Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

VONOCID-10
(Vonoprazan Tablets 10 mg)

2. Qualitative and quantitative composition

Each film-coated tablet contains:
Vonoprazan Fumarate Eq. to Vonoprazan ... 10 mg
Excipients ... q.s.
Colour: Yellow Oxide of Iron and Titanium Dioxide

There are no excipients of known effect in this formulation.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

4. Clinical particulars

4.1 Therapeutic indications

Treatment of gastric ulcer (GU).
Treatment of duodenal ulcer (DU).
Treatment of reflux esophagitis (RE) (erosive esophagitis, EE).
Prevention of recurrence of gastric ulcer or duodenal ulcer during low-dose aspirin administration.
Prevention of recurrence of gastric ulcer or duodenal ulcer during NSAIDs administration.
Adjunct to *Helicobacter pylori* eradication associated with: gastric ulcer, duodenal ulcer, gastric MALT lymphoma, idiopathic thrombocytopenic purpura, the stomach after endoscopic resection of early stage cancer, or *Helicobacter pylori* gastritis.

4.2 Posology and method of administration

Dosage

Adults

Gastric ulcer
The usual dose is 10 mg of vonoprazan once a day. Administration should be limited to 8 weeks.

Duodenal ulcer
The usual dose is 10 mg of vonoprazan once a day. Administration should be limited to 6 weeks.

Reflux esophagitis (erosive esophagitis)
The usual dose is 10 mg of vonoprazan once a day. Administration should be limited to 4 weeks. However, when the effect is insufficient, treatment may be continued for up to 8 weeks.

Prevention of recurrence of gastric ulcer or duodenal ulcer during low-dose aspirin administration
The usual dose is 10 mg of vonoprazan once a day.

Adjunct to Helicobacter pylori eradication
Usually, the following 3 drugs are administered at the same time twice daily for 7 days: 10 mg vonoprazan, 750 mg amoxicillin hydrate, and 200 mg clarithromycin. The dose of clarithromycin may be appropriately increased as required, however, the upper limit is 400 mg twice daily or physician judgement.

When Helicobacter pylori eradication treatment with 3 drugs consisting of a proton pump inhibitor, amoxicillin hydrate, and clarithromycin fails, alternative treatment with the following 3 drugs is recommended: 10 mg vonoprazan, 750 mg amoxicillin hydrate, and 250 mg metronidazole, orally administered at the same time twice daily for 7 days. The doses of antibiotic should follow the respective label recommendations for H. pylori eradication.

Method of administration
For oral use. The tablet should be swallowed whole with a sufficient amount of water, with or without food.

4.3 Contraindications
Hypersensitivity to the active ingredient or to any of the excipients.

4.4 Special warnings and precautions for use
Hepatotoxicity
Hepatic function abnormalities including liver injury have been reported in clinical studies (see section 4.8). Post-marketing reports have also been received in patients treated with vonoprazan, many of which occurred shortly after initiation of treatment. Discontinuation of vonoprazan is recommended in patients who have evidence of liver function abnormalities or if they develop signs or symptoms suggestive of liver dysfunction.

Elevation of intragastric pH
Administration of vonoprazan results in elevation of intragastric pH and is therefore not recommended to be taken with drugs for which absorption is dependent on acidic intragastric pH.

Masking of symptoms associated with gastric malignancy
Gastric malignancy may present with symptoms associated with acid-related disorders which initially respond to drugs that elevate intragastric pH. A symptomatic response to vonoprazan does not exclude the presence of gastric malignancy.

***Clostridium difficile* associated diarrhea, including pseudomembranous colitis**

Drugs that elevate intragastric pH may be associated with an increased risk of *Clostridium difficile* gastrointestinal infection. Pseudomembranous colitis may be due to antibiotics used for Helicobacter pylori eradication in combination with vonoprazan. If abdominal pain and frequent diarrhea occur, appropriate measures, including discontinuation of the treatment, should be taken.

Bone fracture

An increased risk for osteoporosis-related fractures of the hip, wrist, or spine, predominantly in the elderly or in presence of other recognized risk factors, has been reported with the use of proton pump inhibitors, especially with use of high doses over a long-term period (>1 year). The mechanism is not clear and is likely to be multifactorial.

