of Prescription....4-12-24.....
   - Diagnosis/Indication ☒ Yes ☐ No
2. **Drug & Dosage Appropriateness**
   - Indication Appropriate (GERD,PUD, H.pylori,etc): ☒ Yes ☐ No
   - Dose & Strength (10 mg / 20 mg) Appropriate: ☒ Yes ☐ No
   - Duration Specified & Appropriate: ☒ Yes ☐ No

2.1. **H. pylori Eradication Regimen (if applicable):**
   - Vonoprazan + Amoxicillin + Clarithromycin/Metronidazole Correctly Prescribed: ☐ Yes ☐ No
   - Duration of 7-14 Days Mentioned: ☒ Yes ☐ No
3. **Safety & Drug Interactions**
   - Any Contraindications Checked (e.g., Liver Disease, Pregnancy)? ☒ Yes ☐ No
   - Drug Interactions Considered (e.g., CYP3A4 Drugs, Anticoagulants)? ☒ Yes ☐ No
   - Renal/Liver Function Checked (if necessary)? ☒ Yes ☐ No
   - Risk of Long-term Use (Osteoporosis, Hypomagnesemia) Considered? ☒ Yes ☐ No
4. **Patient Instructions & Adherence**
   - Clear Instructions on Timing with Meals: ☒ Yes ☐ No
   - Patient Advised on Possible Side Effects: ☒ Yes ☐ No
   - Advised to Complete Full Course (If for H. pylori)? ☒ Yes ☐ No
5. **Cost & Accessibility Considerations:**
   - Generic or Cost-effective Brand Considered: ☒ Yes ☐ No
   - Availability Confirmed: ☒ Yes ☐ No

Total "Yes" Responses: 14./15

Auditor Name & Date: Dipak Nanaji Pawar (11-3-25)

Version 1.4

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY re[illegible] of ADRs by Healthcare Professionals

[illegible] PHARMACOPOEIA COMMISSION [illegible] Coordination Centre-Pharmacovigilance Programme of India)

Ministry of Health & Family Welfare, Government of India, Sector-23, Raj Nagar, Ghaziabad-201002

PvPI Helpline (Toll Free) :1800-180-3024 (9:00 AM to 5:30 PM, Monday-Friday)

Initial C[illegible] Follow-up Case ☐

A. PATIENT INFORMATION *

1. Patient Initials: [illegible] 2. Age or date of birth: 60

3. Gender: M ☒ F ☐ Other ☐ 4.Weight (in Kg.) 60

B. SUSPECTED ADVERSE REACTION *

5. Event / Reaction start date (dd/mm/yyyy)

6. Event / Reaction stop date (dd/mm/yyyy)

7. Describe Event/Reaction management with details , if any

FOR AMC / NCC USE ONLY

Reg. No. / IPD No. / OPD No. / CR No. :

AMC Report No. :

Worldwide Unique No. :

12. Relevant investigations with dates :

13. Relevant medical / medication history (e.g. allergies, pregnancy, addiction, hepatic, renal dysfunction etc.)

14. [illegible]ousness of the reaction : No☐ If Y[illegible]☐ (please tick anyone)

☐Death (dd/mm/yyyy) ☐Congenital-anomaly

☐Life-threatening ☐Disability

☐Hospitalization-Initial or prolonged ☐Other Medically Important

15. Outcome:

☐Recovered ☐Recovering ☐Not Recovered

☐Fatal ☐Recovered with sequelae ☐Unknown

C. SUSPECTED MEDICATION(S) *

S. No.	8. Name (Brand/ Generic)	Manufacturer (if known)	Batch No. / Lot No.	Expiry Date (if known)	Dose	Route	Frequency	Therapy Dates: Date Started	Therapy Dates: Date Stopped	Indication	Causality Assessment
I	Vonoprazan [illegible]		MKAX003	01/07/26	long	oral		22/11/24	26/11/24	PUD	
II	[illegible]										
III											
Iv #											

9. Action taken after reaction (please tick)

S. No. as per C	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown
I						
II						
III						
Iv						

10. Reaction reappeared after reintroduction of suspected medication (please tick)

Yes	No	Effect unknown	Dose (If re-introduced)

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S. No.	Name (Brand / Generic)	Dose	Route	Frequency (OD, BD, etc.)	Therapy Dates: Date Started	Therapy Dates: Date Stopped	Indication
I							
II							
III #							

Additional Information :

D. REPORTER DETAILS *

16. Name & Address : Tejas Pendse

[illegible] Cuttaeshwar chowk)

Pin : 445202 Email : tejaspendse@gmail.com

Contact No. : —

Occupation : Pharmacist/student Signature : Pendse

17. Date of this report (dd/mm/yyyy) :

Signature and Name of Receiving Personnel :

