Risek® Insta

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[Omeprazole+Sodium Bicarbonate]
20mg + 1680mg & 40mg + 1680mg
Powder for Oral Suspension

DESCRIPTION

Risek Insta (Omeprazole + Sodium Bicarbonate) is a combination of Omeprazole, a proton-pump inhibitor and Sodium Bicarbonate, an antacid. Risek Insta contains immediate-release formulation of Omeprazole and Sodium Bicarbonate. Sodium Bicarbonate raises the gastric pH and thus protect Omeprazole from acid degradation. Omeprazole is substituted benzimidazole 5-methoxy-2-[[(4-methoxy-3, 5-dimethyl-2-pyridinyl) methyl] sulfinyl]-1Hbenzimidazole. Its molecular formula is $C_{17}H_{19}N_3O_3S$ and the structural formula is:

Omeprazole

QUALITATIVE & QUANTITATIVE COMPOSITION

Risek Insta (Omeprazole + Sodium Bicarbonate) Powder for Oral Suspension is available for oral administration as:

Risek Insta Powder for Oral Suspension 20mg + 1680mg
Each sachet contains:
Omeprazole USP…20mg
Sodium Bicarbonate USP…1680mg
(as buffer)

Risek Insta Powder for Oral Suspension 40mg + 1680mg
Each sachet contains:
Omeprazole USP…40mg
Sodium Bicarbonate USP…1680mg
(as buffer)

CLINICAL PHARMACOLOGY

Mechanism of Action

Omeprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that suppress gastric acid secretion by specific inhibition of the H+/K+ ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the gastric mucosa, Omeprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. This effect is dose related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus.

Pharmacokinetics

Absorption

Following single or repeated once-daily dosing, peak plasma concentrations (C_{max}) of Omeprazole were approximately proportional from 20mg to 40mg doses. A greater than dose proportional increase in mean steady-state AUC (more than three-fold increase on Day 7) was observed when doubling the dose to 40mg. The bioavailability of Omeprazole increases upon repeated administration. The percent changes in Cmax and AUC between steady-state (Day 7) and single dose (Day 1) indicate Omeprazole is a time-dependent autoinhibitor of CYP2C19.

When Omeprazole for Oral Suspension 40mg was administered in a two-dose loading regimen, the Omeprazole $AUC_{(0\text{-}inf)}$ (ng hr/mL) was 1665 after Dose 1 and 3356 after Dose 2, while T_{max} was approximately 30 minutes for both Dose 1 and Dose 2. When Omeprazole for Oral Suspension 40mg is administered one hour after a meal, the Omeprazole AUC is reduced by approximately 27% relative to administration one hour prior to a meal.

Distribution

Omeprazole is bound to plasma proteins. Protein binding is approximately 95%.

Metabolism

Omeprazole is extensively metabolized by the cytochrome P450 (CYP) enzyme system. The major part of its metabolism is dependent on the polymorphically expressed CYP2C19, responsible for the formation of hydroxyomeprazole, the major metabolite in plasma. The remaining part is dependent on another specific isoform, CYP3A4, responsible for the formation of omeprazole sulphone. The mean plasma omeprazole half-life following administration in healthy subjects is approximately 1 hour (range 0.4 to 4.2 hours), and the total body clearance is 500 to 600mL/min.

Excretion

Following single-dose oral administration of a buffered solution of Omeprazole, the majority of the dose (about 77%) is eliminated in urine as at least six metabolites. Two metabolites have been identified as hydroxyomeprazole and the corresponding carboxylic acid. The remainder of the dose was recoverable in feces. This implies a significant biliary excretion of the metabolites of Omeprazole. Three metabolites have been identified in plasma – the sulfide and sulfone derivatives of Omeprazole, and hydroxyomeprazole. These metabolites have very little or no antisecretory activity.

Special Population

Pediatric

Safety and effectiveness of Omeprazole + Sodium Bicarbonate have not been established in pediatric patients.

Geriatric Patients

The elimination rate of Omeprazole was somewhat decreased in the elderly, and bioavailability was increased.

Patients with Renal Impairment

In patients with chronic renal impairment (creatinine clearance between 10 and 62mL/min/1.73m^2), the disposition of Omeprazole was very similar to that in healthy subjects, although there was a slight increase in bioavailability. Because urinary excretion is a primary route of excretion of Omeprazole metabolites, their elimination slowed in proportion to the decreased creatinine clearance. This increase in bioavailability is not considered to be clinically meaningful.