4.5 Interaction with other medicinal products and other forms of interaction

Administration of vonoprazan results in elevation of intragastric pH, suggesting that it may interfere with the absorption of drugs where gastric pH is an important determinant of oral bioavailability. Use of vonoprazan is therefore not recommended with some of these drugs for which absorption is dependent on acidic intragastric pH such as atazanavir and nelfinavir, due to significant reduction in their bioavailability.

Vonoprazan is metabolized mainly by hepatic drug-metabolizing enzyme CYP3A4 and partially by CYP2B6, CYP2C19 and CYP2D6.

With strong CYP3A4 inhibitors, e.g., clarithromycin, blood concentration of vonoprazan may increase. It has been reported that blood concentration of vonoprazan increased in concomitant use with clarithromycin by 1.5-fold, but no dose adjustment of vonoprazan is considered necessary.

Coadministration of vonoprazan with the antibiotic regimen clarithromycin and amoxicillin increased concentrations of vonoprazan by up to 1.9-fold. No increase was observed with the antibiotic regimen of metronidazole and amoxicillin. No dose adjustment of vonoprazan is considered necessary.

There were no clinically significant effects of low-dose aspirin or NSAIDs on the pharmacokinetics of vonoprazan, and no clinically significant effects of vonoprazan on the pharmacokinetics of low-dose aspirin or NSAIDs. The effect on platelet-aggregating inhibitory activity of low-dose aspirin was not considered clinically meaningful.

4.6 Fertility, pregnancy and lactation

Pregnancy

No clinical studies have been conducted to date to evaluate vonoprazan in subjects who are pregnant.

In a rat toxicology study, embryo-foetal toxicity was observed following exposure of more than approximately 28 times the exposure (AUC) at the maximum clinical dose (40 mg/day) of vonoprazan. As a precaution, vonoprazan should not be administered to women who are or may be pregnant, unless the expected therapeutic benefit is thought to outweigh any possible risk.

Lactation
No clinical studies have been conducted to date to evaluate vonoprazan in subjects who are lactating. It is unknown whether vonoprazan is excreted in human milk. In animal studies it has been shown that vonoprazan was excreted in milk. During treatment with vonoprazan, nursing should be avoided if the administration of this drug is necessary for the mother.

Fertility
No human fertility data are available. In animal studies, vonoprazan had no effect on sperm parameters, estrous cycles or fertility indices (see section 5.3).

4.7 Effects on ability to drive and use machines
The influence of vonoprazan on the ability to drive or use machines is unknown.

4.8 Undesirable effects
The following convention is used for the classification of the frequency of an adverse drug reaction (ADR) and is based on the Council for International Organizations of Medical Sciences (CIOMS) guidelines: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).

Adverse reactions with vonoprazan in clinical studies

System Organ Class	Adverse Reaction	Frequency
Gastrointestinal disorders		
	Diarrhoea	Common
	Constipation	Common
	Nausea	Uncommon
	Abdominal distension	Uncommon
Investigations		
	Gamma-glutamyl transferase increased	Uncommon
	Aspartate aminotransferase increased	Uncommon
	Liver function test abnormal	Uncommon
	Alanine aminotransferase increased	Uncommon

Post-marketing
Following is a list of ADRs which have been observed in post-marketing (frequency not known):

System Organ Class	Adverse Reaction	Frequency
Immune system disorders		
	Drug hypersensitivity (including anaphylactic shock)	Not known
	Drug eruption	Not known
Hepatobiliary disorders		
	Hepatotoxicity	Not known
	Jaundice	Not known
Skin and subcutaneous tissue disorders		
	Rash	Not known
	Erythema multiforme	Not known
	Stevens-Johnson syndrome	Not known
	Toxic epidermal necrolysis	Not known

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

There is no experience of overdose with vonoprazan.

Vonoprazan is not removed from the circulation by hemodialysis. If overdose occurs, treatment should be symptomatic and supportive.