Confidentiality : The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

Use separate page for more information

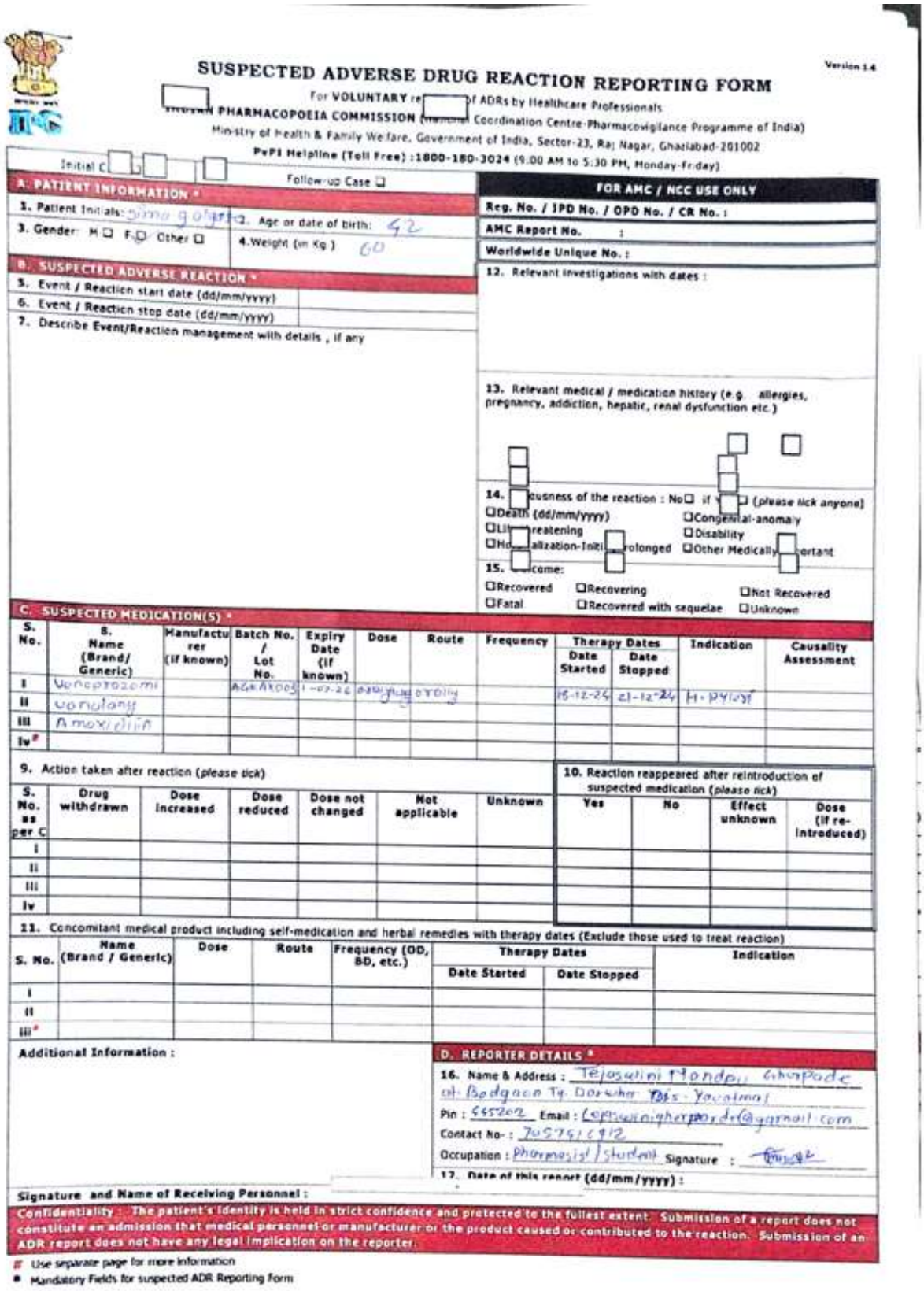
Prescription Audit for Vonoprazan

1. **Prescription Detail**
   - Patient Name ..Kaveeka...Parmar
   - Prescriber Name..Dr...Syed..Akbar...Ahemad
   - Date of Prescription..27.01.24.....
   - Diagnosis/Indication ☑ Yes ☐ No
2. **Drug & Dosage Appropriateness**
   - Indication Appropriate (GERD,PUD, H.pylori,etc): ☑ Yes ☐ No
   - Dose & Strength (10 mg / 20 mg) Appropriate: ☑ Yes ☐ No
   - Duration Specified & Appropriate: ☑ Yes ☐ No