Patients with Hepatic Impairment

In patients with chronic hepatic disease, the bioavailability of Omeprazole increased to approximately 100% compared to healthy subjects, reflecting decreased first-pass effect, and the plasma half-life of the drug increased to nearly 3 hours compared to the in healthy subjects of 0.5 to 1 hour. Plasma clearance averaged 70mL/min, compared to a value of 500 to 600mL/min in healthy subjects.

THERAPEUTIC INDICATIONS

Risek Insta (Omeprazole + Sodium Bicarbonate) Powder for Oral Suspension are indicated in adults for the:

1. Short-term treatment of active duodenal ulcer. Most patients heal within four weeks. Some patients may require an additional four weeks of therapy.
2. Short-term treatment (4 to 8 weeks) of active benign gastric ulcer.
3. Treatment of heartburn and other symptoms associated with GERD for up to 4 weeks.
4. Short-term treatment (4 to 8 weeks) of EE (Erosive Esophagitis) due to acid-mediated GERD which has been diagnosed by endoscopy in adults. The efficacy of Risek Insta (Omeprazole + Sodium Bicarbonate) used for longer than 8 weeks in patients with EE has not been established. If a patient does not respond to 8 weeks of treatment, an additional 4 weeks of treatment may be given. If there is recurrence of EE or GERD symptoms (e.g., heartburn), additional 4 to 8-week courses of Risek Insta (Omeprazole + Sodium Bicarbonate) may be considered.
5. Maintenance of healing of EE (Erosive Esophagitis) due to acid-mediated GERD.
6. Reduction of risk of upper GI bleeding in critically ill adult patients.

DOSAGE & ADMINISTRATION

Important Administration Points

- The sodium content of Risek Insta (Omeprazole + Sodium Bicarbonate) Powder for Oral Suspension should be taken into consideration when prescribing this product.
- Do not substitute two packets of 20mg Risek Insta (Omeprazole + Sodium Bicarbonate) Powder for Oral Suspension with one packet of 40mg Risek Insta (Omeprazole + Sodium Bicarbonate) Powder for Oral Suspension.
- Risek Insta (Omeprazole + Sodium Bicarbonate) Powder for Oral Suspension is intended to be mixed with water and administered orally or via a nasogastric (NG) or orogastric (OG) tube.
- If administered orally, take on an empty stomach at least one hour before a meal.
- If administered via NG or OG tube, suspend enteral feeding approximately 3 hours before and 1 hour after administration of Risek Insta (Omeprazole + Sodium Bicarbonate) Powder for Oral Suspension.

Dosage Regimen

The recommended dosage regimen by indication in adults of Risek Insta (Omeprazole + Sodium Bicarbonate) Powder for Oral Suspension is summarized in Table 1. Only 40mg Risek Insta (Omeprazole + Sodium Bicarbonate) Powder for Oral Suspension is indicated for the reduction of risk of upper GI bleeding in critically ill adult patients and the dosage regimen is summarized in Table 2. All recommended dosages are based upon Omeprazole content. Risek Insta (Omeprazole + Sodium Bicarbonate) Powder for Oral Suspension should be taken on an empty stomach at least one hour before a meal.

Table 1: Recommended Dosage Regimen of Risek Insta Powder for Oral Suspension in Adults by Indication

Indication	Dosage of Risek Insta for oral suspension	Treatment Duration
Treatment of Active Duodenal Ulcer	20mg once daily	4 weeks[1,2]
Treatment of Active Benign Gastric Ulcer	40mg once daily	4 to 8 weeks
Treatment of Symptomatic GERD	20mg once daily	Up to 4 weeks
Treatment of EE due to Acid-Mediated GERD	20mg once daily	4 to 8 weeks[2]
Maintenance of Healing of EE due to Acid-Mediated GERD	20mg once daily	Controlled studies do not extend beyond 12 months

[1] Most patients heal within 4 weeks. Some patients may require an additional 4 weeks of therapy.
[2] The efficacy of Omeprazole + Sodium Bicarbonate used for longer than 8 weeks in patients with EE has not been established. If a patient does not respond to 8 weeks of treatment, an additional 4 weeks of treatment may be given. If there is recurrence of EE or GERD symptoms (e.g., heartburn), additional 4 to 8-week courses of Omeprazole + Sodium Bicarbonate may be considered.