Drug abuse and dependence
Vonoprazan has no known potential for abuse or dependence.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Mechanism of action
Vonoprazan is a potassium-competitive acid blocker (PCAB) and inhibits H+, K+-ATPase in a reversible and potassium-competitive manner. It does not require activation by acid. Vonoprazan is a strong base with a high affinity for the acid pump of gastric cells, inhibiting gastric acid production.

Serum gastrin and serum pepsinogen effects
Increased serum gastrin and serum pepsinogen concentrations are physiological responses to treatment with acid suppression therapy,

including vonoprazan. Increased serum gastrin and serum pepsinogen concentrations were reported with a higher incidence in the vonoprazan treatment groups compared with lansoprazole treatment groups. Serum gastrin and serum pepsinogen concentrations returned to baseline over time upon discontinuation of vonoprazan. The increase in serum gastrin concentration occurred early in treatment with vonoprazan and remained stable for the remainder of treatment.

Clinical studies

The efficacy of vonoprazan has been demonstrated in a number of clinical studies across several indications including GU, DU, RE, prevention of GU/DU during low-dose aspirin or NSAID administration and as an adjunct to H. pylori eradication (see section 4.1). Clinical efficacy in completed phase 2 and 3 studies is summarized below. These data are divided into categories based upon the specific indication.

Following administration of vonoprazan at a dose of 10 mg or 20 mg in healthy adult male subjects for 7 days, pH4 HTR (pH4 holding time ratio, i.e. the percentage of time pH is maintained at a level ≥ 4 in 24 hours) was 63±9% and 83±17% respectively.

A phase 1 open-label pharmacodynamics study to investigate the acid-inhibitory effect of vonoprazan 10 mg compared with esomeprazole 10 mg or rabeprazole sodium 10 mg in healthy adult male Japanese subjects showed that the acid-inhibitory effect of vonoprazan was greater than that of esomeprazole or rabeprazole. After all treatments, the mean 24-hour pH4 HTRs increased from Baseline to Day 1 and from Day 1 to Day 7. The mean pH4 HTRs were higher after administration of vonoprazan on Day 1 than after administration of esomeprazole or rabeprazole on Day 7. The mean 24-hour pH4 HTRs for vonoprazan and rabeprazole at Baseline were both 8.9%, and on Day 1 and on Day 7 were 84.16% vs 26.29%, and 93.79% vs 65.09%, respectively.

Overview of clinical efficacy of vonoprazan (TAK-438) and comparators in completed phase 2 and 3 studies

Indication / Study	**Vonoprazan Dose(s)**	**Comparator**	**Duration (weeks)**	**Efficacy Findings**
Reflux esophagitis (EE) – CCT-001 (Phase 2, dose-ranging)	5, 10, 20, 40 mg	Lansoprazole 30 mg	8	Non-inferior to lansoprazole at all doses; 4-week EE healing rates: 5 mg 92.3%, 10 mg 92.5%, 20 mg 94.4%, 40 mg 97.0%
Reflux esophagitis (EE) – CCT-002 (Phase 3)	10 mg	Lansoprazole 30 mg	8	Non-inferior to lansoprazole: 99.0% vs 95.5% ($p<0.0001$) 8-week EE healing rate
Reflux esophagitis (EE) – CCT-003	10 mg	N/A	8	EE healing rate 98.9%