2.1. **H. pylori Eradication Regimen (if applicable):**
   - Vonoprazan + Amoxicillin + Clarithromycin/Metronidazole Correctly Prescribed: ☐ Yes ☐ No
   - Duration of 7-14 Days Mentioned: ☐ Yes ☐ No
3. **Safety & Drug Interactions**
   - Any Contraindications Checked (e.g., Liver Disease, Pregnancy)? ☑ Yes ☐ No
   - Drug Interactions Considered (e.g., CYP3A4 Drugs, Anticoagulants)? ☑ Yes ☐ No
   - Renal/Liver Function Checked (if necessary)? ☑ Yes ☐ No
   - Risk of Long-term Use (Osteoporosis, Hypomagnesemia) Considered? ☑ Yes ☐ No
4. **Patient Instructions & Adherence**
   - Clear Instructions on Timing with Meals: ☑ Yes ☐ No
   - Patient Advised on Possible Side Effects: ☑ Yes ☐ No
   - Advised to Complete Full Course (If for H. pylori)? ☐ Yes ☐ No
5. **Cost & Accessibility Considerations:**
   - Generic or Cost-effective Brand Considered: ☑ Yes ☐ No
   - Availability Confirmed: ☑ Yes ☐ No

Total "Yes" Responses: 12.../15

Auditor Name & Date:..Tejas...V..Fendar [28-01-2025



SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

Version 1.4

For VOLUNTARY reporting of ADRs by Healthcare Professionals

PHARMACOPOEIA COMMISSION (National Coordination Centre-Pharmacovigilance Programme of India)

Ministry of Health & Family Welfare, Government of India, Sector-23, Raj Nagar, Ghaziabad-201002

PvPI Helpline (Toll Free) :1800-180-3024 (9.00 AM to 5:30 PM, Monday-Friday)

Initial C ☐ ☐ ☐ Follow-up Case ☐

A. PATIENT INFORMATION *

1. Patient Initials: [illegible] 2. Age or date of birth: 42

3. Gender: M ☐ F ☐ Other ☐ 4. Weight (in Kg) 60

B. SUSPECTED ADVERSE REACTION *

5. Event / Reaction start date (dd/mm/yyyy)

6. Event / Reaction stop date (dd/mm/yyyy)

7. Describe Event/Reaction management with details , if any

FOR AMC / NCC USE ONLY

Reg. No. / IPD No. / OPD No. / CR No. :

AMC Report No. :

Worldwide Unique No. :

12. Relevant investigations with dates :

13. Relevant medical / medication history (e.g. allergies, pregnancy, addiction, hepatic, renal dysfunction etc.)

14. [illegible]usness of the reaction : No ☐ if Y[illegible] ☐ (please tick anyone)
☐ Death (dd/mm/yyyy) ☐ Congenital anomaly
☐ Li[illegible]reatening ☐ Disability
☐ Ho[illegible]alization-Initi[illegible]rolonged ☐ Other Medically [illegible]ortant

15. [illegible]come:
☐ Recovered ☐ Recovering ☐ Not Recovered
☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S) *

S. No.	8. Name (Brand/ Generic)	Manufacturer (If known)	Batch No. / Lot No.	Expiry Date (If known)	Dose	Route	Frequency	Therapy Dates: Date Started	Therapy Dates: Date Stopped	Indication	Causality Assessment
I	Pantoprazole		AGAX005	1-07-26	40mg	PO	OD/1d	15-12-24	21-12-24	H. pylori	
II	Ondansetron										
III	Amoxicillin										
Iv*											

9. Action taken after reaction (please tick)

S. No. as per C	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown
I						
II						
III						
Iv						

10. Reaction reappeared after reintroduction of suspected medication (please tick)

Yes	No	Effect unknown	Dose (If re-introduced)

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S. No.	Name (Brand / Generic)	Dose	Route	Frequency (OD, BD, etc.)	Therapy Dates: Date Started	Therapy Dates: Date Stopped	Indication
I							
II							
III*							

Additional Information :

D. REPORTER DETAILS *

16. Name & Address : Tejaswini Mandar Ghorpade
at Badgaon Ta. Darwha Dis. Yavatmal
Pin : 445202 Email : tejaswinighorpade@gmail.com
Contact No- : 7057516912
Occupation : Pharmacist / student Signature :

17. Date of this report (dd/mm/yyyy) :

Signature and Name of Receiving Personnel :

Confidentiality : The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

Use separate page for more information

* Mandatory Fields for suspected ADR Reporting Form

Prescription Audit for Vonoprazan

1. **Prescription Detail**
   - Patient Name Sima Gaidare
   - Prescriber Name....Sunil Mandan
   - Date of Prescription....15.12.25
   - Diagnosis/Indication ☐ Yes ☐ No
2. **Drug & Dosage Appropriateness**
   - Indication Appropriate (GERD,PUD, H.pylori,etc): ☐ Yes ☐ No
   - Dose & Strength (10 mg / 20 mg) Appropriate: ☐ Yes ☐ No
   - Duration Specified & Appropriate: ☐ Yes ☐ No