Table 2: Recommended Dosage Regimen of 40mg Risek Insta Powder for Oral Suspension in Adults by Indication

Indication	Dosage of 40mg Risek Insta Powder for Oral Suspension	Treatment Duration
Reduction of Risk of Upper GI Bleeding in Critically ill Patients	40mg initially; followed by 40mg 6 to 8 hours later; and 40mg once daily thereafter	14 days

Preparation and Administration

Oral Administration

- Empty the sachet contents into a small cup containing 1-2 tablespoons (15 - 30mL) of water to form suspension. Stir well and drink immediately. Refill cup with water and drink.
- DO NOT USE OTHER LIQUIDS OR FOODS.

Nasogastric (NG) or Orogastric (OG) Tube Administration

- Add 25mL of water to a catheter tipped syringe and then add the contents of a packet. Use an appropriately-sized catheter tipped syringe. Do not mix with liquids or foods other than water.
- Shake the syringe to dissolve the powder.
- Administer through the NG or orogastric tube into the stomach right away.
- Refill the syringe with an equal amount of water.
- Shake and flush any remaining contents from the NG tube or orogastric tube into the stomach.

ADVERSE REACTIONS

The following adverse reactions have been reported with the use of Omeprazole:

Body as a Whole

Hypersensitivity reactions, including anaphylaxis, anaphylactic shock, angioedema, bronchospasm, urticaria (see also Skin below), fever, pain, fatigue, malaise, and systemic lupus erythematosus.

Cardiovascular

Chest pain or angina, tachycardia, bradycardia, palpitation, elevated blood pressure, and peripheral edema.

Gastrointestinal

Pancreatitis (some fatal), anorexia, irritable colon, flatulence, fecal discoloration, esophageal candidiasis, mucosal atrophy of the tongue, dry mouth, stomatitis, abdominal swelling and fundic gland polyps. Gastroduodenal carcinoids have been reported in patients with Zollinger-Ellison syndrome on long-term treatment with omeprazole. This finding is believed to be a manifestation of the underlying condition, which is known to be associated with such tumors.

Hepatic

Mild and, rarely, marked elevations of liver function tests [ALT (SGPT), AST (SGOT), γ-glutamyl transpeptidase, alkaline phosphatase, and bilirubin (jaundice)]. In rare instances, overt liver disease has occurred, including hepatocellular, cholestatic, or mixed hepatitis, liver necrosis (some fatal), hepatic failure (some fatal), and hepatic encephalopathy.

Infections and Infestations

Clostridium difficile-associated diarrhea.

Metabolism and Nutritional Disorders

Hypomagnesemia, hypocalcemia, hypokalemia, hyponatremia, hypoglycemia, and weight gain.

Musculoskeletal

Muscle cramps, myalgia, muscle weakness, joint pain, bone fracture, and leg pain.

Nervous System/Psychiatric

Psychic disturbances including depression, agitation, aggression, hallucinations, confusion, insomnia, nervousness, tremors, apathy, somnolence, anxiety, dream abnormalities; vertigo; paresthesia; and hemifacial dysesthesia.

Respiratory

Epistaxis, pharyngeal pain.

Skin

Severe generalized skin reactions including TEN (some fatal), SJS, DRESS, AGEP, cutaneous lupus erythematosus and erythema multiforme (some severe); purpura and/or petechiae (some with rechallenge); skin inflammation, urticaria, angioedema, pruritus, photosensitivity, alopecia, dry skin, and hyperhidrosis.

Special Senses

Tinnitus, and taste perversion.

Ocular

Blurred vision, ocular irritation, dry eye syndrome, optic atrophy, anterior ischemic optic neuropathy, optic neuritis, and double vision.

Urogenital

Tubulointerstitial nephritis, urinary tract infection, microscopic pyuria, urinary frequency, elevated serum creatinine, proteinuria, hematuria, glycosuria, testicular pain, gynecomastia, and erectile dysfunction.

Hematologic

Rare instances of pancytopenia, agranulocytosis (some fatal), thrombocytopenia, neutropenia, leukopenia, anemia, leukocytosis, and hemolytic anemia have been reported.