(Phase 3, treatment period)				
Reflux esophagitis (EE) – TAK-438-303 (Phase 3)	20 mg	Lansoprazole 30 mg	Up to 8	Non-inferior to lansoprazole; 8-week EE healing rates: 92.4% vs 91.3%
Gastric ulcer – CCT-101 (Phase 3)	10 mg	Lansoprazole 30 mg	8	Non-inferior to lansoprazole: 93.5% vs 93.8% (p=0.011) ulcer healing rate
Duodenal ulcer – CCT-102 (Phase 3)	10 mg	Lansoprazole 30 mg	6	Non-inferiority not confirmed in FAS (p=0.0654); confirmed in PPS
NSAID ulcer recurrence prevention – CCT-301 (Phase 3)	10, 20 mg	Lansoprazole 15 mg	24	Non-inferior to lansoprazole at both doses: 10 mg 3.3% vs 5.5% (p<0.0001); 20 mg 3.4% vs 5.5%
NSAID ulcer recurrence prevention – OCT-301 (Phase 3 extension)	10, 20 mg	Lansoprazole 15 mg	28–80	Ulcer recurrence rates lower at all visits in vonoprazan groups than lansoprazole group
LDA ulcer recurrence prevention – CCT-302 (Phase 3)	10, 20 mg	Lansoprazole 15 mg	24	Non-inferior to lansoprazole at both doses: 10 mg 1.0% vs 2.8% (p<0.0001)
LDA ulcer recurrence prevention – CCT-302 extension	10 mg	Lansoprazole 15 mg	28–80	Recurrence rate numerically lower in vonoprazan groups; significantly lower in the 10 mg group than lansoprazole at Weeks 76 and beyond
H. pylori eradication, first-line – CCT-401 (Phase 3)	10 mg + amoxicillin + clarithromycin	Lansoprazole 30 mg + amoxicillin + clarithromycin	1	Non-inferior to lansoprazole: 92.6% vs 75.9% (p<0.0001) 4-week eradication rate
H. pylori eradication, second-line – CCT-401 (Phase 3)	10 mg + amoxicillin + metronidazole	N/A	1	4-week eradication rate: 98%
NERD – CCT-201 (Phase 3)	10, 20 mg	Placebo	4	Proportion of days without heartburn numerically higher in vonoprazan groups than placebo
NERD – Vonoprazan 3001 (Phase 3)	10 mg	Placebo	4	Proportion of days without heartburn numerically higher in vonoprazan group than placebo group

LDA = low-dose aspirin; N/A = not assessed; PPS = per protocol set; FAS = full analysis set; EE = erosive esophagitis = reflux esophagitis (RE).

5.2 Pharmacokinetic properties

Following 7-day repeat once-daily doses of vonoprazan at doses of 10–40 mg in healthy adult male subjects, AUCτ,ss and Cmax increase in a slightly greater than dose-proportional manner. Steady state has been reached by day 3 of administration, since the trough level of the blood concentration of vonoprazan is constant between day 3 and day 7 of administration.

In addition, vonoprazan does not exhibit time-dependent pharmacokinetics. The following table shows pharmacokinetic parameters of vonoprazan on day 7 of administration (mean ± S.D. of 9 subjects; tmax,ss expressed as median (minimum, maximum)):

Parameter	**10 mg**	**20 mg**
tmax,ss (h)	1.5 (0.75, 3.0)	1.5 (0.75, 3.0)
Cmax,ss (ng/mL)	12.0±1.8	23.3±6.6
t1/2z (h)	7.0±1.6	6.1±1.2
AUCτ,ss (h·ng/mL)	79.5±16.1	151.6±40.3

Absorption

Absolute bioavailability has not been determined. The pharmacokinetic parameters of vonoprazan following single administration of vonoprazan to healthy adult male subjects at 10 mg under fasting and fed conditions are presented below (mean ± S.D. of 12 subjects; tmax,ss expressed as median (minimum, maximum)):

Parameter	**Under fasting**	**After meal**
tmax,ss (h)	1.5 (1.0, 3.0)	3.0 (1.0, 4.0)
Cmax,ss (ng/mL)	24.3±6.6	26.8±9.6
t1/2z (h)	7.7±1.0	7.7±1.2
AUC48 (h·ng/mL)	222.1±69.7	238.3±71.1

Distribution

The mean binding rate is 85.2 to 88.0% when [14C] vonoprazan in the range of 0.1 to 10 μg/mL is added to human plasma (in vitro).

Metabolism

Vonoprazan is metabolized mainly by hepatic drug-metabolizing enzyme CYP3A4 and partially by CYP2B6, CYP2C19 and CYP2D6. Vonoprazan is also metabolized by sulfotransferase SULT2A1 (in vitro).

Vonoprazan exhibits time-dependent inhibitory effect on CYP2B6, CYP2C19 and CYP3A4/5 (in vitro). In addition, vonoprazan shows a slight concentration-dependent inductive effect on CYP1A2, but it shows little inductive effect on CYP2B6 and CYP3A4/5 (in vitro).

Excretion and elimination

When radioactive-labeled drug (15 mg as vonoprazan) is orally administered to healthy adult male subjects, 98.5% of the radioactivity

administered is excreted into urine and feces by 168 hours after administration: 67.4% into urine and 31.1% into feces.