2.1. **H. pylori Eradication Regimen (if applicable):**
   - Vonoprazan + Amoxicillin + Clarithromycin/Metronidazole Correctly Prescribed: ☐ Yes ☐ No
   - Duration of 7-14 Days Mentioned: ☐ Yes ☐ No
3. **Safety & Drug Interactions**
   - Any Contraindications Checked (e.g., Liver Disease, Pregnancy)? ☐ Yes ☐ No
   - Drug Interactions Considered (e.g., CYP3A4 Drugs, Anticoagulants)? ☐ Yes ☐ No
   - Renal/Liver Function Checked (if necessary)? ☐ Yes ☐ No
   - Risk of Long-term Use (Osteoporosis, Hypomagnesemia) Considered? ☐ Yes ☐ No
4. **Patient Instructions & Adherence**
   - Clear Instructions on Timing with Meals: ☐ Yes ☐ No
   - Patient Advised on Possible Side Effects: ☐ Yes ☐ No
   - Advised to Complete Full Course (If for H. pylori)? ☐ Yes ☐ No
5. **Cost & Accessibility Considerations:**
   - Generic or Cost-effective Brand Considered: ☐ Yes ☐ No
   - Availability Confirmed: ☐ Yes ☐ No

Total "Yes" Responses: 15/15

Auditor Name & Date: Tejaswini M. Ghorpade [15/12/25]

Version 1.4

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of ADRs by Healthcare Professionals

INDIAN PHARMACOPOEIA COMMISSION (National Coordination Centre-Pharmacovigilance Programme of India)

Ministry of Health & Family Welfare, Government of India, Sector-23, Raj Nagar, Ghaziabad-201002

PvPI Helpline (Toll Free) :1800-180-3024 (9:00 AM to 5:30 PM, Monday-Friday)

Initial Case ☐ Follow-up Case ☐

A. PATIENT INFORMATION *

1. Patient Initials: Nitu Shaikh
2. Age or date of birth: 21
3. Gender: M ☐ F ☐ Other ☐
4. Weight (in Kg.) 38 kg

FOR AMC / NCC USE ONLY

Reg. No. / IPD No. / OPD No. / CR No. :

AMC Report No. :

Worldwide Unique No. :

12. Relevant investigations with dates :

13. Relevant medical / medication history (e.g. allergies, pregnancy, addiction, hepatic, renal dysfunction etc.)

14. Seriousness of the reaction : No ☐ if Yes ☐ (please tick anyone)
☐Death (dd/mm/yyyy) ☐Congenital-anomaly
☐Life threatening ☐Disability
☐Hospitalization-Initial/Prolonged ☐Other Medically important

15. Outcome:
☐Recovered ☐Recovering ☐Not Recovered
☐Fatal ☐Recovered with sequelae ☐Unknown

B. SUSPECTED ADVERSE REACTION *

5. Event / Reaction start date (dd/mm/yyyy)
6. Event / Reaction stop date (dd/mm/yyyy)
7. Describe Event/Reaction management with details , if any

C. SUSPECTED MEDICATION(S) *

S. No.	8. Name (Brand/ Generic)	Manufacturer (if known)	Batch No. / Lot No.	Expiry Date (if known)	Dose	Route	Frequency	Therapy Dates: Date Started	Therapy Dates: Date Stopped	Indication	Causality Assessment
I	Vonolong		Adkp[illegible]	1-7-25	10 mg	Oral		5-12-24	12-12-24	H. Pylori	
II	(vonoprazan)										
III	Amoxicillin										
Iv#											

9. Action taken after reaction (please tick)

10. Reaction reappeared after reintroduction of suspected medication (please tick)

S. No. as per C	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	Yes	No	Effect unknown	Dose (if re-introduced)
I										
II										
III										
Iv										

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S. No.	Name (Brand / Generic)	Dose	Route	Frequency (OD, BD, etc.)	Therapy Dates: Date Started	Therapy Dates: Date Stopped	Indication
I							
II							
III#							

Additional Information :

D. REPORTER DETAILS *

16. Name & Address : Prem Dilip Fendar Uttareshwar chowk Parcuha

Pin :445202 Email : premfendar15@gmail.com

Contact No- :

Occupation : pharmacist / student Signature :

17. Date of this report (dd/mm/yyyy) :

Signature and Name of Receiving Personnel :