The following adverse reactions have been reported with the use of Sodium Bicarbonate:

Metabolic alkalosis, seizures, and tetany.

"To report SUSPECTED ADVERSE REACTIONS to Getz Pharma's pharmacovigilance Section, please contact at dsafety@getzpharma.com or +92-21-38636363"

CONTRAINDICATIONS

Omeprazole + Sodium Bicarbonate is contraindicated in:

- Patients who are hypersensitive to the active substance or to any of the excipient of the product.
- Patients with known hypersensitivity to substituted benzimidazoles.
- In patients receiving rilpivirine & nelfinavir containing products.

PRECAUTIONS

Presence of Gastric Malignancy

In adults, symptomatic response to therapy with Omeprazole + Sodium Bicarbonate does not preclude the presence of gastric malignancy. Consider additional follow-up and diagnostic testing in adult patients who have a suboptimal response or an early symptomatic relapse after completing treatment with a proton pump inhibitor (PPI). In older patients, also consider an endoscopy.

Acute Tubulointerstitial Nephritis

Acute tubulointerstitial nephritis (TIN) has been observed in patients taking PPIs and may occur at any point during PPI therapy. Patients may present with varying signs and symptoms from symptomatic

hypersensitivity reactions to non- specific symptoms of decreased renal function (e.g., malaise, nausea and anorexia). In reported case series, some patients were diagnosed on biopsy and in the absence of extra-renal manifestations (e.g., fever, rash or arthralgia). Discontinue Omeprazole + Sodium Bicarbonate and evaluate patients with suspected acute TIN.

Sodium Bicarbonate Buffer Content
Chronic administration of Bicarbonate with calcium or milk can cause milk-alkali syndrome. Chronic use of Sodium Bicarbonate may lead to systemic alkalosis, and increased sodium intake can produce edema and weight gain. The sodium content of Omeprazole + Sodium Bicarbonate products should be taken into consideration when administering to patients on a sodium-restricted diet or those at risk for developing congestive heart failure. Avoid Omeprazole + Sodium Bicarbonate in patients with Bartter's syndrome, hypokalemia, hypocalcemia, and problems with acid-base balance.

Clostridium difficile-Associated Diarrhea
PPI therapy like Omeprazole + Sodium Bicarbonate may be associated with an increased risk of Clostridium difficile-associated diarrhea, especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Bone Fracture
Proton pump inhibitor (PPI) therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Severe Cutaneous Adverse Reactions
Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with the use of PPIs. Discontinue Omeprazole + Sodium Bicarbonate at the first signs or symptoms of severe cutaneous adverse reactions or other signs of hypersensitivity and consider further evaluation.

Cutaneous and Systemic Lupus Erythematosus
Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) have been reported in patients taking PPIs, including Omeprazole. These events have occurred as both new onset and an exacerbation of existing autoimmune disease. The majority of PPI-induced lupus erythematosus cases were CLE. Avoid administration of PPIs for longer than medically indicated. If signs or symptoms consistent with CLE or SLE are noted in patients receiving Omeprazole + Sodium Bicarbonate, discontinue the drug and refer the patient to the appropriate specialist for evaluation. Most patients improve with discontinuation of the PPI alone in 4 to 12 weeks. Serological testing (e.g., ANA) may be positive and elevated serological test results may take longer to resolve than clinical manifestations.

Interaction with Clopidogrel
Avoid concomitant use of Omeprazole + Sodium Bicarbonate with clopidogrel. The metabolism of clopidogrel to its active metabolite can be impaired by use with concomitant medications, such as Omeprazole, that interfere with CYP2C19 activity. Concomitant use of clopidogrel with 80mg Omeprazole reduces the pharmacological activity of clopidogrel, even when administered 12 hours apart. When using Omeprazole + Sodium Bicarbonate, consider alternative antiplatelet therapy.

Cyanocobalamin (Vitamin B-12) Deficiency
Daily treatment with any acid-suppressing medications over a long period of time (e.g., longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B-12) caused by hypo- or achlorhydria.

