Central Administration of Pharmaceutical Care
General Administration for Drug Utilization and Pharmacy Practice

Egyptian National Drug Formulary

Gastrointestinal Tract Medications

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Preface

The *Egyptian National Drug Formulary* is published by the **Egyptian Drug Authority (EDA)**. It has been developed by the **General Administration of Drug Utilization and Pharmacy Practice**, under the supervision of the **Central Administration of Pharmaceutical Care**, and reviewed by the **Committee of Pharmacy Practice Guides and National Drug Lists** at the EDA.

The *Egyptian National Drug Formulary* aims to provide pharmacists and other healthcare professionals with accessible, evidence-based, and reliable information on medications available in the Egyptian drug database, supporting sound clinical decision-making and promoting the rational use of medicines across healthcare settings.

This formulary serves as a reference guide that should be applied in conjunction with professional clinical judgment. Every effort has been made to ensure the accuracy and completeness of the information at the time of publication. However, as medical knowledge and best practices continue to evolve, users are encouraged to apply their professional judgment when using this formulary.

Egyptian National Drug Formulary Manual Gastrointestinal Drugs

The Egyptian Drug Formulary (gastrointestinal medications) contains a list of medicines registered in the Egyptian drug database, included in the essential medicines list, or widely used in the Egyptian pharmaceutical market. It is designed as drug monographs classified pharmacologically and arranged alphabetically. There is a pharmacologically classified drug index at the beginning of the document and another alphabetically classified index at the end.

The Egyptian National Drug Formulary (gastrointestinal medications) presents detailed practical information for healthcare providers about each medicine. Each monograph includes:

1. Generic name.
2. Dosage forms/strengths available in Egypt from the EDA database.
3. Route of administration.
4. Pharmacological category and ATC code.
5. Indications: Labeled indications.
6. Dosage regimens for adults and pediatrics.
7. Dosage adjustments if needed.
8. Contraindications.
9. Adverse drug reaction.
10. Monitoring parameters.
11. Drug interactions: That imply avoidance or considering modifications.
12. Pregnancy and lactation.
13. Administration: Detailed administration information for all routes [parenteral (preparation concentrations, compatibility with diluents, infusion rate, precautions during administration), oral (food correlation)].
14. Warnings/precautions.
15. Storage conditions:
    - For reconstituted vials, apply the mentioned storage conditions only if prepared in aseptic techniques and ISO-controlled conditions according to USP 797 standards; otherwise, discard immediately if not used.
    - USP develops standards for compounding medications to help ensure patient benefit and reduce risks such as contamination, infection, or incorrect dosing.

N.B.: Referral to the product leaflet is needed for other specific formulation considerations.

Gastrointestinal Disorders Formulary

This document includes medications that contribute to the management of gastrointestinal disorders. Therapeutic classes include: anti-diarrheal agents, antiemetics, antiflatulent, antispasmodic, bile and liver therapy, acid suppressants, intestinal anti-inflammatory agents, and laxatives, in addition to a miscellaneous group.

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Abbreviations

ACE	Angiotensin-Converting Enzyme
AGEP	Acute Generalized Exanthematous Pustulosis
AIDS	Acquired Immunodeficiency Syndrome
ARB	Angiotensin Receptor Blocker
ATC	Anatomical Therapeutic Chemical
BSA	Body Surface Area
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CgA	Chromogranin A
CIC	Chronic Idiopathic Constipation
CINV	Chemotherapy-Induced Nausea and Vomiting
CLE	Cutaneous Lupus Erythematosus
COVID-19	Coronavirus Disease 2019
CrCl	Creatinine Clearance
CNS	Central Nervous System
CT	Computed Tomography
CYP	Cytochrome P
DRESS	Drug Reaction with Eosinophilia and Systemic Symptoms
ECG	Electrocardiogram
EE	Erosive Esophagitis
ESRD	End-Stage Renal Disease
G-6-PD	Glucose-6 Phosphate Dehydrogenase
GERD	Gastroesophageal Reflux Disease
GI	Gastrointestinal
GIT	Gastrointestinal Tract
gm	Gram
HIV	Human Immunodeficiency Virus
IBD	Inflammatory Bowel Disease
IM	Intramuscular
INR	International Normalized Ratio
IV	Intravenous
mcg	microgram
mcg/kg	microgram per kilogram
m Eq/h	milliequivalents per hour
mg	milligram
m^2	meter square
mL	milliliter

NADH	Nicotinamide Adenine Dinucleotide Hydrogen
NS	Normal Saline
NSAIDs	Non-selective Non-Steroidal Anti-Inflammatory Drugs
PBC	Primary Biliary Cholangitis
PEG	Polyethylene Glycol
PIL	Patient Information Leaflet
PONV	Post-Operative Nausea and Vomiting
PPI	Proton Pump Inhibitors
PT	Prothrombin Time
QTc	Corrected QT Interval
RINV	Radiotherapy-Induced Nausea and Vomiting
SC	Subcutanous
SCLE	Subacute Cutaneous Lupus Erythematosus
SJS	Stevens-Johnson Syndrome
SS	Serotinin Syndrome
TEN	Toxic Epidermal Necrolysis
TIN	Tubulointerstitial Nephritis

Anti-diarrheal Agent

Loperamide

Generic Name	Loperamide
Dosage Form/Strengths	**Oro-dispersible tablet:** 2 mg **Oro-dispersible Film:** 2 mg **Capsule:** 2 mg
Route of Administration	Oral
Pharmacologic Category	Antidiarrheal **ATC:** A07DA03
Indications	N.B. (Pediatrics and treatment for more than 2 days should be under medical advice and follow-up monitoring). • For the symptomatic treatment of acute diarrhoea in adults and children aged **12 years** and over. • For the symptomatic treatment of acute episodes of diarrhoea associated with Irritable Bowel Syndrome IBS in adults aged **18 years** and over, following initial diagnosis by a doctor. • In the adjunctive short-term, control of post-surgical diarrhoea, including ileostomies.
Dosage Regimen	**Acute diarrhea** • **Dosing: Adults** – **Initial dose**: 4 mg, followed by 2 mg after each loose stool. – **Maximum daily dose**: 12-16 mg/day. • **Dosing: Adolescents 12-18 years age** – **Initial**: 2-4 mg, followed by 2 mg after each loose stool. – **Maximum daily dose**: 8-16 mg/day. • **Dosing: Pediatrics 6 to 12 years of age** – **Initial dose** ○ Age 6-8 years (20 to 30 kg): 2 mg twice daily. (4 mg a day). ○ Age 8-12 years (greater than 30kg): 2 mg 3 times daily (6 mg a day). – **Subsequent doses** **Oral**: 1 mg/10 kg body weight administered only after a loose stool. The total daily dosage should not exceed the recommended dosages for the first day. **Chronic diarrhea** • **Dosing: Adults** – **Initial dose**: 4 mg, followed by 2 mg after each loose stool. Dose should be reduced after symptoms are controlled. – **Maintenance dosage (usual dose):** 4 to 8 mg/day.

Loperamide

	N.B. Once diarrhea is controlled, use the lowest dosage required to control symptoms. If clinical improvement is not observed within 48 hours, the patient should consult a physician. After ≥10 days of maximally tolerated dosage (16 mg/day), symptoms are unlikely to be controlled by further administration.
Dosage Adjustment	**Renal Impairment** No dosage adjustment is necessary. Unlikely to be dialyzed. **Hepatic Impairment** No adequate data. Caution. Monitor closely for signs of CNS toxicity.
Contra-indications	• Hypersensitivity to Loperamide or any component of the formulation. • Children <2 years. • Abdominal pain without diarrhea. • Acute dysentery (blood in stools and high fever). • Acute ulcerative colitis. • Bacterial intestinal inflammation caused by pathogens invading the intestinal wall (e.g., Salmonella, Shigella, and Campylobacter) • Diarrhea occurring during or after use of antibiotics (pseudomembranous [antibiotic-associated] colitis) • If inhibition of peristalsis is to be avoided due to the possible risk of significant sequelae, including ileus, megacolon, and toxic megacolon.
Adverse Drug Reactions	**1% to 10%** **Central nervous system**: Dizziness (1%). **Gastrointestinal**: Constipation (2% to 5%), abdominal cramps (≤3%), nausea (≤3%).
Monitoring Parameters	Monitor signs of CNS toxicity in patients with hepatic impairment.
Drug Interactions	***Risk X: Avoid combination*** Kratom. ***Risk D: Consider therapy modification*** Alvimopan, Lonafarnib, Sincalide.
Pregnancy and Lactation	**Pregnancy** No adequate data. Consider the risk/benefit ratio. Avoid use during the first trimester of pregnancy, while it may be used during the second and third trimester of pregnancy. **Lactation** Loperamide is not recommended during lactation as it may appear in breast milk.
Administration	**Oral Administration** **Capsule:** Administer with plenty of fluids to prevent dehydration.

Loperamide

	Oro-dispersible tablet/film: Placed directly onto the tongue to be dissolved and swallowed the medicine with saliva without water intake. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Cardiac disorders** • Avoid use in higher than recommended doses and duration due to the risk of serious cardiac adverse reactions (some are fatal), including QT interval prolongation, Torsades de Pointes, and cardiac arrest. • Avoid use in patients with risk factors for cardiac conditions, including patients with electrolyte abnormalities and patients taking products known to prolong the QT intervals (e.g., antipsychotics, antibiotics...). **Abuse and misuse** Abuse and misuse of loperamide as an opioid substitute have been reported in patients with opioid dependence. Caution. **Dehydration** Prevention of fluid and electrolyte depletion during acute diarrhea is a priority even during loperamide administration. Patients, particularly young children and the elderly, should drink plenty of clear fluids. **Gastrointestinal Disorders** • Loperamide should not be used when inhibition of peristalsis is to be avoided due to the possible risk of significant sequelae, including ileus, megacolon, and toxic megacolon. It must be discontinued immediately when constipation, abdominal distention, or ileus develops. • Loperamide is only a symptomatic treatment. Whenever an underlying etiology can be determined, specific treatment should be given. • Discontinue if diarrhea lasts longer than 2 days with worsening of symptoms, or abdominal swelling or bulging develops, and should consult a healthcare provider. **CNS effects** Loperamide may cause drowsiness or dizziness, which may impair physical or mental abilities; use with caution with activities that require mental alertness.
Storage	Store between 15°C and 30°C. Refer to the manufacturer's PIL if there are specific considerations.