Confidentiality : The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

Use separate page for more information
* Mandatory Fields for suspected ADR Reporting Form

Prescription Audit for Vonoprazan

1. Prescription Detail
   - Patient Name ....Hina...Shaikh.....
   - Prescriber Name..Dr..Sahish...Jaiswal
   - Date of Prescription.....5.12.24.....
   - Diagnosis/Indication ☐ Yes ☐ No
2. Drug & Dosage Appropriateness
   - Indication Appropriate (GERD,PUD, H.pylori,etc): ☐ Yes ☐ No
   - Dose & Strength (10 mg / 20 mg) Appropriate: ☐ Yes ☐ No
   - Duration Specified & Appropriate: ☐ Yes ☐ No

2.1. H. pylori Eradication Regimen (if applicable):
   - Vonoprazan + Amoxicillin + Clarithromycin/Metronidazole Correctly Prescribed: ☐ Yes ☐ No
   - Duration of 7-14 Days Mentioned: ☐ Yes ☐ No
3. Safety & Drug Interactions
   - Any Contraindications Checked (e.g., Liver Disease, Pregnancy)? ☐ Yes ☐ No
   - Drug Interactions Considered (e.g., CYP3A4 Drugs, Anticoagulants)? ☐ Yes ☐ No
   - Renal/Liver Function Checked (if necessary)? ☐ Yes ☐ No
   - Risk of Long-term Use (Osteoporosis, Hypomagnesemia) Considered? ☐ Yes ☐ No
4. Patient Instructions & Adherence
   - Clear Instructions on Timing with Meals: ☐ Yes ☐ No
   - Patient Advised on Possible Side Effects: ☐ Yes ☐ No
   - Advised to Complete Full Course (If for H. pylori)? ☐ Yes ☐ No
5. Cost & Accessibility Considerations:
   - Generic or Cost-effective Brand Considered: ☐ Yes ☐ No
   - Availability Confirmed: ☐ Yes ☐ No

Total "Yes" Responses: 15.../15

Auditor Name & Date: pharm...Nitin...Pandey (10-3-25)

Version 1.4

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY re... of ADRs by Healthcare Professionals

... PHARMACOPOEIA COMMISSION (... Coordination Centre-Pharmacovigilance Programme of India)

Ministry of Health & Family Welfare, Government of India, Sector-23, Raj Nagar, Ghaziabad-201002

PvPI Helpline (Toll Free) :1800-180-3024 (9:00 AM to 5:30 PM, Monday-Friday)

Initial C... Follow-up Case ☐

A. PATIENT INFORMATION *

1. Patient Initials:
2. Age or date of birth: 20
3. Gender: M ☐ F ☑ Other ☐
4. Weight (in Kg.) 47 kg

B. SUSPECTED ADVERSE REACTION *

5. Event / Reaction start date (dd/mm/yyyy)
6. Event / Reaction stop date (dd/mm/yyyy)
7. Describe Event/Reaction management with details, if any

FOR AMC / NCC USE ONLY

Reg. No. / IPD No. / OPD No. / CR No. :

AMC Report No. :

Worldwide Unique No. :

12. Relevant investigations with dates :

13. Relevant medical / medication history (e.g. allergies, pregnancy, addiction, hepatic, renal dysfunction etc.)

14. ...usness of the reaction : No ☐ if Y... ☐ (please tick anyone)
☐ Death (dd/mm/yyyy) ☐ Congenital-anomaly
☐ Li... hreatening ☐ Disability
☐ Ho... alization-Initi... rolonged ☐ Other Medically ...ortant

15. ...come:
☐ Recovered ☐ Recovering ☐ Not Recovered
☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S) *

S. No.	8. Name (Brand/ Generic)	Manufacturer (if known)	Batch No. / Lot No.	Expiry Date (if known)	Dose	Route	Frequency	Therapy Dates		Indication	Causality Assessment
								Date Started	Date Stopped		
I	vonolong		AAFAXC03	1-7-26	10 mg	Oral		30-11-24	03-12-24	PUD	
II	(vonoprazan)										
III											
IV#											

9. Action taken after reaction (please tick)

S. No. as per C	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown
I						
II						
III						
IV						

10. Reaction reappeared after reintroduction of suspected medication (please tick)

Yes	No	Effect unknown	Dose (if re-introduced)

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S. No.	Name (Brand / Generic)	Dose	Route	Frequency (OD, BD, etc.)	Therapy Dates		Indication
					Date Started	Date Stopped	
I							
II							
III#							

Additional Information :

D. REPORTER DETAILS *

16. Name & Address : Gayatri vilas Jadhav
At - palashi , po lakh (khind) , Ta - Darwha
Pin : 445202 Email : jadhavvilas...@gmail.com
Contact No- : 9405147742
Occupation : pharmacist/student Signature : Jadhav