Hypomagnesemia and Mineral Metabolism
Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Hypomagnesemia may lead to hypocalcemia and/or hypokalemia and may exacerbate underlying hypocalcemia in at-risk patients.
For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.
Consider monitoring magnesium and calcium levels prior to initiation of Omeprazole + Sodium Bicarbonate and periodically while on treatment in patients with a preexisting risk of hypocalcemia (e.g., hypoparathyroidism). Supplement with magnesium and/or calcium as necessary. If hypocalcemia is refractory to treatment, consider discontinuing the PPI.

Interaction with St. John's wort or Rifampin
Drugs which induce CYP2C19 or CYP3A4 (such as St. John's wort or rifampin) can substantially decrease Omeprazole concentrations. Avoid concomitant use of Omeprazole + Sodium Bicarbonate with St. John's wort or rifampin.

Interactions with Investigations for Neuroendocrine Tumors
Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors. Providers should temporarily stop Omeprazole + Sodium Bicarbonate treatment for at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high. If serial tests are performed (e.g., for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.

Interaction with Methotrexate
Concomitant use of PPIs with methotrexate (primarily at high dose) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of the PPI may be considered in some patients.

Fundic Gland Polyps
PPI use is associated with an increased risk of fundic gland polyps that increases with long-term use, especially beyond one year. Most PPIs users who developed fundic gland polyps were asymptomatic and fundic gland polyps were identified incidentally on endoscopy. Use the shortest duration of PPI therapy appropriate to the condition being treated.

Pregnancy
There are no adequate and well controlled studies on the use of Omeprazole in pregnant women. Omeprazole should be used during pregnancy only if the potential benefit to pregnant women justifies the potential risk to the fetus.

Nursing Mothers
Omeprazole + Sodium Bicarbonate is present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Omeprazole + Sodium Bicarbonate and any potential adverse effects on the breastfed infant from Omeprazole + Sodium Bicarbonate or from the underlying maternal condition.

DRUG INTERACTIONS
Antiretrovirals
Clinical Impact
The effect of PPIs on antiretroviral drugs is variable. The clinical importance and the mechanisms behind these interactions are not always known.
- Decreased exposure of some antiretroviral drugs (e.g., rilpivirine, atazanavir and nelfinavir) when used concomitantly with Omeprazole may reduce antiviral effect and promote the development of drug resistance.
- Increased exposure of other antiretroviral drugs (e.g., saquinavir) when used concomitantly with Omeprazole may increase toxicity.
- There are other antiretroviral drugs which do not result in clinically relevant interactions with Omeprazole.

Intervention
- Rilpivirine-containing products: Concomitant use with Omeprazole + Sodium Bicarbonate is contraindicated.
- Atazanavir: Avoid concomitant use with Omeprazole + Sodium Bicarbonate.
- Nelfinavir: Avoid concomitant use with Omeprazole + Sodium Bicarbonate.
- Saquinavir: See the prescribing information for saquinavir for monitoring of potential saquinavir-related toxicities.
- Other antiretrovirals: See prescribing information for specific antiretroviral drugs.

Warfarin
Clinical Impact
Increased INR and prothrombin time in patients receiving PPIs, including Omeprazole, and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death.
Intervention
Monitor INR and prothrombin time and adjust the dose of warfarin, if needed, to maintain target INR range.

Methotrexate
Clinical Impact
Concomitant use of Omeprazole with methotrexate (primarily at high dose) may elevate and prolong serum concentrations of methotrexate and/or its metabolite hydroxymethotrexate, possibly leading to methotrexate toxicities. No formal drug interaction studies of high-dose methotrexate with PPIs have been conducted.
Intervention
A temporary withdrawal of Omeprazole + Sodium Bicarbonate may be considered in some patients receiving high-dose methotrexate.

Clopidogrel
Clinical Impact
Concomitant use of Omeprazole 80mg results in reduced plasma concentrations of the active metabolite of clopidogrel and a reduction in platelet inhibition. There are no adequate combination studies of a lower dose of Omeprazole or a higher dose of clopidogrel in comparison with the approved dose of clopidogrel.
Intervention
Avoid concomitant use with Omeprazole + Sodium Bicarbonate. Consider use of alternative antiplatelet therapy.

Citalopram
Clinical Impact
Increased exposure of citalopram leading to an increased risk of QT prolongation.
Intervention
Limit the dose of citalopram to a maximum of 20mg per day. See prescribing information for citalopram.

Cilostazol
Clinical Impact
Increased exposure of one of the active metabolites of cilostazol (3,4-dihydrocilostazol).
Intervention
Reduce the dose of cilostazol to 50mg twice daily.