Antiemetics

NK Receptor Antagonists

Aprepitant

Generic Name	Aprepitant
Dosage Form/Strengths	**Capsule (containing immediate release pellets):** 40mg, 125 mg **Capsule**: 80 mg, 125 mg
Route of Administration	Oral
Pharmacologic Category	Antiemetic; Substance P/Neurokinin 1 Receptor Antagonist. ATC: A04AD12.
Indications	1. Aprepitant is used in combination with other medicines in the prevention of **nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy** in adults and adolescents aged 12 and older. 2. Prevention of postoperative nausea and vomiting in adults. **N.B.** Aprepitant has not been studied for the treatment of established nausea and vomiting. **N.B**. Chronic continuous administration of aprepitant is not recommended.
Dosage Regimen	**Doses: Adults and adolescents aged 12 and older** **Prevention of nausea and vomiting associated with highly or moderately emetogenic chemotherapy** ○ **Day 1**: 125 mg 1 hour before chemotherapy. ○ **Days 2 and 3**: 80 mg once daily (1 hour before chemotherapy, or in the morning if no chemotherapy to be given). ○ Aprepitant is taken as part of a regimen that includes a 5-HT3 antagonist (day 1) and a corticosteroid (dexamethasone) (day 1 with moderately emetogenic chemotherapy or day 1 to 4 with highly emetogenic chemotherapy).
Dosage Adjustment	**Renal Impairment** No dose adjustment is necessary with renal impairment or for patients undergoing hemodialysis. **Hepatic Impairment** **Mild to moderate impairment**: No dose adjustment is needed. **Severe impairment**: No data available; may require additional monitoring for adverse reactions.
Contra-indications	• Hypersensitivity to aprepitant or any component of the formulation. • Concurrent use with pimozide.
Adverse Drug Reactions	**>10%** **Hematologic & oncologic**: Neutropenia (children and adolescents: 13%; adults: <3%).

Aprepitant

	Nervous system: Fatigue (children and adolescents: 5%; adults: 13%). **1% to 10%:** **Cardiovascular**: Flushing (<3%), hypotension (PONV: 6%), palpitations (<3%), peripheral edema (<3%). **Dermatologic**: Alopecia (<3%), hyperhidrosis (<3%), skin rash (<3%). **Endocrine & metabolic**: Decreased serum sodium (<3%), dehydration (3%), hot flash (<3), hypokalemia (<3%), weight loss (<3%). **Gastrointestinal**: Abdominal pain (6%), decreased appetite (children and adolescents: 5%; adults: <3%), diarrhea (children and adolescents: 6%; adults: 9%), dysgeusia (<3%), dyspepsia (7%), eructation (<3%), flatulence (<3%), gastritis (<3%), gastroesophageal reflux disease (<3%), hiccups (children and adolescents: 4%; adults: 5%), oral candidiasis (<3%), xerostomia (<3%). **Genitourinary**: Proteinuria (<3%). **Hematologic & oncologic**: Anemia (<3%), febrile neutropenia (<3%), thrombocytopenia (<3%). **Hepatic**: Increased serum alanine aminotransferase (3%), increased serum alkaline phosphatase (<3%), increased serum aspartate aminotransferase (<3%). **Nervous system**: Anxiety (<3%), asthenia (7%), dizziness (children and adolescents: 5%; adults: <3%), headache (4-9%), malaise (<3%), peripheral neuropathy (<3%). **Neuromuscular & skeletal**: Musculoskeletal pain (<3%). **Renal**: Increased blood urea nitrogen (<3%). **Respiratory**: Cough (children and adolescents: 5%; adults: <3%), dyspnea (<3%), oropharyngeal pain (<3%), pharyngitis (<3%).
Monitoring Parameters	• INR and PT in patients who are taking warfarin for 2 weeks, especially the first seven to ten days after starting aprepitant. • Monitor for hypersensitivity reactions and for adverse reactions in patients with severe liver impairment.
Drug Interactions	***Risk X: Avoid Combination*** Asunaprevir, Budesonide (Topical), CYP3A4 Inducers (Strong), CYP3A4 Inhibitors (Moderate), CYP3A4 Inhibitors (Strong), Domperidone, Elacestrant, Eletriptan, Ensartinib, Flibanserin, Fosaprepitant, Grapefruit Juice, Ivabradine, Lemborexant, Lomitapide, Lonafarnib, Methysergide, Nirogacestat, Nisoldipine, Orelabrutinib, Pacritinib, Pimozide, Repotrectinib, Sertindole, Simeprevir. ***Risk D: Consider Therapy Modification*** Acalabrutinib, ALfentanil, Alprazolam, Avanafil, Avapritinib, Brigatinib, Bromocriptine, Budesonide (Systemic), Capivasertib, Cariprazine, Cilostazol, Cisapride, Cobimetinib, Colchicine, Dapoxetine, Daridorexant, Dexamethasone (Systemic), Elexacaftor, Tezacaftor, And Ivacaftor, Eliglustat, Entrectinib, Eplerenone, Fentanyl, Fexinidazole, Fusidic Acid (Systemic), Gepirone,

Aprepitant

	Guanfacine, Hormonal Contraceptives, Ibrutinib, Ivacaftor, Ivosidenib, Lumateperone, Lurasidone, Lurbinectedin, Mavacamten, Methadone, Methylprednisolone, Midazolam, Mitapivat, Mobocertinib, Naloxegol, Olaparib, Omaveloxolone, Palovarotene, Pemigatinib, Pexidartinib, Pralsetinib, Ranolazine, Rimegepant, Selpercatinib, Selumetinib, Sirolimus (Conventional), Sirolimus (Protein Bound), Sonidegib, Suvorexant, Tazemetostat, Tezacaftor and Ivacaftor, Tolvaptan, Triazolam, Ubrogepant, Tezacaftor, and Deutivacaftor, Vardenafil, Vanzacaftor, Venetoclax, Voclosporin, Zanubrutinib.
Pregnancy and Lactation	**Pregnancy** Insufficient human data. No adverse developmental effects were observed in animals. Aprepitant should not be used during pregnancy unless clearly necessary. Non-hormonal methods of contraception should be used during and for a month after administration of aprepitant due to reduced efficacy. **Lactation** No human data. Aprepitant is excreted in the milk of lactating rats. Breastfeeding is not recommended during treatment with aprepitant**.**
Administration	**Oral Administration** The capsule should be swallowed whole. Aprepitant may be taken with or without food. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Hypersensitivity reaction** • There have been reports of hypersensitivity responses, including anaphylactic reactions. • Patients should stop taking aprepitant and seek immediate medical attention if they experience signs of a hypersensitivity reaction, such as rash and itching, skin sores, or difficulty in breathing or swallowing. **Co-administration with warfarin (a CYP2C9 substrate)** • When taking warfarin medication concurrently, there may be a clinically significant decrease in INR or PT. • Monitor INR in patients on chronic warfarin therapy at 7 to 10 days, following initiation of aprepitant with each chemotherapy cycle. **CYP3A4 interactions** • Aprepitant is a substrate, a weak-to-moderate (dose-dependent) inhibitor, and an inducer of CYP3A4. • Use of aprepitant with other drugs that are CYP3A4 substrates may result in increased plasma concentration of the concomitant drug. Caution with narrow therapeutic range agents, such as cyclosporine, tacrolimus, sirolimus, everolimus, alfentanil, ergot alkaloid derivatives, fentanyl, and quinidine. • Use of pimozide is contraindicated due to the risk of significantly increased

Aprepitant

	plasma concentrations of pimozide, potentially resulting in prolongation of the QT interval. • Use of aprepitant with strong or moderate CYP3A4 inhibitors (e.g., ketoconazole, diltiazem) may increase plasma concentrations of aprepitant and its associated adverse reactions. • Use of aprepitant with strong CYP3A4 inducers (e.g., rifampin) may result in a reduction in aprepitant plasma concentrations and decreased efficacy of aprepitant. • Concomitant administration with irinotecan may result in increased toxicity. Caution. **Hormonal Contraceptives** The efficacy of hormonal contraceptives may be reduced during and for a month after administration of aprepitant. Alternative non-hormonal methods of contraception should be used.
Storage	Store between 15°C and 30°C in a dry place. Refer to the manufacturer's PIL if there are specific considerations.

Serotonin Receptor Antagonists

Granisetron

Generic Name	Granisetron
Dosage Form/ Strengths	**Solution for IV injection \Infusion**: 1mg/1ml, 3mg/3ml. **Tablet**: 1mg, 2mg. **Oral Solution**: 1mg/5ml. **Transdermal Patch**: 34.3 mg.
Route of Administration	IV, Oral, Transdermal.
Pharmacologic Category	Antiemetic; Selective 5-HT3 Receptor Antagonist. ATC: A04AA02.
Indications	**Oral** • Prevention and treatment of acute nausea and vomiting associated with chemotherapy and radiotherapy in adults. • Prevention of delayed nausea and vomiting associated with chemotherapy and radiotherapy in adults. **Injection** • Prevention and treatment of - acute nausea and vomiting associated with chemotherapy and radiotherapy in adults and children aged 2 years and above. - post-operative nausea and vomiting in adults. • Prevention of delayed nausea and vomiting associated with chemotherapy and radiotherapy in adults and children aged 2 years and above. **Transdermal** • Prevention of nausea and vomiting associated with moderately or highly emetogenic chemotherapy, for a planned duration of 3 to 5 consecutive days (where oral antiemetic swallowing is difficult).
Dosage Regimen	**Adult dosing** **Oral** • **Oral**: 1 mg twice a day or 2 mg once a day. • The first dose should be taken 1 hour before the start of therapy. • **Duration:** for up to one week following radiotherapy or chemotherapy. **Injection** **Prevention (acute and delayed nausea)** • **IV:** 1-3 mg (10-40 µg/kg) as a slow intravenous injection or as a diluted intravenous infusion given over 5 minutes before the start of chemotherapy. **Treatment (acute nausea)** • **IV:** 1-3 mg (10-40 µg/kg) as a slow intravenous injection or as a diluted intravenous infusion given over 5 minutes.

Granisetron

	• Further maintenance doses of granisetron may be administered at least 10 minutes apart. • **The maximum dose** in 24 hours should not exceed 9 mg. **Post-operative nausea and vomiting (PONV)** • **IV**: 1 mg (10 µg/kg) as slow intravenous injection. • The maximum dose in 24 hours should not exceed 3 mg. • For the prevention of PONV, administration should be completed before the induction of anesthesia **Transdermal patch** Apply a single transdermal patch 24 to 48 hours before chemotherapy, as appropriate. The patch should be removed a minimum of 24 hours after completion of chemotherapy and can be worn for up to 7 days. **Pediatric dosing (IV)** **Treatment and Prevention (acute and delayed nausea)** • **IV**: 10-40 µg/kg (up to 3 mg) as an IV infusion, diluted in 10-30 ml infusion fluid and administered over 5 minutes before the start of chemotherapy. • If required, one additional dose may be administered within 24 hours in not less than 10 minutes after initial infusion.
Dosage Adjustment	**Renal Impairment** No dosage adjustment necessary. **Hepatic Impairment** No dosage adjustment necessary. **Dosing: Adjustment for Toxicity** • Serotonin syndrome: If serotonin syndrome occurs, discontinue 5-HT3 receptor antagonist treatment and begin supportive management. • Transdermal patch: Skin reaction, severe or generalized (allergic rash, including erythematous or papular rash, or pruritus): Remove the patch.
Contra-indications	Hypersensitivity to granisetron or any of the excipients or to other 5-HT_3 receptor antagonists.
Adverse Drug Reactions	**>10%** **Gastrointestinal**: Constipation (IV, oral, transdermal: 3% to 22%; including fecal impaction), nausea (20%), vomiting (12%). **Local**: Injection site reaction (IV: 37% to 62%; including bleeding at injection site [2% to 4%], bruising at injection site [≤45%], erythema at injection site [11% to 17%], hematoma at injection site [≤45%], induration at injection site ≤10%], injection-site infection ≤1%], injection-site nodule [≤18%], injection-site pruritus [≤2%], injection-site scarring [≤2%], irritation at injection site [≤2%], lipohypertrophy at injection site [≤2%], localized vesiculation [≤2%], pain at injection site [3% to 20%], paresthesia [injection site: ≤2%], rash at injection site [≤2%], residual mass at injection site [≤18%], skin discoloration at injection site [≤2%], swelling at injection site [≤10%], tenderness at injection