Special population – impaired renal function
The effect of renal disorders on pharmacokinetics of vonoprazan was evaluated in subjects with normal renal function and patients with mild, moderate or severe renal disorder and patients with end-stage renal disease (ESRD). When administered a single dose of vonoprazan 10 mg, the AUC∞ was higher by 1.3 to 2.4 times and the Cmax higher by 1.2 to 1.8 times in patients with mild, moderate or severe renal disorder compared to subjects with normal renal function, indicating an increase in vonoprazan exposure with a reduction in renal function. The AUC∞ was higher by 1.3 times and the Cmax higher by 1.2 times in ESRD patients compared to those in subjects with normal renal function.

Impaired hepatic function
The effect of hepatic disorders on pharmacokinetics of vonoprazan was evaluated in subjects with normal hepatic function and patients with mild, moderate or severe hepatic disorder. When administered a single dose of vonoprazan 10 mg, the AUC∞ was higher by 1.2 to 2.6 times and the Cmax were higher by 1.2 to 1.8 times in patients with mild, moderate or severe hepatic disorder, compared to subjects with normal hepatic function.

Age, gender, race
Vonoprazan has not been studied in patients under 18 years of age. There are no clinically relevant gender effects of vonoprazan.

No dedicated ethnic comparison studies have been conducted with vonoprazan. The ethnic sensitivity analysis based on the International Conference for Harmonization (ICH) E5 principles was conducted to assess whether the molecular properties of vonoprazan were sensitive to ethnic factor differences, and whether the diagnosis, medical practice, treatment options, and other epidemiological factors for acid-related disorders would vary dramatically in areas other than Japan. It was concluded that vonoprazan is insensitive to ethnic factor differences.

Drug interactions – vonoprazan and clarithromycin
Healthy adult male subjects were administered with a single dose of vonoprazan (40 mg), 30 minutes after breakfast on day 1 and day 8, and with repeated dose of clarithromycin 500 mg (potency) 2 times daily 30 minutes before breakfast and dinner on day 3–9. The AUC∞ and Cmax of vonoprazan increased by 1.6 times and 1.4 times, respectively, when concomitantly administered with clarithromycin compared to those of vonoprazan when administered alone.

Vonoprazan, amoxicillin hydrate and clarithromycin

The drug interaction study in healthy adult male subjects administered twice daily with vonoprazan 10 mg, amoxicillin hydrate 750 mg (potency) and clarithromycin 400 mg (potency) concomitantly for 7 days shows no effect on pharmacokinetics of unchanged amoxicillin; however, AUC12 and Cmax of vonoprazan increased by 1.8 times and 1.9 times, respectively, and AUC12 and Cmax of unchanged clarithromycin increased by 1.5 times and 1.6 times, respectively.

Vonoprazan, amoxicillin hydrate and metronidazole
The drug interaction study in healthy adult male subjects administered twice daily with vonoprazan 10 mg, amoxicillin hydrate 750 mg (potency) and metronidazole 250 mg concomitantly for 7 days showed little difference in the pharmacokinetics of vonoprazan, when administered alone or as triple therapy. No difference was observed in the pharmacokinetics of metronidazole or amoxicillin when administered alone or as triple therapy.

Vonoprazan, bismuth, clarithromycin and amoxicillin
The drug interaction study in Helicobacter pylori positive adult subjects administered twice daily vonoprazan 10 mg or lansoprazole 30 mg with tripotassium bismuth dicitrate 600 mg, clarithromycin 500 mg, and amoxicillin 1000 mg concomitantly for 14 days shows the lack of a clinically meaningful effect of vonoprazan on the pharmacokinetics of bismuth compared with lansoprazole.

Vonoprazan and low-dose aspirin or vonoprazan and NSAIDs
The drug interaction study in healthy adult male subjects administered with vonoprazan 40 mg and aspirin 100 mg or NSAID (loxoprofen sodium 60 mg, diclofenac sodium 25 mg or meloxicam 10 mg) concomitantly showed no clear effect of low-dose aspirin or NSAIDs on pharmacokinetics of vonoprazan and of vonoprazan on pharmacokinetics of low-dose aspirin or NSAIDs.