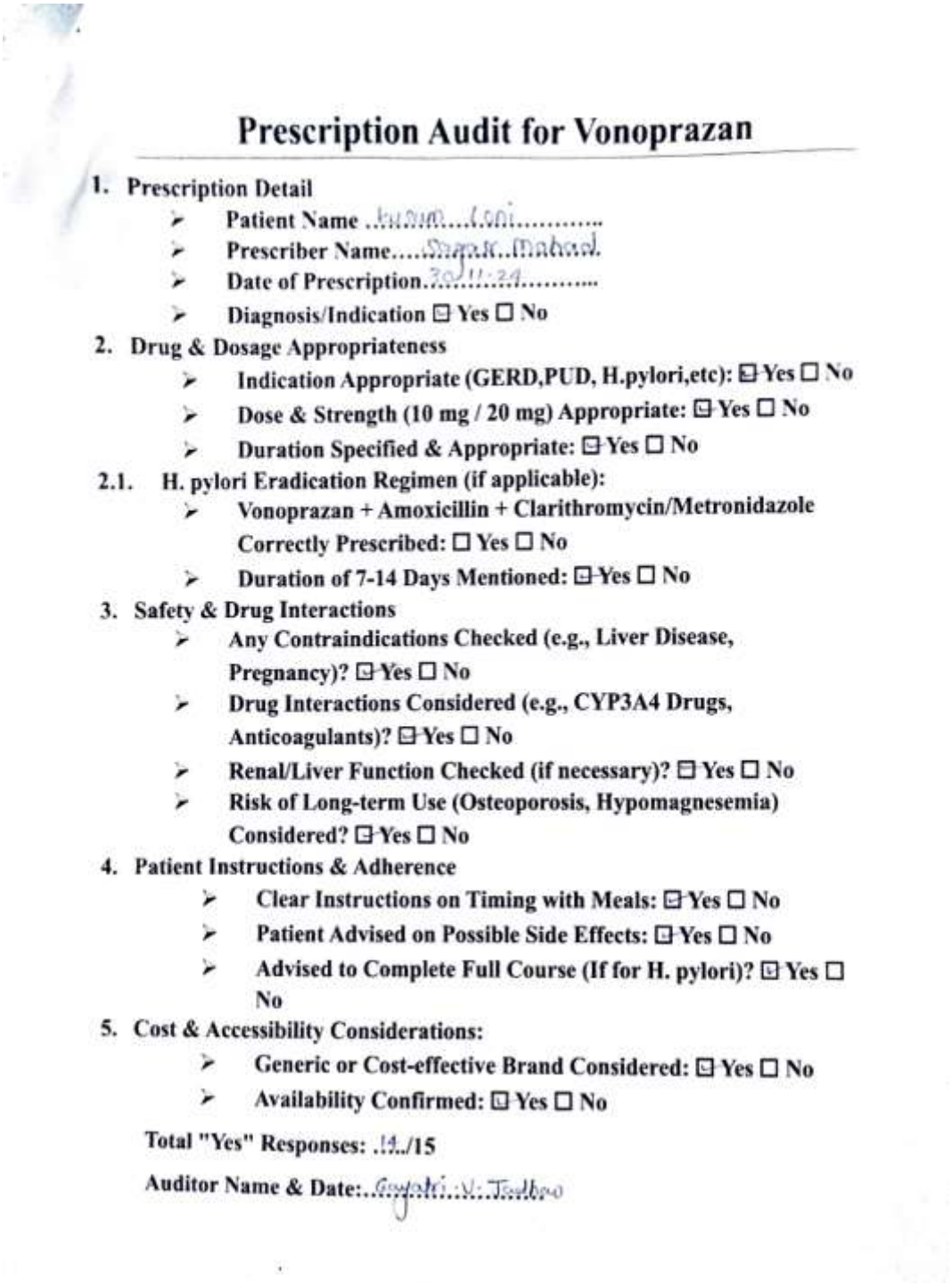
17. Date of this report (dd/mm/yyyy) :

Signature and Name of Receiving Personnel :

Confidentiality : The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

Use separate page for more information

* Mandatory Fields for suspected ADR Reporting Form



Prescription Audit for Vonoprazan

1. Prescription Detail
   - Patient Name .....
   - Prescriber Name.....
   - Date of Prescription.....
   - Diagnosis/Indication ☑ Yes ☐ No
2. Drug & Dosage Appropriateness
   - Indication Appropriate (GERD,PUD, H.pylori,etc): ☑ Yes ☐ No
   - Dose & Strength (10 mg / 20 mg) Appropriate: ☑ Yes ☐ No
   - Duration Specified & Appropriate: ☑ Yes ☐ No