Granisetron

	site [4% to 27%], warm sensation at injection site [≤2%]). **Nervous system:** Asthenia (IV: 2% to 5%; oral: 14% to 18%), fatigue (IV: 11% to 21%), headache (IV, oral: 9% to 21%; transdermal: 1%). **1% to 10%** **Cardiovascular**: Atrial fibrillation (IV: <3%), flushing (IV: <3%), hypertension (IV, oral: 1% to 2%), prolonged QT interval on ECG (IV, oral, transdermal: 1% to 3%; >450 milliseconds), syncope (IV: <3%). **Dermatologic**: Alopecia (3%), skin rash (IV: 1%). **Gastrointestinal**: Abdominal pain (IV, oral: 4% to 7%), decreased appetite (6%), diarrhea (IV, oral: 4% to 9%), dysgeusia (IV: 2%), dyspepsia (IV, oral: 3% to 6%), gastroesophageal reflux disease (IV: 1% to 5%), pancreatitis (IV: <3%). **Hematologic & oncologic**: Anemia (4%), leukopenia (9%), thrombocytopenia (2%). **Hepatic**: Increased serum alanine aminotransferase (IV, oral: >2 x ULN: 3% to 6%), increased serum aspartate aminotransferase (IV, oral: >2 x ULN: 3% to 5%). **Hypersensitivity**: Hypersensitivity reaction (including anaphylaxis; IV: <3%) **Nervous system**: Agitation (IV: <2%), anxiety (IV, oral: ≤2%), central nervous system stimulation (IV: <2%), dizziness (IV, oral: 3% to 5%), drowsiness (IV, oral: ≤4%), insomnia (IV, oral: 4% to 5%). **Miscellaneous**: Fever (IV, oral: 3% to 9%). **Frequency not defined** **Cardiovascular**: Angina pectoris, atrioventricular block, cardiac arrhythmia, ECG abnormality, hypotension, sinus bradycardia, ventricular ectopy (includes no sustained ventricular tachycardia).
Monitoring Parameters	• Monitor for decreased bowel activity. • Monitor for signs of hypersensitivity and serotonin syndrome. • Monitor both ECG and clinical abnormalities when treating patients with electrolyte abnormalities, congestive heart failure, bradyarrhythmia, or patients taking other medicinal products that lead to QT prolongation.
Drug Interactions	***Risk X: Avoid Combination*** Apomorphine.
Pregnancy and Lactation	**Pregnancy** Limited human data. No evidence of harm in animal studies. As a precautionary measure, it is preferable to avoid the use of granisetron during pregnancy unless clearly needed. **Lactation** No data. It is unknown whether granisetron or its metabolites are excreted in human milk. Breastfeeding should be discontinued during treatment.
Administration	**Administration: IV** Administer IV push over 30 seconds (for adults), or as a diluted infusion over 5 minutes (for adults and children). **Preparation for administration** **Diluted solution for infusion**: The Solution should be diluted to 5 mL per mg in

Granisetron

	neutral saline or 5% dextrose to a volume of 10-30 mL for pediatrics or 20 to 50 mL in adults. **Administration: Oral** Tablets should be swallowed whole with water. Doses should be administered up to 1 hour before initiation of chemotherapy or radiation. **Administration: Transdermal** • Apply patch to clean, dry, nearly hairless, intact skin on the upper outer arm or abdomen. • Do not apply to red, irritated, or damaged skin. • The transdermal patch should not be cut into pieces. • The release liner is removed before application. • If the patch became completely or partially detached, the original transdermal patch should be reattached in the same position using medical tape (if necessary). • Contact with water while bathing or showering will not affect the patch; however, avoid swimming, saunas, hot tubs, and strenuous exercise. • Do not apply heat (e.g., heating pad, heating lamp) over or in the area of the transdermal patch; avoid prolonged exposure to heat. Avoid direct light. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Cardiovascular events** As for other 5-HT_3 antagonists, ECG changes, including QT interval prolongation, have been reported with granisetron. Caution in patients with cardiac co-morbidities, cardiotoxic therapy, and/or concomitant electrolyte abnormalities, as this might lead to clinical consequences. **Gastrointestinal disorders** • Granisetron may reduce lower bowel motility. Caution in patients with signs of sub-acute intestinal obstruction. Monitor. • It may mask a progressive ileus or gastric distension caused by an underlying condition (evaluate risks/benefits in patients who have recently undergone abdominal surgery). **Hypersensitivity** • Granisetron has been associated with hypersensitivity responses (including anaphylaxis, shortness of breath, and urticaria). • Cross-sensitivity between 5-HT_3 antagonists (e.g., ondansetron) has been reported. **Serotonin Syndrome** • 5-HT_3 receptor antagonists have been associated with serotonin syndrome (SS) (some are fatal), mainly when used in conjunction with other serotonergic medications (such as methylene blue, fentanyl, lithium, tramadol, selective serotonin reuptake inhibitors, and serotonin and norepinephrine reuptake inhibitors). • Symptoms include Mental status changes (agitation, hallucinations, delirium,

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	and coma), autonomic instability (e.g., tachycardia), neuromuscular changes (tremors, rigidity), seizures with or without GI symptoms (nausea, vomiting, diarrhea). Monitor. • If developed, discontinue and initiate supportive treatment. **Transdermal Patch** • Local mild reactions may occur and do not require stopping. If a severe or generalized skin reaction (e.g., allergic rash, including erythematous, macular, papular rash or pruritus) develops, patch removal is required. • The granisetron patch could be impacted by either direct natural or artificial sunlight. The patient should cover the patch area for 10 days following its removal. Avoid external heat. • The transdermal patch should only be applied to patients whose chemotherapy treatment (after routine hematological monitoring) is unlikely to be delayed, reducing the possibility of unnecessary exposure to granisetron. **Combination with an adrenocortical steroid** The efficacy of granisetron may be enhanced by an additional corticosteroid, e.g., 8-20 mg dexamethasone or 250 mg methylprednisolone.
Storage	**Injection** • Store between 15°C to 30°C. Do not freeze vials. • After dilution: Stable when mixed in NS or 5% Dextrose for at least 24 hours at room temperature. **Oral** Store tablet or oral solution between 15°C and 30 30°C. **Transdermal patch** • Store between 15°C to 30°C. Protect from light. • Keep the patch in original packaging until immediately before use. Refer to the manufacturer's PIL if there are specific considerations.

Ondansetron

Generic Name	Ondansetron
Dosage Form/ Strengths	**Solution for I.M Injection, IV Injection/Infusion:** 4mg/2ml, 8mg/4ml **Tablet:** 4 mg, 8 mg, 24 mg **Orally disintegrating, dispersible, or fast-melting tablet**: 4 mg, 8 mg **Oral soluble film**: 4 mg, 8 mg **Oral Syrup or solution**: 4 mg/5 ml **Rectal Suppositories:** 16 mg
Route of Administration	Oral, Parenteral, Rectal
Pharmacologic Category	Antiemetic; Selective 5-HT_3 Receptor Antagonist **ATC:** A04AA01
Indications	• Management and prevention of nausea and vomiting associated with emetogenic chemotherapy or radiotherapy in adults (IV, Oral, Rectal) and in children aged ≥6 months (IV, Oral). • Prevention and treatment of postoperative nausea and vomiting (PONV) in adults (IV, Oral) and in children aged ≥ 1 month (IV only).
Dosage Regimen	**Doses in adults** **Chemotherapy and radiotherapy induced nausea and vomiting** **Oral**: 8 mg administered 30 minutes (up to 2 hours) before chemotherapy, and 1 to 2 hours before radiation treatment. After 8 hours, it can be followed by 8 mg doses either every 12- or 8-hours during therapy. **IV**: 8 mg immediately before treatment. • Given either as a slow IV injection (over not less than 30 seconds) or as a short IV infusion over 15 minutes. • Initial dose can be followed by two further IV injections of 8 mg orally every twelve hours. **Rectal**: 8 mg can be continued every 12 hours up to 5 days to protect against delayed or prolonged emesis. **Highly Emetogenic Chemotherapy** **Oral**: A single 24-mg dose given 30 minutes (up to 2 hours) before the start of single-day chemotherapy. **IV**: Single dose of 8 mg over not less than 30 seconds (or maximum 16 mg diluted infusion over 15 minutes) immediately before chemotherapy. Initial dose can be followed by two further IV injections of 8 mg four hours apart, or by a constant infusion of 1 mg/hour for up to 24 hours. **N.B**. To protect against delayed emesis, oral or rectal doses may be given 8 mg every 12 hours up to 5 days. **N.B.** The efficacy of ondansetron in highly emetogenic chemotherapy may be

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enhanced by the addition of a single IV dose of dexamethasone, 20 mg, administered before chemotherapy.

N.B. A single dose greater than 16 mg must not be given due to a dose-dependent increase in QT-prolongation risk.

Postoperative Nausea and Vomiting (PONV) in adults

Oral: 16 mg given 1 hour before induction of anesthesia.

IV or IM: 4 mg over at least 30 seconds (undiluted) before, at, or after induction of anesthesia.

N.B. For the treatment of established PONV, IV or IM administration is recommended

Doses in pediatrics

Chemotherapy-induced nausea and vomiting (CINV) (6 months to 17 years of age)

N.B. The dose for CINV can be calculated based on (BSA) or weight, or fixed dosing.

- **Dosing by body surface area (BSA)**

Initial: IV single dose: 5 mg/m^2 given immediately before chemotherapy (must not exceed 8 mg) over 15 minutes.

Oral dosing can start 12 hours later and may be continued for up to 5 days.

BSA	Days 1-6 starting after 12 hours of IV dose
< 0.6 m^2	2 mg syrup every 12 hours
> 0.6 m^2 to ≤ 1.2 m^2	4 mg syrup or tablet every 12 hours
> 1.2 m^2	8 mg syrup or tablet every 12 hours

- **Dosing by body weight**

Initial: IV single dose: 0.15 mg/kg given immediately before chemotherapy (must not exceed 8 mg) over 15 minutes. Two further IV doses may be given in 4-hourly intervals.

Oral dosing can commence 12 hours later and may be continued up to 5 days.

Weight	Day 1	Days 2-6
≤ 10 kg	Up to 3 doses of 0.15 mg/kg IV every 4 hours	2 mg syrup every 12 hours
> 10 kg	Up to 3 doses of 0.15 mg/kg IV every 4 hours	4 mg syrup or tablet every 12 hours

- **Fixed dosing**

Indication	Dosage Regimen
Moderately Emetogenic Chemotherapy	• **12 to 17 years age**: **Oral**: 8 mg given 30 minutes before starting chemotherapy, with a subsequent 8-mg dose 8 hours after the first dose. **Then** 8 mg twice a day for 1 to 2 days after completion of chemotherapy. • **4 to 11 years age**: 4 mg given 30 minutes before starting chemotherapy, with subsequent 4-mg doses

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	4 and 8 hours after the first dose. **Then** administer 4 mg 3 times a day for 1 to 2 days after completion of chemotherapy.