Phenytoin
Clinical Impact
Potential for increased exposure of phenytoin.
Intervention
Monitor phenytoin serum concentrations. Dose adjustment may be needed to maintain therapeutic drug concentrations.

Diazepam
Clinical Impact
Increased exposure of diazepam.
Intervention
Monitor patients for increased sedation and reduce the dose of diazepam as needed.

Digoxin
Clinical Impact
Potential for increased exposure of digoxin.
Intervention
Monitor digoxin concentrations. Dose adjustment may be needed to maintain therapeutic drug concentrations. See digoxin prescribing information.

Drugs Dependent on Gastric pH for Absorption (e.g., iron salts, erlotinib, dasatinib, nilotinib, mycophenolate mofetil, ketoconazole/itraconazole)
Clinical Impact
Omeprazole can reduce the absorption of other drugs due to its effect on reducing intragastric acidity.
Intervention
Mycophenolate mofetil (MMF): Co-administration of Omeprazole in healthy subjects and in transplant patients receiving MMF has been reported to reduce the exposure to the active metabolite, mycophenolic acid (MPA), possibly due to a decrease in MMF solubility at an increased gastric pH. The clinical relevance of reduced MPA exposure on organ rejection has not been established in transplant patients receiving Omeprazole + Sodium Bicarbonate and MMF. Use Omeprazole + Sodium Bicarbonate with caution in transplant patients receiving MMF.

Tacrolimus
Clinical Impact
Potential for increased exposure of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19.
Intervention
Monitor tacrolimus whole blood concentrations. Dose adjustment may be needed to maintain therapeutic drug concentrations.

Interactions with Investigations of Neuroendocrine Tumors
Clinical Impact
Serum chromogranin A (CgA) levels increase secondary to PPI-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors.
Intervention
Temporarily stop Omeprazole + Sodium Bicarbonate treatment at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high. If serial tests are performed (e.g., for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.

Interaction with Secretin Stimulation Test
Clinical Impact
Hyper-response in gastrin secretion in response to secretin stimulation test, falsely suggesting gastrinoma.
Intervention
Temporarily stop Omeprazole + Sodium Bicarbonate treatment at least 14 days before assessing to allow gastrin levels to return to baseline.

False Positive Urine Tests for THC
Clinical Impact
There have been reports of false positive urine screening tests for tetrahydrocannabinol (THC) in patients receiving PPIs.
Intervention
An alternative confirmatory method should be considered to verify positive results.

Other
Clinical Impact
There have been clinical reports of interactions with other drugs metabolized via the cytochrome P450 system (e.g., cyclosporine, disulfiram).
Intervention
Monitor patients to determine if it is necessary to adjust the dosage of these other drugs when taken concomitantly with Omeprazole + Sodium Bicarbonate.

CYP2C19 or CYP3A4 Inducers
Clinical Impact
Decreased exposure of Omeprazole when used concomitantly with strong inducers.
Intervention
St. John's wort, rifampin: Avoid concomitant use with Omeprazole + Sodium Bicarbonate.
Ritonavir-containing products: See prescribing information for specific drugs.

CYP2C19 or CYP3A4 Inhibitors
Clinical Impact
Increased exposure of Omeprazole.
Intervention
Voriconazole: Dosage adjustment of Omeprazole + Sodium Bicarbonate is not required.

OVERDOSAGE
Omeprazole
Symptoms were transient, and no serious clinical outcome has been reported when Omeprazole was taken alone. No specific antidote for Omeprazole overdosage is known. Omeprazole is extensively protein bound and is, therefore, not readily dialyzable. In the event of overdosage, treatment should be symptomatic and supportive.

Sodium Bicarbonate
Overdosage of sodium Bicarbonate can cause electrolyte abnormalities (hypocalcemia, hypokalemia, hypernatremia), metabolic alkalosis, and seizures. Institute supportive care and correct electrolyte abnormalities.

STORAGE
Do not store above 30ºC.
Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
Risek Insta (Omeprazole + Sodium Bicarbonate) 20mg Powder for Oral Suspension is available as sachets in packs of 50's.
Risek Insta (Omeprazole + Sodium Bicarbonate) 40mg Powder for Oral Suspension is available as sachets in packs of 50's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

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