2.1. H. pylori Eradication Regimen (if applicable):
   - Vonoprazan + Amoxicillin + Clarithromycin/Metronidazole Correctly Prescribed: ☐ Yes ☐ No
   - Duration of 7-14 Days Mentioned: ☑ Yes ☐ No

3. Safety & Drug Interactions
   - Any Contraindications Checked (e.g., Liver Disease, Pregnancy)? ☑ Yes ☐ No
   - Drug Interactions Considered (e.g., CYP3A4 Drugs, Anticoagulants)? ☑ Yes ☐ No
   - Renal/Liver Function Checked (if necessary)? ☑ Yes ☐ No
   - Risk of Long-term Use (Osteoporosis, Hypomagnesemia) Considered? ☑ Yes ☐ No
4. Patient Instructions & Adherence
   - Clear Instructions on Timing with Meals: ☑ Yes ☐ No
   - Patient Advised on Possible Side Effects: ☑ Yes ☐ No
   - Advised to Complete Full Course (If for H. pylori)? ☑ Yes ☐ No
5. Cost & Accessibility Considerations:
   - Generic or Cost-effective Brand Considered: ☑ Yes ☐ No
   - Availability Confirmed: ☑ Yes ☐ No

Total "Yes" Responses: 14/15

Auditor Name & Date:.....

For more patient detail here are the link are attached https://drive.google.com/file/d/1gfr5jexsHDuXzEJAJgumizwidZMM1Idj/view

3. Result

3.1 clinical trial

Vonoprazan, a potassium-competitive acid blocker (P-CAB), has been extensively evaluated in Phase I–III clinical trials to assess its safety and efficacy in treating acid-related gastrointestinal conditions. Here's a summary of the pharmacovigilance data from these trials:

Phase III Clinical Trials: Safety Outcomes

1. Erosive Esophagitis (EE):

Study Design: A Phase III, randomized, double-blind, multicentre study compared vonoprazan 20 mg to lansoprazole 30 mg in Asian patients with EE.

Results: At 8 weeks, EE healing rates were 92.4% for vonoprazan and 91.3% for lansoprazole, demonstrating non-inferiority.

Safety: Treatment-emergent adverse events (TEAEs) occurred in 38.1% of vonoprazan-treated patients and 36.6% of those on lansoprazole, indicating similar safety profiles.[37]

2. Gastric and Duodenal Ulcers:

Study Design: Randomized clinical trials assessed vonoprazan 20 mg versus lansoprazole 30 mg for healing gastric (GU) and duodenal ulcers (DU).

Results: Vonoprazan was non-inferior to lansoprazole in GU healing and had similar efficacy in DU healing.

Safety: TEAEs were slightly lower for GU and slightly higher for DU with vonoprazan compared to lansoprazole. One death (subarachnoid hemorrhage) occurred in the vonoprazan group, with the possibility of a relationship to the study drug not ruled out.

Long-Term Safety: VISION Trial

Study Design: The VISION trial is a Phase IV, open-label, multicenter study in Japan, evaluating the long-term safety of vonoprazan as maintenance therapy for healed EE over a 5-year period.

Interim Results (3-Year Analysis):

Histopathology: Gastric mucosal evaluations showed that hyperplasia of parietal, foveolar, and G cells was more common with vonoprazan than with lansoprazole at week 156. However, no neoplastic changes were observed in either group.

regulatory Review and Approval

FDA Review: The U.S. FDA reviewed data from pivotal studies, including Protocol EE-301, which evaluated the efficacy and safety of vonoprazan 20 mg compared to lansoprazole 30 mg for healing EE, and vonoprazan (10 mg and 20 mg) compared to lansoprazole 15 mg for maintenance of healing.[38]

3.2 Post-marketing surveillance

Post-marketing surveillance of vonoprazan, a potassium-competitive acid blocker (P-CAB), has provided valuable insights into its safety profile beyond clinical trials. Real-world data have identified both common and rare adverse events (AEs), contributing to a comprehensive understanding of the drug's risk-benefit balance.

Common Adverse Events

In routine clinical practice, vonoprazan is generally well-tolerated. Commonly reported adverse drug reactions (ADRs) include: Gastrointestinal symptoms: Diarrhea, nausea, dysgeusia (altered taste), soft **stools**

These ADRs are typically mild and transient. For instance, a post-marketing surveillance study in Japan reported ADR incidences of 3.22% for first-line therapy and 1.89% for second-line therapy in Helicobacter pylori eradication regimens

Serious and Rare Adverse Events

While serious AEs are uncommon, post-marketing data have identified several rare but noteworthy events:

Hypersensitivity reactions: Anaphylactic shock, urticaria, drug eruptions

Hepatic disorders: Hepatic injury, hepatic failure, jaundice

Severe skin reactions: Erythema multiforme, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN)[39]

vonoprazan and proton pump inhibitors (PPIs) from a pharmacovigilance perspective, emphasizing safety outcomes, post-marketing data, and adverse drug reactions (ADRs):

1. Mechanism of Action

Vonoprazan: Potassium-Competitive Acid Blocker (P-CAB) — offers rapid, strong, and sustained acid suppression by competitively inhibiting H+/K+-ATPase.