N.B. The total daily dose over 24 hours must not exceed the adult dose of 32 mg.

Prevention of PONV in pediatric patients (aged 1 month to 17 years)

IV: Single dose 0.1 mg/kg up to a maximum of 4 mg (over at least 30 seconds) prior to, at or after induction of anesthesia.
Patients of 12 years of age and above may be given a 4 mg IM dose instead of IV.

Treatment of PONV after surgery in pediatric patients (aged 2 years and above)

IV: Single dose 0.1 mg/kg up to a maximum of 4 mg (over at least 30 seconds).

Doses in geriatrics

- **In patients 65 and older**: All IV doses should be diluted in 50-100 ml of infusion fluid and infused over 15 minutes.
- **In patients 75 years or older:** IV doses of ondansetron should not exceed 8 mg.

Dosage Adjustment

Renal impairment
No dose adjustment is needed**.**

Hepatic impairment

- **Mild impairment**: No dose adjustment is needed**.**
- **Moderate to severe impairment**: It is recommended not to exceed a total daily dose of 8 mg (oral or parenteral).

Contra-indications

- Hypersensitivity to ondansetron or any component of the formulation.
- Concomitant use with Apomorphine.

Adverse Drug Reactions

>10%

Gastrointestinal: Constipation (9% to 11%).
Nervous system: Fatigue (oral: ≤13%), headache (9% to 24%), malaise (oral: ≤13%)

1% to 10%

Dermatologic: Pruritus (2% to 5%), skin rash (1%).
Gastrointestinal: Diarrhea (oral: 6%; IV: children 1 to 24 months of age: 2%).
Genitourinary: Gynecologic disease (oral: 7%), urinary retention (oral: 5%).
Hepatic: Increased serum alanine aminotransferase (>2 times ULN: 1% to 5%; transient), increased serum aspartate aminotransferase (>2 times ULN: 1% to 5%; transient).
Hypersensitivity: Anaphylaxis (<2%).
Local: Injection site reaction (4%; includes burning sensation at injection site, erythema at injection site, injection site pain).
Nervous system: Agitation (oral: ≤6%), anxiety (oral: ≤6%), dizziness (7%),

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	drowsiness (IV: ≤8%), paresthesia (IV: 2%), sedated state (IV: ≤8%), sensation of cold (IV: 2%). **Respiratory**: Bronchospasm (<2%), hypoxia (oral: 9%). **Miscellaneous**: Fever (2% to 8%). **<1%** **Cardiovascular**: Hypotension. **Nervous system**: Extrapyramidal reaction. **Frequency not defined** **Cardiovascular**: Angina pectoris, peripheral vascular disease, tachycardia. **Endocrine & metabolic**: Hypokalemia. **Nervous system**: Tonic-clonic epilepsy.
Monitoring Parameters	• Monitor for decreased bowel activity. • Monitor for signs of hypersensitivity and serotonin syndrome. • Monitor both ECG and clinical abnormalities when treating patients with electrolyte abnormalities, congestive heart failure, bradyarrhythmia, or patients taking other medicinal products that lead to QT prolongation. • Signs /symptoms of myocardial ischemia.
Drug Interactions	***Risk X: Avoid combination*** Apomorphine, Domperidone, Levoketoconazole, Pimozide, Piperaquine, Sertindole, Thioridazine. ***Risk D: Consider therapy modification*** Amiodarone, QT-prolonging Agents (Highest Risk), QT-prolonging Class IA Antiarrhythmics (Highest Risk), QT-prolonging Class III Antiarrhythmics (Highest Risk).
Pregnancy and Lactation	**Pregnancy** Ondansetron should not be used during the first trimester of pregnancy due to the risk of oral clefts. **Lactation** No human data. Breastfeeding during treatment with ondansetron is not recommended unless the benefits and possible risks are considered.
Administration	**Administration: Intramuscular** Should be given undiluted. **Administration: Intravenous** • **IV push:** IV injection as an undiluted solution over at least 30 seconds but preferably over 2 to 5 minutes. • **IV infusion:** Infuse diluted solution over 15 minutes. o Adults: Dilute in 50 – 100 mL dextrose 5% or NS. o Pediatrics: Dilute in 25 to 50 ml dextrose 5% or NS. **Administration: Oral** Administer without regard to meals. • **Oral dosage forms** should be given 30 minutes (up to 2 hours in adults) before chemotherapy; 1 to 2 hours before radiation; and 1 hour before induction of anesthesia. Bioavailability is slightly enhanced by the presence of food. • **Orally disintegrating forms:** The tablet (or film) should be placed on top of the tongue. It will disperse within seconds, then swallow.

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	Administration: Rectal Suppository: Bowel is better to be emptied before administration. N.B. Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Hypersensitivity Reactions** • Reactions including anaphylaxis and bronchospasm have been reported. Monitor and treat immediately until signs and symptoms resolve. • Cross-sensitivity between 5-HT_3 antagonists has been reported. **QT Interval Prolongation and Torsade de Pointes** • Ondansetron prolongs the QT interval dose-dependently. Risk increases with a single dose greater than 16 mg. Avoid ondansetron in patients with congenital long QT syndrome. Torsade de Pointes has been reported. • Caution should be taken and ECG monitored when ondansetron is administered to patients who have or may develop prolongation of QTc, including patients with electrolyte abnormalities, congestive heart failure, bradyarrhythmia, or patients taking other medicinal products that lead to QT prolongation. • Hypokalemia and hypomagnesemia should be corrected before ondansetron administration. **Serotonin Syndrome** • 5-HT_3 receptor antagonists have been associated with serotonin syndrome (SS) (some are fatal), mainly when used in conjunction with other serotonergic medications (such as methylene blue, fentanyl, lithium, tramadol, selective serotonin reuptake inhibitors, and serotonin and norepinephrine reuptake inhibitors). • Symptoms include Mental status changes (agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia), neuromuscular changes (tremors, rigidity), seizures with or without GI symptoms (nausea, vomiting, diarrhea). Monitor. • If developed, discontinue and initiate supportive treatment. **Myocardial Ischemia** • Cases of myocardial ischemia have been reported immediately after patients treated with ondansetron, especially in the case of IV administration. Do not exceed the recommended infusion rate and monitor patients during and after administration. Symptoms are mostly resolved with prompt treatment. • Patients should be alerted to the signs and symptoms of myocardial ischemia after oral administration. **Masking of Progressive Ileus and Gastric Distension** • The use of ondansetron in patients may mask a progressive ileus and gastric distension. Monitor for decreased bowel activity, particularly in patients with risk factors for gastrointestinal obstruction.

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	• In patients with adenotonsillar surgery prevention of nausea and vomiting with ondansetron may mask occult bleeding. Therefore, such patients should be followed carefully after ondansetron.
Storage	• **Suppository:** Store below 30 °C. Store in the original package. • **Oral Dispersible Tablet:** Store below 30°C in a dry place. • **Oral soluble film**: Store below 30°C. • **Oral solution**: Store below 30°C in the original package. Protect from light. • **Tablet**: Store below 30°C. • **Vial**: Store below 30°C. Protect from light. • **After dilution**: use immediately. Other recommendations may vary according to the product manufacturer. Refer to the manufacturer's PIL if there are specific considerations.

Palonosetron

Generic Name	Palonosetron
Dosage Form/ Strengths	**Solution for IV injection or Infusion:** 0.05 mg/mL (1.5 mL, 5 mL) **Capsules:** 0.5 mg
Route of Administration	**IV, Oral**
Pharmacologic Category	Antiemetic; Selective 5-HT3 Receptor Antagonist ATC: A04AA05
Indications	**Oral** • Prevention of acute and delayed nausea and vomiting associated with moderately emetogenic cancer chemotherapy in adults. • Prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based chemotherapy in adults. **IV** • Prevention of acute nausea and vomiting associated with highly emetogenic cancer chemotherapy (in patients 1 month of age and older). • Prevention of acute and delayed nausea and vomiting associated with moderately emetogenic cancer chemotherapy (in patients 1 month of age and older).
Dosage Regimen	**Adult dosing** • **Chemotherapy-Induced Nausea and Vomiting** **IV**: 0.25 mg as a single dose over 30 seconds, given 30 minutes before the start of chemotherapy. **Oral**: 0.5 mg taken 1 hour before the start of the chemotherapy cycle. • **Postoperative Nausea and Vomiting** **IV**: 0.075 mg as a single dose over 10 seconds immediately before the induction of anesthesia. **Pediatric dosing** (aged 1 month to 17 years) **Chemotherapy-Induced Nausea and Vomiting** **IV infusion**: 20 mcg/kg administered as a single dose over 15 minutes, given 30 minutes before the start of chemotherapy. The maximum total dose should not exceed 1500 micrograms.
Dosage Adjustment	**Renal impairment** No dose adjustment is necessary. **Hepatic impairment** • No dose adjustment is necessary. • End-stage renal disease with hemodialysis: No available data.
Contra-indications	Hypersensitivity to the active substance or to any of the excipients.

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Adverse Drug Reactions	**1% to 10%** **Cardiovascular**: Bradycardia (≤1%), distended vein (≤1%), extrasystoles (≤1%), hypertension (≤1%), hypotension (≤1%), ischemic heart disease (≤1%), nonsustained ventricular tachycardia (≤1%), prolonged QT interval on ECG (5%), sinoatrial nodal rhythm disorder (≤1%), sinus tachycardia (≤1%), supraventricular extrasystole (≤1%), vein discoloration (≤1%). **Dermatologic**: Allergic dermatitis (infants, children, adolescents, and adults: ≤1%), pruritus (≤1%), skin rash (≤1%). **Endocrine & metabolic**: Electrolyte disturbance (≤1%), hot flash (≤1%), hyperglycemia (≤1%), hyperkalemia (≤1%), hypokalemia (≤1%), metabolic acidosis (≤1%). **Gastrointestinal**: Abdominal pain (≤1%; including upper abdominal pain), anorexia (≤1%), constipation (5%), decreased appetite (≤1%), decreased gastrointestinal motility (≤1%), diarrhea (≤1%), dyspepsia (≤1%), flatulence (≤1%), hiccups (≤1%), motion sickness (≤1%), sialorrhea (≤1%), xerostomia (≤1%). **Genitourinary**: Glycosuria (≤1%), urinary retention (≤1%). **Hepatic**: Increased liver enzymes (≤1%; including increased serum alanine aminotransferase, increased serum aspartate aminotransferase), increased serum bilirubin (≤1%). **Nervous system**: Anxiety (≤1%), asthenia (≤1%), chills (≤1%), dizziness (infants, children, adolescents, and adults: ≤1%), drowsiness (≤1%), euphoria (≤1%), headache (adults: 9%; infants, children, and adolescents <1%), hypersomnia (≤1%), paresthesia (≤1%). **Neuromuscular & skeletal**: Arthralgia (≤1%), laryngospasm (≤1%). **Ophthalmic**: Amblyopia (≤1%), eye irritation (≤1%). **Otic**: Tinnitus (≤1%). **Respiratory**: Flu-like symptoms (≤1%), hypoventilation (≤1%). **Miscellaneous**: Fever (≤1%).
Monitoring Parameters	• Monitor for decreased bowel activity. • Monitor for signs of serotonin syndrome.
Drug Interactions	***Risk X: Avoid combination*** Apomorphine
Pregnancy and Lactation	**Pregnancy**: No human data. No harmful effects in animal studies. **Lactation**: No data. Consider risk and benefit.
Administration	**IV administration** • May be diluted with 0.9% sodium chloride solution for infusion. • Inspect visually for particulate matter and discoloration before administration. **Oral administration** Capsule can be taken with or without food. N.B. Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Hypersensitivity Reactions** • Reactions, including anaphylaxis, have been reported. Monitor and treat