5.3 Preclinical safety data

Carcinogenicity
Vonoprazan was non-carcinogenic in a long-term carcinogenicity study in mice when administered the drug daily via oral gavage for up to 2 years at 0.6, 20, 60, and 200 mg/kg/day. Treatment-related tumors, related to exaggerated pharmacology or species-specificity, were noted in the stomach and liver. In the stomach, benign and malignant neuroendocrine cell tumors were observed at ≥20 (males) and ≥60 (females) mg/kg/day and ≥6 (males) and ≥60 (females) mg/kg/day, respectively. In the liver, increased incidences of hepatocellular adenoma and carcinoma were observed at ≥20 (males) and ≥60 (females) mg/kg/day, and at ≥60 (males) and 200 (females) mg/kg/day, respectively. Hyperplasia of the neuroendocrine cells and associated tumors in the stomach may be due to hypergastrinemia as a consequence of inhibiting gastric acid secretion. The hepatocellular tumors are likely rodent-specific findings that are

attributed to prolonged induction of hepatic drug-metabolizing enzymes. The NOAEL was <6 mg/kg/day.

Vonoprazan was non-carcinogenic in a long-term carcinogenicity study in rats administered the drug via oral gavage at 5, 15, 50, and 150 mg/kg/day. Treatment-related tumors, related to exaggerated pharmacology or species-specificity, were noted in the stomach and liver. In the stomach, benign and malignant neuroendocrine cell tumors were observed at ≥5 mg/kg/day except for malignant neuroendocrine tumor at 50 mg/kg/day (males). In some instances in benign and malignant neuroendocrine cell tumors, tumor cells showed eosinophilic change but these tumors were also judged to be of neuroendocrine cell origin. In the liver, increased incidences of hepatocellular adenoma and carcinoma were observed at ≥50 mg/kg/day except for hepatocellular carcinoma at 50 mg/kg/day (females). Tumor findings in the stomach and liver are believed to be due to hypergastrinemia as a consequence of inhibiting gastric acid secretion and rodent-specific induction of hepatic drug-metabolizing enzymes, respectively. The occurrence of 4 hepatocholangiocellular tumors at ≥50 mg/kg/day (males) were considered to be treatment-related because they were considered to be associated with induction of hepatocellular tumor, but pairwise comparison did not demonstrate a statistically significant effect.

Mutagenicity
Vonoprazan did not exhibit any mutagenic or clastogenic activity in the in vitro Ames assay, in vitro mammalian chromosome aberration assay, and in vivo rat micronucleus assay.

Impairment of fertility
When administered daily via oral gavage to male and female rats there were no effects on sperm analysis, estrous cycles or number of corpora lutea observed at doses up to 300 mg/kg/dose. Males were administered vonoprazan prior to and during mating and females dosed for 2 weeks pre-mating through Gestation Day (GD) 6. The NOAEL for male and female general toxicity was 30 mg/kg/day and ≥ 300 mg/kg/day for reproductive function and early embryonic development.

6. Pharmaceutical particulars

6.1 List of excipients

Mannitol
Microcrystalline Cellulose PH-101
Hydroxypropyl Cellulose
Purified water
Croscarmellose Sodium
Hydrophilic Pyrogenic Silica
Fumaric Acid
Magnesium stearate
DR Coat FCU (C/026/315) Yellow
Iso Propyl Alcohol

Methylene Dichloride

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
24 months.

6.4 Special precautions for storage
Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container
The immediate container of the product is an Alu-Alu blister pack of 10 tablets. Two blister packs are placed in one printed duplex board carton, along with pack insert.

6.6 Special precautions for disposal and other handling
No special requirements for disposal.

7. Marketing authorisation holder
HOF Pharmaceuticals Limited
Survey No.211-4/5/6, Village: Pipan,
Sanand-Bavla Road,
Sanand, Ahmedabad, Gujarat-382110, India

8. Marketing authorisation number
H2022/CTD10755/24430

9. Date of first authorisation/renewal of the authorisation
1st October, 2023

10. Date of revision of the text
24th August, 2026