PPIs (e.g., omeprazole, lansoprazole): Irreversibly bind H+/K+-ATPase — require acid activation and take longer to reach maximal effect.

Clinical Relevance: Faster onset with vonoprazan may contribute to different ADR patterns, especially early in treatment.

3.3 Drug-Drug Interactions

Vonoprazan: Lower interaction potential with CYP enzymes (mainly CYP3A4).

PPIs: Metabolized mainly via CYP2C19 and CYP3A4; higher interaction risk with drugs like clopidogrel.[39]

4. Discussion

Interpretation of the Safety Data:

Clinical trials and post-marketing surveillance suggest that vonoprazan is generally well-tolerated, with an adverse event (AE) profile similar to that of traditional proton pump inhibitors (PPIs). Common AEs include gastrointestinal symptoms (e.g., diarrhea, nausea) and skin reactions, typically mild and self-limiting.

Comparison to Traditional PPIs:

Vonoprazan offers faster and more potent acid suppression compared to PPIs. Safety data show comparable rates of adverse events, though vonoprazan may be associated with slightly higher rates of dysgeusia and rare gastrointestinal events like hemorrhagic enterocolitis. PPIs have a well-established link to long-term risks (e.g., hypomagnesemia, kidney disease), which are not yet confirmed for vonoprazan.

Limitations in Current Data:

Long-term safety data are limited, especially outside of Japan.

Most available studies involve short-duration use or specific populations, limiting generalizability.

Real-world data are still emerging, and rare adverse events may be underreported.

Need for Continued Monitoring:

As vonoprazan use expands globally, ongoing pharmacovigilance and real-world evidence are crucial to detect delayed or rare adverse effects, ensure patient safety, and better define its risk-benefit profile compared to PPIs.

Conclusion

The overall safety profile of vonoprazan appears acceptable based on data from Phase I–III clinical trials and early post-marketing surveillance. Adverse events are generally mild and comparable to those seen with traditional proton pump inhibitors (PPIs). While some rare and serious events have been reported—such as hypersensitivity reactions and gastrointestinal complications—these are uncommon and not clearly more frequent than with PPIs.

However, the limited long-term safety data, particularly outside of Japan, highlight the need for continued monitoring. As global use increases, further real-world evidence and post-marketing studies will be essential to fully establish its safety over extended treatment periods.

In summary, vonoprazan represents a promising alternative to PPIs with a favorable short-term safety profile, but long-term vigilance is warranted

Reference

1. Hori Y, Imanishi A, Matsukawa J, Tsukimi Y, Nishida H, Arikawa Y, et al. 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. J Pharmacol Exp Ther
2. Shin JM, Inatomi N, Munson K, Strugatsky D, Tokhtaeva E, Vagin O, et al. Characterization of a novel potassium-competitive acid blocker of the gastric H, K-ATPase, 1-[5-(2-fuorophenyl)-1-(pyridin-3-ylsulfonyl)-1H-pyr-rol-3-yl]-N-methylmethanamine monofumarate (TAK-438). J Pharmacol Exp Ther. 2011
3. Sugano K. Vonoprazan fumarate, a novel potassium-competitive acid blocker, in the management of gastroesophageal refux dis-ease: safety and clinical evidence to date. Therap Adv Gastroenterol. 2018
4. Iwakiri K, Sakurai Y, Shiino M, Okamoto H, Kudou K, Nishimura A, et al. A randomized, double-blind study to evaluate the acid-inhibitory efect of vonoprazan (20 mg and 40 mg) in patients with proton-pump inhibitor-resistant erosive esophagitis. Therap Adv Gastroenterol. 2017;
5. Mizuno H, Yamada K, Minouchi K, Kamiyamamoto S, Hinoue Y. Efcacy of vonoprazan for 24-week maintenance therapy of patients with healed refux esophagitis refractory to proton pump inhibitors. Biomed Rep.2018
6. Tanabe T, Hoshino S, Kawami N, Hoshikawa Y, Hanada Y, Takenouchi N, et al. Efcacy of long-term maintenance therapy with 10-mg vonoprazan for proton pump inhibitor-resistant refux esophagitis. Esophagus.2019
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