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	immediately until signs and symptoms resolve. • Cross-sensitivity between 5-HT_3 antagonists has been reported. **Serotonin Syndrome** • 5-HT_3 receptor antagonists have been associated with serotonin syndrome (SS) (some are fatal), mainly when used in conjunction with other serotonergic medications (such as methylene blue, fentanyl, lithium, tramadol, selective serotonin reuptake inhibitors, and serotonin and norepinephrine reuptake inhibitors). • Symptoms include mental status changes (agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia), neuromuscular changes (tremors, rigidity), and seizures with or without GI symptoms (nausea, vomiting, diarrhea). Monitor. • If developed, discontinue and initiate supportive treatment. **QT Interval Prolongation** • Palonosetron did not induce clinically relevant prolongation of the QTc interval in healthy volunteers at all dose levels tested. • However, as for other 5-HT3 antagonists, caution should be exercised in the use of palonosetron in patients who are at risk of developing prolongation of the QT interval. Hypokalemia and hypomagnesemia should be corrected before 5-HT3-antagonist administration. **GIT effects** Monitor for decreased bowel activity, particularly in patients with risk factors for gastrointestinal obstruction.
Storage	Store between 15 and 30 °C. Protect from freezing. Protect from light. Refer to the manufacturer's PIL if there are specific considerations.

Dopamine Receptor Antagonists

Domperidone

Generic Name	Domperidone
Dosage Form/Strengths	**Oral suspension:** 5 mg/ 5 ml **Film-coated tablet:** 10 mg alone and in combination with (ergotamine tartrate 1 mg, paracetamol 250 mg, caffeine anhydrous 50 mg) **Oro-dispersible tablets:** 10 mg **Effervescent granules:** 10 mg **Soft gelatin capsule:** 10 mg **Rectal suppository:** 30 mg
Route of Administration	*Oral, Rectal*
Pharmacologic Category	• Dopamine Antagonist; Gastrointestinal Agent, Prokinetic • ATC: A03FA03
Indications	• Relief of the symptoms of nausea and vomiting.
Dosage Regimen	**Adults and adolescents (12 years of age and older and weighing 35 kg or more)** Tablets/capsule:10 mg up to three times per day with a maximum daily dose of 30 mg per day. Suspension: 10 ml up to three times per day with a maximum daily dose of 30 ml per day. Granules: 10 mg sachet up to three times a day for a maximum dose of 3 sachets per day. Suppository: 30 mg twice daily • Children < 12 years and adolescents weighing less than 35 Kg are not recommended. • Domperidone should be used at the lowest effective dose for the shortest duration necessary to control nausea and vomiting, maximum duration of one week. Check the dosage regimen in the manufacturer's labelling of combination products available.
Dosage Adjustment	**Altered kidney function** • Mild to moderate impairment: No dosage adjustments • Severe impairment: On repeated administration, the dosing frequency should be reduced to once or twice daily depending on severity. **Hepatic impairment** Mild (Child-Pugh 5 to 6): Dose modification is not needed Moderate (Child-Pugh 7 to 9) or severe (Child-Pugh > 9): Contraindicated

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Contra-indications	• Hypersensitivity to domperidone or to any of the excipients • Indications in which stimulation of gastric motility is dangerous, e.g., gastrointestinal haemorrhage, mechanical obstruction, or perforation • Patients with prolactin-releasing pituitary tumors (prolactinoma) • Patients with moderate or severe hepatic impairment • Patients who have known existing prolongation of cardiac conduction intervals, particularly QTc, patients with significant electrolyte disturbances, or underlying cardiac diseases such as congestive heart failure. • Co-administration with QT-prolonging drugs, except apomorphine. • Co-administration with ketoconazole, erythromycin, or other potent CYP3A4 inhibitors (regardless of their QT-prolonging effects), such as fluconazole, voriconazole, clarithromycin, and amiodarone. • Confirmed or suspected pheochromocytoma due to the risk of severe hypertension episodes. **Suppository:** In the first months of life, when the metabolic functions of the blood-brain barrier are not fully developed, the risk of neurological side effects in young children is higher.
Adverse Drug Reactions	1% to 10% • Dermatologic: Pruritus, skin rash, urticaria • Endocrine and metabolic: Galactorrhea not associated with childbirth, gynecomastia, hot flash, increased thirst, menstrual disease • Gastrointestinal: Abdominal pain, acid regurgitation, change in appetite, constipation, diarrhea, dyspepsia, nausea, stomatitis, xerostomia • Genitourinary: Mastalgia • Nervous system: Dizziness, headache, insomnia, irritability, lethargy, migraine, nervousness • Ophthalmic: Conjunctivitis
Monitoring Parameters	• Renal function; ECG (baseline and then periodically during therapy). Check monitoring parameters in the manufacturer's labelling in case of combination products available.
Drug Interactions	*Risk X: Avoid combination* CYP3A4 Inhibitors (Strong), Grapefruit Juice, Haloperidol, Lefamulin, Levoketoconazole, Ondansetron, Pentamidine (Systemic), Pimozide, Posaconazole, QT-prolonging Agents (Highest Risk, Moderate Risk), QT-prolonging Moderate, strong CYP3A4 Inhibitors, Sertindole, Triptorelin. *Risk D: Consider therapy modification* CYP3A4 Inhibitors (Moderate), Fusidic Acid (Systemic)
Pregnancy and Lactation	Pregnancy considerations There is little post-marketing data on the use of domperidone in pregnant women. The potential risk for humans is unknown. Therefore, it should only be used in pregnancy if justified by the expected therapeutic benefit.

Domperidone

	Lactation considerations Domperidone passes into breast milk in very small amounts (<0.1% of the maternal dose), but cardiac adverse effects in the infant cannot be ruled out Caution should be exercised in case of QTc prolongation risk factors in breast-fed infants.
Administration	• Domperidone should be used at the lowest effective dose for the shortest duration necessary to control nausea and vomiting. • It is recommended to take oral domperidone 15-30 minutes before meals. If taken after meals, absorption of the drug is somewhat delayed. • If a scheduled dose is missed, the missed dose should be omitted and the usual dosing schedule resumed. The dose should not be doubled to make up for a missed dose. • Usually, the maximum treatment duration should not exceed one week. Refer to the manufacturer's PIL if there are specific considerations
Warnings/ Precautions	**Altered cardiac conduction** Domperidone may be associated with an increased risk of serious ventricular arrhythmias or sudden cardiac death, particularly with doses >30 mg or when used in patients >60 years of age. Use the lowest possible dose for the shortest duration necessary. **Elevated prolactin levels** May increase prolactin levels (dose-dependent response); may be asymptomatic (clinical consequence of chronically elevated prolactin is unknown) or may present symptomatically as galactorrhea, gynecomastia, amenorrhea, or impotence (reversible upon decreasing dose or discontinuing drug). Use is contraindicated in patients with prolactinomas. **Hepatic impairment** Undergoes extensive hepatic metabolism; use is contraindicated in patients with moderate to severe hepatic impairment; use with caution in mild impairment. **Renal impairment** Use with caution in patients with severe renal impairment; dosage and/or frequency of administration may need to be adjusted with repeated use and/or long-term therapy. Monitor renal function regularly, particularly with long-term therapy.
Storage	Store at a temperature not exceeding 25 °C. Store in the original container or package to protect from moisture. Refer to the manufacturer's PIL if there are specific considerations.

Metoclopramide

Generic Name	Metoclopramide
Dosage Forms/ Strengths	**Tablets, Scored tablet**: 10 mg **Oral solution**: 1 mg/1 ml **Oral drops**: 1mg/1 mL, 2 mg/1 ml **Rectal Suppositories**: 10 mg, 20 mg **Solution for IM or IV Injection:** 10 mg/2 ml
Route of Administration	Oral, Rectal, Parenteral
Pharmacologic Category	Antiemetic; Dopamine Antagonist; Gastrointestinal Agent, Prokinetic; Serotonin 5-HT4 Receptor Agonist. **ATC:** A03FA01
Indications	**Oral** **Adults** • Prevention of delayed chemotherapy-induced nausea and vomiting (CINV). • Prevention of radiotherapy-induced nausea and vomiting (RINV). • Symptomatic treatment of nausea and vomiting, including acute migraine-induced nausea and vomiting. **Pediatrics** • Prevention of delayed chemotherapy-induced nausea and vomiting (CINV). **Injection/ Rectal** **Adults** • Prevention of post-operative nausea and vomiting (PONV). • Prevention of radiotherapy-induced nausea and vomiting (RINV). • Symptomatic treatment of nausea and vomiting, including acute migraine-induced nausea and vomiting. **Pediatrics** • Prevention of post-operative nausea and vomiting (PONV) • Treatment of established postoperative nausea and vomiting (PONV) as a second-line option. • Prevention of delayed chemotherapy-induced nausea and vomiting (CINV) as a second-line option. **N.B.** Pediatric indications are considered only as a second-line option.
Dosage Regimen	**Adult dosing** **Nausea and vomiting indications** **Oral, IV, IM**: 10 mg, repeated up to three times daily. Maximum daily dose: 30 mg or 0.5mg/kg body weight. Maximum duration: 5 days. **Rectal:** The usual dose of conventional formulations is 10 mg up to 3 times daily. The maximum dose in 24 hours is: 0.5 mg per kg body weight. The maximum recommended duration of treatment is 5 days. A minimum interval of 6 hours between 2 administrations must be respected, even in case of vomiting or rejection of the dose.

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	Pediatric Dosing **Pediatric patients aged 1-18 years** **Nausea and vomiting indications (as a second-line agent)** • **Oral, IM, IV:** 0.1 to 0.15 mg/kg, repeated up to three times daily. • **Maximum dose**: 0.5 mg/kg in 24 hours. **Maximum duration:** 48 hours for (PONV) (injection). **Maximum duration:** 5 days for (CINV) (oral or injection). N.B. The safety and efficacy of Metoclopramide in children below 1 year have not yet been established.
Dosage Adjustment	**Elderly** A dose reduction should be considered, taking into account the kidney and liver function and overall fragile health. **Renal Impairment** **Nausea and vomiting indications** • **CrCl >60 mL/minute:** No dosage adjustment necessary. • **CrCl >15 to 60 mL/minute** (Moderate to severe impairment): Dose should be reduced by 50%. • **CrCl ≤ 15 ml/min** (End-stage renal disease): Daily dose should be reduced by 75%. **Gastroesophageal reflux disease (GERD)** • **CrCl >60 mL/minute:** No dosage adjustment necessary. • **CrCl ≤ 60 mL/minute** (Moderate or severe renal impairment)**:** 5 mg four times daily or 10 mg taken three times daily. Maximum: 30 mg/day. • **End-Stage Renal Disease (ESRD),** including those treated with hemodialysis and continuous ambulatory peritoneal dialysis: 5 mg four times daily or 10 mg twice daily. Maximum dose: 20 mg/ day. **Acute and Recurrent Diabetic Gastroparesis** • **CrCl >60 mL/minute:** No dosage adjustment necessary. • **CrCl ≤ 60 mL/minute** (Moderate or severe renal impairment)**:** 5 mg four times daily. Maximum: 20 mg/day. • **End-Stage Renal Disease (ESRD),** including those treated with hemodialysis and continuous ambulatory peritoneal dialysis: 5 mg twice daily. Maximum: 10 mg/day. **Hepatic impairment** **Nausea and vomiting indications** • **Mild hepatic impairment:** No dose adjustments necessary. • **Severe hepatic impairment**: Dose should be reduced by 50%. **Gastroesophageal reflux disease (GERD)** • **Mild hepatic impairment (Child-Pugh A):** No dose adjustments necessary.

Metoclopramide

	• **Moderate or severe hepatic impairment (Child-Pugh B or C):** 5 mg four times daily or 10 mg taken three times daily. Maximum: 30 mg/day. **<u>CYP2D6 poor metabolizers, or Concomitant use with strong CYP2D6 inhibitors (e.g., quinidine, bupropion, fluoxetine, and paroxetine)</u>** **Gastroesophageal Reflux Disease (GERD)** **Oral**: 5 mg four times daily, or 10 mg taken three times daily. Maximum dose: 30 mg/day. **Acute and Recurrent Diabetic Gastroparesis** **Oral**: 5 mg four times daily. Maximum dose: 20 mg/day.
Contra-indications	• Hypersensitivity to metoclopramide or any component of the formulation. • Circumstances in which gastrointestinal (GI) motility stimulation may be hazardous, such as mechanical GI obstruction, perforation, or hemorrhage. • Pheochromocytoma (confirmed or suspected), due to the risk of severe hypertension episodes. • History of neuroleptic or metoclopramide-induced tardive dyskinesia. • Epilepsy. • Parkinson's disease. • Combination with levodopa or dopaminergic agonists. • Known history of methemoglobinemia with metoclopramide or NADH cytochrome b5 deficiency. • Use in neonates or children aged < 1 year due to an increased risk of extrapyramidal disorders and methemoglobinemia. **N.B.** Metoclopramide should not be used during the first three to four days following operations such as pyloroplasty or gut anastomosis to avoid vigorous muscular contractions, which may not help healing.
Adverse Drug Reactions	**<u>>10%</u>** **Nervous system:** Drowsiness (10% to 70%), dystonic reaction (≤25%; dose and age related). **<u>1% to 10%</u>** **Nervous system (**dose related**):** Fatigue (10%), lassitude (10%), restlessness (10%).
Monitoring Parameters	• Kidney functions. • Liver functions. • Signs of cardiac or nervous disorders.
Drug Interactions	***Risk X: Avoid combination*** Anti-Parkinson Agents (Dopamine Agonist), Antipsychotic Agents, Cabergoline, Droperidol, Mavorixafor, Metyrosine, Monoamine Oxidase Inhibitors, Promethazine, Rivastigmine, Tetrabenazine, Trimetazidine, Triptorelin. ***Risk D: Consider therapy modification*** Atovaquone, CYP2D6 Inhibitors (Strong), Primaquine, Thiopental.

Metoclopramide

Pregnancy and Lactation	**Pregnancy** • Metoclopramide can be used during pregnancy if clinically needed, as human data reveal no harm. Administration at the end of pregnancy, extrapyramidal syndrome in the newborn cannot be excluded. • Maternal administration during delivery should be avoided. Monitor neonates for extrapyramidal signs if metoclopramide is used. **Lactation** • Limited human data. Infants have experienced adverse effects. Metoclopramide is therefore not recommended during lactation. • During lactation, discontinuation of metoclopramide should be considered.
Administration	**IV or IM Administration** • The solution can be administered intravenously or intramuscularly. • IV doses should not be administered in less than 3 minutes to reduce the risk of adverse effects (e.g., hypotension, akathisia). • Dilute if needed with compatible solution, e.g., sodium chloride (preferred), dextrose 5% or 4%, lactated Ringer solutions. **Oral Administration** • Dose should be administered 30 minutes before meals and at bedtime. • A minimal interval of 6 hours between two doses is to be respected, even in case of vomiting of the dose. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Cardiac Disorders** • Serious cases have been reported, particularly after the IV route administration (including cases of circulatory collapse, severe bradycardia, cardiac arrest, and QT prolongation). • Electrolyte disturbances (hypokalemia, hyperkalemia, hypomagnesemia) or bradycardia increases the proarrhythmic risk. Caution. • At any signs of cardiac symptoms, the patient should consult their physician. **Neurological Disorders** Avoid concomitant use of other drugs known to cause neurological disorders, and avoid use in patients with Parkinson's Disease. If symptoms occur, metoclopramide should be discontinued, and immediate medical treatment should be started. • **Tardive dyskinesia** Treatment should not exceed 3 months because of the risk of tardive dyskinesia. Tardive dyskinesia, which may be irreversible, may occur with prolonged treatment, especially in the elderly. If clinical signs of tardive dyskinesia appeared, metoclopramide should be discontinued. • **Other Extrapyramidal disorders** ○ Extrapyramidal disorders may occur, particularly in children and young adults or when high doses are used. These effects may occur at any time during therapy.

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- Metoclopramide should be discontinued immediately if extrapyramidal symptoms have developed. These effects are reversible after treatment discontinuation, but may require a symptomatic treatment (benzodiazepines in children or anti-Parkinson anticholinergics in adults).

- **Neuroleptic malignant syndrome**
  Metoclopramide should be discontinued immediately if symptoms of neuroleptic malignant syndrome develop, and appropriate treatment should be started.

Depression

Depression has occurred in patients with or without a history of depression, after administration of metoclopramide. Symptoms have included suicidal ideation and suicide. Avoid use in patients with a history of depression.

Methemoglobinemia

- If developed, metoclopramide should be immediately and permanently discontinued, and appropriate treatment should be started (e.g., methylene blue but not in G6PD-deficient patients).
- Risk factor is Nicotinamide Adenine Dinucleotide Hydrogen (NADH)-cytochrome b5 reductase deficiency.

Renal and Hepatic Impairment

In patients with renal impairment or with severe hepatic impairment, a dose reduction is recommended.

Hypertension

Metoclopramide may increase blood pressure. Avoid use in patients with hypertension or in patients taking monoamine oxidase inhibitors. Discontinue in any patient with a rapid rise in blood pressure.

Fluid retention

Patients with cirrhosis or congestive heart failure may be at risk of developing fluid retention and volume overload due to a transient increase in plasma aldosterone. Discontinue if any of these adverse reactions occur.

Precautions

If vomiting persists, the possibility of an underlying disorder should be excluded, e.g., cerebral irritation.

Elderly

A dose reduction should be considered according to the kidney and liver function and overall fragile health.

Prolactin levels

Metoclopramide may cause elevation of serum prolactin levels during prolonged treatment, which may be asymptomatic or symptomatic. Clinical

Metoclopramide

	signs include amenorrhea, galactorrhea, gynecomastia, or impotence. **Effects on the Ability to Drive and Operate Machinery** Metoclopramide may impair the mental and/or physical abilities required for the performance of hazardous tasks such as operating machinery or driving a motor vehicle.
Storage	**Injection** • Store between 15°C to 30°C. Protect from light. • All dilutions may be stored under normal light conditions up to 24 hours after preparation. **Oral dosage forms** • Store between 15°C to 30°C. Protect from light and moisture. • Do not freeze the oral solution. **Rectal dosage forms** Store between 15°C and 30°C. Refer to the manufacturer's PIL if there are specific considerations.

Itopride

Generic Name	Itopride
Dosage Form/ Strengths	**Tablets**: 50 mg
Route of Administration	Oral
Pharmacologic Category	Gastrointestinal Agent, Prokinetic ATC: A03FA07
Indications	Treatment of gastrointestinal symptoms of functional, caused by gastric dysmotility and delayed gastric emptying, like sensation of bloating, early satiety, postprandial fullness, upper abdominal pain or discomfort, anorexia, heartburn, nausea, and vomiting: functional non-ulcer dyspepsia or chronic gastritis.
Dosage Regimen	**Adult dosing** **Oral**: 50 mg three times daily. This dose can be reduced according to the patient's age and symptoms if required. **Maximum duration**: 8 weeks. **Pediatrics** The safety and efficacy of itopride in pediatrics has not been established.
Dosage Adjustment	**Renal Impairment** Monitor carefully. Dose may be reduced or discontinued in case of adverse effects. **Hepatic Impairment** Monitor carefully. Dose may be reduced or discontinued in case of adverse effects.
Contra-indications	• Hypersensitivity to the active substance or to any of the excipients. • Patients in whom increased gastrointestinal motility could be harmful, e.g., in patients with gastrointestinal hemorrhage, mechanical obstruction, or perforation
Adverse Drug Reactions	**0.1-1%** **Endocrine disorders**: Hyperprolactinemia. **Psychiatric disorders**: Irritability. **Nervous system disorders:** Headache, sleep disorders, dizziness. **Gastrointestinal disorders:** Diarrhea, constipation, abdominal pain, hypersalivation. **Musculoskeletal and connective tissue disorders:** Chest or back pain. **Renal and urinary disorders:** BUN (blood urea nitrogen) and creatinine increased. **Miscellaneous:** Fatigue.
Monitoring Parameters	No monitoring data needed.
Drug Interactions	**Notes**

Itopride

	• Itopride has a gastrokinetic effect that could influence the absorption of concomitantly orally administered medicines. Caution in narrow therapeutic index, medicines with prolonged-release and enteric-coated drug formulations. • Anticholinergic agents may reduce the action of itopride.
Pregnancy and Lactation	**Pregnancy** No data. Only use if therapeutic benefits outweigh possible risks. **Lactation** No data. Use is not recommended during lactation.
Administration	Tablets should be swallowed whole with a sufficient amount of liquid. N.B. Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Cholinergic effects** Itopride potentiates acetylcholine action and can induce side cholinergic effects. **Safety issues** Data about long-term administration of itopride is not available. **Effects on the ability to drive and use machines** No effects, but impairment of alertness cannot be excluded since dizziness may occur very rarely.
Storage	Store between 15-30 ^{o}C. Protect from moisture. Refer to the manufacturer's PIL if there are specific considerations.

Serotonin-4 Agonists

Prucalopride

Generic Name	Prucalopride
Dosage Form/Strengths	**Film-coated tablets:** 1mg, 2 mg
Route of Administration	Oral
Pharmacologic Category	Gastrointestinal Agent, Prokinetic; Serotonin 5-HT4 Receptor Agonist ATC: A06AX05
Indications	Symptomatic treatment of Chronic Idiopathic Constipation (CIC) in adults in whom laxatives fail to provide adequate relief.
Dosage Regimen	**Dosing: Adult** 2 mg once daily. * Due to the specific mode of action of prucalopride (stimulation of propulsive motility), exceeding the daily dose of 2 mg is not expected to increase efficacy. * In case of prolonged treatment (> 3 months), the benefit should be reassessed at regular intervals. **Dosing: Children** – Prucalopride should not be used in children and adolescents younger than 18 years
Dosage Adjustment	• **Dosing: elderly (> 65 years)** – Start with 1 mg once daily; if needed, the dose can be increased to 2 mg once daily. • **Dosing: Altered Kidney Function** – No dose adjustment is required for patients with mild to moderate renal impairment. – Severe renal impairment (CrCl <30 mL/minute): 1 mg once daily – ESRD requiring hemodialysis: Avoid use. • **Dosing: Hepatic Impairment** – Mild to moderate hepatic impairment: No dose adjustment is required for patients. – Severe hepatic impairment (Child-Pugh class C): Start with 1 mg once daily, which may be increased to 2 mg if required to improve efficacy and if the 1 mg dose is well tolerated.
Contra-indications	• Hypersensitivity to the active ingredient or to any of the excipients. • Renal impairment requiring dialysis. • Intestinal perforation or obstruction due to structural or functional disorder of the gut wall, obstructive ileus, severe inflammatory conditions of the intestinal

Prucalopride

	tract, such as Crohn's disease, ulcerative colitis, and toxic megacolon/megarectum.
Adverse Drug Reactions	• **>10%:** – Gastrointestinal: Abdominal pain, nausea, diarrhea – Nervous system: Headache • **1% to 10%:** – Gastrointestinal: Abdominal distension, abnormal bowel sounds, decreased appetite, flatulence, vomiting – Genitourinary: Pollakiuria – Nervous system: Dizziness, fatigue, migraine
Monitoring Parameters	• Frequency of bowel movements; worsening of depression or emergence of suicidal thoughts and behavior.
Drug Interactions	• Risk X: Avoid combination None. • Risk D: Consider therapy modification: None.
Pregnancy and Lactation	• **Pregnancy** – There is a limited amount of data from the use of prucalopride in pregnant women. – Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (including pregnancy, embryonal development, parturition, or postnatal development). – Prucalopride is not recommended during pregnancy. • **Lactation** – Prucalopride is excreted in human milk. – At therapeutic doses of prucalopride, no effects on breast-fed newborns/infants are anticipated. – In the absence of human data in women who actively breastfed while taking prucalopride, it can be taken when the potential benefits outweigh the potential risks.
Administration	• To be taken orally. • May be administered with or without food. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	• Women of childbearing potential have to use effective contraception during treatment with prucalopride. • Use with caution in severe renal or hepatic impairment.

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	• Use with caution in patients with severe and unstable concomitant disease (e.g., cardiovascular or lung disease, neurological or psychiatric disorders, cancer or AIDS, and other endocrine disorders) or in patients with a history of arrhythmias or ischaemic cardiovascular disease. • Women of childbearing potential using oral contraceptives have to use a different effective method of contraception in case of severe diarrhea to avoid potential oral contraceptive failure. • Monitor all patients treated with prucalopride for persistent worsening of depression or the emergence of suicidal thoughts and behaviors.
Storage	• Store in the original container to protect from moisture. • Keep out of the reach of children. Refer to the manufacturer's PIL if there are specific considerations.

Glucocorticoids: Dexamethasone, refer to the endocrine system formulary

You can access it through the following link

https://edaegypt.gov.eg/media/wcbezfpv/4-new-code-endocrine-egyptian-national-formulary.pdf

Antiflatulent

Simethicone

Generic Name	Simethicone
Dosage Form /Strengths	**Chewable Tablets:** 40 mg, 125 mg **Oro-dispersible Film**: 62.5 mg **Oral Drops:** 20 mg/ 1mL, 40 mg, 66.6 mg/ 1mL **Oral Suspension**: 42 mg/ 5mL **Oral Emulsion:** 100 mg/ 5mL
Route of Administration	Oral
Pharmacologic Category	Antiflatulent
Indications	Symptomatic relief of flatulence, wind pains, bloating, abdominal distension, and other symptoms associated with intestinal gas.
Dosage Regimen	**Adults, the elderly, and children:** **Oral:** 100- 200 mg taken 3 or 4 times daily or as required.
Dosage Adjustment	**Renal Impairment** No dose adjustment necessary. The drug is not absorbed. **Hepatic Impairment** No dose adjustment necessary. The drug is not absorbed.
Contra-indications	Hypersensitivity to Simethicone or to any of the ingredients.
Adverse Drug Reactions	Minor adverse effects: nausea and constipation.
Monitoring Parameters	No monitoring data needed.
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	**Pregnancy and Lactation** Not absorbed. Not anticipated that it will cause any harm during pregnancy and lactation. However, as with all drugs, caution should be exercised in these conditions.
Administration	**Oral Administration** **Chewable tablet:** Chew thoroughly and swallow. **Suspension (drops**): Shake well before using. May mix with 30 mL of water or other liquids. **Strips**: Allow to dissolve on the tongue.

Simethicone

	N.B. Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Benzyl alcohol and derivatives** Some dosage forms may contain sodium benzoate/benzoic acid;
Storage	Store below 30ºC. Protect from moisture. Refer to the manufacturer's PIL if there are specific considerations.

Antispasmodic

Hyoscine-N-butyl bromide/ Scopolamine butylbromide

Generic Name	Hyoscine-N-butyl bromide/ Scopolamine butylbromide
Dosage Form /Strengths	**Solution for I.M., S.C., or Slow IV injection:** 20 mg/mL **Tablet:** 10 mg **Oral Syrup:** 5 mg/5mL **Rectal Suppositories:** 15 mg
Route of Administration	Oral, Parenteral, Rectal
Pharmacologic Category	Anticholinergic Agent. ATC: A03BA03
Indications	**Injection (adult only)** • Treatment of acute spasm, as in renal or biliary colic. • To reduce spasm and pain during radiology diagnosis, e.g., pyelography, and other diagnostic procedures, e.g., gastroduodenal endoscopy. **Oral** • Relief of spasm of the genitourinary tract or gastrointestinal tract. • Symptomatic relief of irritable bowel syndrome.
Dosage Regimen	**Adult dosing** **Oral** • **Initial:** 10 mg three times daily. • Dose can be increased up to 20 mg four times daily if necessary. **Injection** • **IV, IM:** 20 mg, repeated after half an hour if necessary. • In endoscopy, this dose may need to be repeated more frequently. • **Maximum** daily dose is 100 mg. **Pediatric dosing (6-12 years)** **Oral**: 10 mg three times daily. **N.B.** should not be taken on a continuous daily basis or for extended periods without investigating the cause of abdominal pain.
Dosage Adjustment	**Renal impairment** No dose adjustments required. Caution. **Hepatic impairment** No dose adjustments required. Caution.
Contra-Indications	• Hypersensitivity to the active substance or to any of the excipients • Narrow-angle glaucoma • Mechanical stenosis in the gastrointestinal tract • Paralytic or obstructive ileus • Megacolon • Myasthenia gravis

Hyoscine-N-butyl bromide/ Scopolamine butylbromide

	• Prostate hypertrophy with urinary retention • Tachycardia
Adverse Drug Reactions	**>10%** **Gastrointestinal**: Xerostomia (29% to 67%). **Nervous system**: Dizziness (12%), drowsiness (8% to 17%). **1% to 10%** **Nervous system**: Agitation (6%), confusion (4%). **Ophthalmic**: Mydriasis (4%), visual impairment (5%). **Respiratory**: Pharyngitis (3%).
Monitoring Parameters	• Intraocular pressure in patients with open-angle glaucoma. • Monitor for intestinal or urinary obstruction, and monitor for CNS adverse reactions.
Drug Interactions	***Risk X: Avoid combination*** Aclidinium, Azelastine (Nasal), Bromperidol, Cimetropium, Dronabinol, Eluxadoline, Flunarizine, Glycopyrrolate (Oral Inhalation), Glycopyrronium (Topical), Ipratropium (Oral Inhalation), Kratom, Levosulpiride, Nabilone, Noscapine, Olopatadine (Nasal), Orphenadrine, Oxatomide, Oxomemazine, Paraldehyde, Potassium Chloride, Potassium Citrate, Pramlintide, Revefenacin, Sofpironium, Thalidomide, Umeclidinium. ***Risk D: Consider therapy modification*** Articaine, Blonanserin, Buprenorphine, Chlormethiazole, Clozapine, Daridorexant, Dexmedetomidine, Droperidol, Flunitrazepam, Hydroxyzine, Lemborexant, Loxapine, Methotrimeprazine, Opioid Agonists, Oxybate Salt Products, Oxycodone, Rivastigmine, Ropeginterferon Alfa-2b, Secretin, Suvorexant, Zolpidem, Zuranolone.
Pregnancy and Lactation	**Pregnancy** Limited human and animal data. As a precautionary measure, it is not recommended during pregnancy. **Lactation** Limited data. Use of Hyoscine butyl bromide during breastfeeding is not recommended.
Administration	**Oral administration** Tablets should be swallowed whole with adequate water. **Intramuscular or Subcutaneous Administration (IM, SC)** • Administer without dilution. • Injection site pain may occur, particularly after intramuscular use.

Hyoscine-N-butyl bromide/ Scopolamine butylbromide

	• Avoid IM administration in patients receiving anticoagulant therapy to avoid hematoma. **Intravenous Administration (IV)** • Intravenous injection should be performed slowly to avoid a potentially severe infusion reaction (i.e., hypotension). • May be used diluted with glucose 5% or with sodium chloride 0.9% solution for injection. N.B. Refer to the manufacturer's PIL for other specific considerations.
Warnings/ Precautions	**Cardiovascular disorders** • Hyoscine butylbromide can cause tachycardia, hypotension, and anaphylaxis. • Use with caution in patients with cardiac conditions such as cardiac failure, coronary heart disease, cardiac arrhythmia, or hypertension, and in cardiac surgery. Monitoring of these patients is recommended. **Anticholinergic effects** • Caution should be used in patients susceptible to intestinal or urinary outlet obstructions. Discontinue if the patient develops difficulty in urination. • Anticholinergics may reduce sweating. Caution in patients with pyrexia. • Elevation of intraocular pressure may occur in untreated narrow-angle glaucoma patients. Patients should have urgent ophthalmological advice if they develop a painful, red eye with loss of vision. • Consider more frequent monitoring during treatment in patients receiving other anticholinergic drugs **Neuropsychiatric effects** • May cause psychiatric and cognitive effects. Seizures and impaired mental abilities may occur. Monitor for new or worsening psychiatric symptoms. • Use with caution with tasks that need alertness as driving. Drowsiness, dizziness, and blurred vision may occur. **The patient should seek medical advice in case of** Severe, unexplained abdominal pain persists or worsens, with or without symptoms like fever, nausea, vomiting, changes in bowel movements, abdominal tenderness, decreased blood pressure, fainting, or blood in stool. **Hypersensitivity reactions** Parenteral administration of hyoscine butylbromide may be associated with anaphylaxis and shock. Monitor.

Hyoscine-N-butyl bromide/ Scopolamine butylbromide

	Pediatric, elderly, hepatic, or renal impairment patients Use with caution. These patients are particularly susceptible to the adverse reactions of scopolamine.
Storage	**Injection** • Store at a temperature not exceeding 30°C. • After opening, any unused solution must be discarded. **Tablet** Store at a temperature not exceeding 30°C. Protect from light and moisture. **Syrup** Store at a temperature not exceeding 30°C. **Suppository** Store at a temperature not exceeding 30°C, in a dry place. Refer to the manufacturer's PIL if there are specific considerations.

Mebeverine

Generic Name	Mebeverine
Dosage Form/ Strengths	**Tablets:** 100 mg, 135 mg **Modified Release capsule or tablet:** 200 mg **Oral Suspension:** 50 mg/ 5mL
Route of Administration	Oral
Pharmacologic Category	Antispasmodic Agent, Gastrointestinal **ATC Code:** A03AA04
Indications	• Symptomatic treatment of irritable bowel syndrome and other included conditions, such as chronic irritable colon, spastic constipation, nervous diahrres, mucous colitis, and spastic colitis. Symptoms include abdominal pain and cramps, persistent, non-specific diarrhea (with or without alternating constipation), and flatulence. • Symptomatic treatment of gastrointestinal spasms secondary to functional disorders of GIT and bile ducts.
Dosage Regimen	**Adult dosing** **Immediate release forms** **Oral**: 100-150 mg three times daily, preferably 20 minutes before meals. **N.B.** The dose may be gradually reduced after several weeks of symptomatic relief. **Modified-release forms** (used for irritable bowel syndrome) **Oral**: 200 mg twice daily (morning and evening). **Duration** of use is not limited. **Pediatric dosing** **Children 10 years and above** **Oral suspension**: 150 mg three times daily, preferably 20 minutes before meals. The dose may be gradually reduced after several weeks of symptomatic relief.
Dosage Adjustment	**Renal impairment** No dosage adjustment is necessary. **Hepatic impairment** No dosage adjustment is necessary.
Contra-indications	Hypersensitivity to mebeverine or any component of the formulation.
Adverse Drug Reactions	• **Allergic reactions,** mainly but not exclusively limited to the skin • **Immune system disorders:** Hypersensitivity

Mebeverine

	• **Skin and subcutaneous tissue disorders:** Urticaria, angioedema, face edema, exanthema.
Monitoring Parameters	No monitoring is needed.
Drug Interactions	No interaction studies have been performed.
Pregnancy and Lactation	**Pregnancy** Limited data. Mebeverine is not recommended during pregnancy. **Lactation** No data**.** Mebeverine is not recommended during breastfeeding.
Administration	**Oral administration** **Immediate release forms (suspension or tablets)**: Administered preferably 20 minutes before meals. **Tablets and capsules** • Do not crush or chew immediate or modified-release capsules/tablets. • Tablets and capsules should be swallowed whole with at least 100 mL of water. **Suspension** • Shake well before use. N.B. Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	• Mebeverine solid dosage forms are not recommended to be used in children and adolescents < 18 years of age. • Some formulations may contain fructose, sucrose, or lactose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption, or sucrose-isomaltase insufficiency should not take the solid dosage forms of this medicine.
Storage	Store at a temperature not exceeding 30 °C. Refer to the manufacturer's PIL if there are specific considerations.

Dicyclomine (Dicycloverine)

Generic Name	Dicyclomine (Dicycloverine) hydrochloride
Dosage Form/ Strengths	**Oral syrup:** 10 mg/5mL **Tablets:** 10 mg, 20 mg
Route of Administration	Oral
Pharmacologic Category	Anticholinergic Agent ATC: A03AA07
Indications	Antispasmodic for the treatment of functional conditions involving smooth muscle spasm of the GIT.
Dosage Regimen	**Adult Dosing** **Oral**: 10 – 20 mg three times daily before or after meals. **Pediatric Dosing** **Children (2-12 years)** **Oral:** 10 mg three times daily. **Children (6 months - 2 years)** **Oral:** 5 – 10 mg three or four times daily, 15 minutes before feeds. The maximum daily dose: 40 mg.
Dosage Adjustment	**Renal Impairment** No dosage adjustments. Unlikely to be significantly dialyzable. Not studied. Caution. **Hepatic Impairment** No dosage adjustments. Not studied. Caution.
Contra-indications	• Hypersensitivity to active ingredients or any of the excipients. • Known idiosyncrasies to the active ingredients. • Infants <6 months of age.
Adverse Drug Reactions	**>10%** **Gastrointestinal**: Nausea (14%), xerostomia (33%). **Nervous system**: Dizziness (40%). **Ophthalmic**: Blurred vision (27%). **1% to 10%** **Nervous system**: Drowsiness (9%), nervousness (6%). **Neuromuscular and skeletal**: Asthenia (7%).
Monitoring Parameters	Monitor for anticholinergic effects, intestinal or urinary obstruction, and CNS adverse reactions.
Drug Interactions	***Risk X: Avoid combination*** Aclidinium, Cimetropium, Dronabinol, Eluxadoline, Glycopyrrolate (Oral Inhalation), Glycopyrronium (Topical), Ipratropium (Oral Inhalation), Levosulpiride, Oxatomide, Potassium Chloride, Potassium Citrate, Pramlintide, Revefenacin, Sofpironium, Tiotropium, Umeclidinium.

Dicyclomine (Dicycloverine)

	Risk D: Consider therapy modification Clozapine, Rivastigmine, Secretin, Sincalide.
Pregnancy and Lactation	**Pregnancy** Studies have not shown fetal harm upon 40 mg/day in first-trimester pregnant women or higher doses in animals. Dicyclomine should be used during pregnancy only if clearly needed, as teratogenicity cannot be excluded. **Lactation** No data. Caution due to potential toxicity.
Administration	**Oral Administration** • Adults and children above 2 years: Taken with or without food. • Children (6 months - 2 years): Taken 15 minutes before feeds. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Anticholinergic effects** • Caution in patients with or suspected of having glaucoma. Patients should have urgent ophthalmological advice if they develop a painful, red eye with loss of vision. • Caution in patients with prostatic hypertrophy and in patients susceptible to urinary outlet obstructions. • Anticholinergics may reduce sweating. Fever and heat prostration may occur in high-temperature environments. • Caution in patients with hiatus hernia associated with reflux esophagitis because anticholinergic drugs may aggravate the condition. • Treatment with this drug to control diarrhea (an early symptom of intestinal obstruction) would be inappropriate and possibly harmful in this case. **Neuropsychiatric effects** • May cause psychiatric and cognitive effects. Seizures and impaired mental abilities may occur. Monitor for new or worsening psychiatric symptoms. • Use with caution with tasks that need alertness as driving. Drowsiness, dizziness, and blurred vision may occur. **Infants** • Serious respiratory reactions, central nervous system symptoms, and deaths have been reported following administration to infants; use in infants <6 months of age is contraindicated. **Hereditary problems** • This medicine may contain lactose. Patients with rare hereditary problems of fructose intolerance, glucose, galactose malabsorption, or sucrase-isomaltase insufficiency should not take this medicine.
Storage	• **Tablet:** Store between 15-30°C. Protect light. • **Oral solution:** Store between 15-30°C in the original container. Refer to the manufacturer's PIL if there are specific considerations.

Trimebutine

Generic Name	Trimebutine
Dosage Form/Strengths	• **Oral Suspension:** 24 mg/5 mL • **Tablets:** 100 mg, 200 mg • **I.M. and I.V. Injection:** 50 mg
Route of Administration	**Oral, IM, IV**
Pharmacologic Category	**Pharmacologic category:** Antispasmodic Agent, Gastrointestinal; Opioid Agonist, Peripherally-Acting **ATC Classification:** A03AA05
Indications	• Treatment and relief of pain, transit disorders, and intestinal discomfort associated with functional intestinal disorders.
Dosage Regimen	**Dosing: Adults, adolescents, and children ≥12 years:** • **Oral:** – Initial dose: 100 mg every 8 hours taken before meals. – Maximum dose: 200 mg every 8 hours. • **IM, IV:** One ampoule during the acute phase.
Dosage adjustment	• **Dosing: Altered Kidney Function:** – **Oral:** No dose adjustment is needed. – **IM and IV:** Use with caution in renal impairment. • **Dosing: Hepatic Impairment:** – **Oral**: No dose adjustment is needed. – **IM and IV**: Use with caution in hepatic impairment.
Contra-indications	• Hypersensitivity to the active ingredient. • Children under 2 years of age.
Adverse Drug Reactions	• **1% to 10%:** – Central nervous system: Mood change, dizziness, drowsiness, fatigue, feeling hot, sensation of cold, taste disorder. – Gastrointestinal: Constipation, diarrhea, dyspepsia, epigastric distress, nausea, xerostomia.
Monitoring Parameters	• None
Drug Interactions	• **Risk X: Avoid combination** None. • **Risk D: Consider therapy modification:** None.
Pregnancy and Lactation	• **Pregnancy:** ○ **Oral:** – Animal studies have not shown any teratogenic effect.

Trimebutine

	– Currently, there are no sufficient and relevant data to evaluate the possible malformities or fetotoxic effects of trimebutine when administered during pregnancy. – As a precaution, trimebutine should not be used during the first trimester of pregnancy. – During the 2nd and 3rd trimesters, trimebutine should only be used, if necessary, as no harmful effect is expected for the mother or child. ○ **IM/ IV:** – If the product contains benzyl alcohol, it can cross the placenta, and the teratogenic risk of benzyl alcohol has not been studied. In addition, in pregnant women, there is a risk of accumulation and toxicity of benzyl alcohol that may cause metabolic acidosis. – t is preferable not to use the injection during pregnancy. • **Lactation:** – It is unknown whether trimebutine passes into breast milk. – As a precaution, it is preferable to avoid using trimebutine while breastfeeding.
Administration	• **Oral:** Administer before meals. • **IM/ IV:** It must be administered slowly for over 3 to 5 minutes. **N.B** Refer to the manufacturer's PIL if there are specific considerations**.**
Warnings/ Precautions	• Use with caution in tasks that require mental alertness (e.g., operating machinery or driving), because it may cause CNS depression, which may impair physical or mental abilities • In IM and IV administration, use with caution in patients with hepatic or kidney impairment.
Storage	• **Oral:** Store at room temperature of 15°C to 30°C • **IM & IV:** Store in a refrigerator (between 2°C and 8°C). Refer to the manufacturer's PIL if there are specific considerations**.**

Bile and Liver Therapy

Ursodeoxycholic

Generic Name	Ursodeoxycholic acid
Dosage Form/ Strengths	**Tablets**: 250 mg, 450 mg, 500 mg **Capsules**: 250 mg, 300 mg, 450 mg, 500 mg **Prolonged Release Tablet**: 450 mg **Oral Suspension**: 250 mg/5mL
Route of Administration	Oral
Pharmacologic Category	Gallstone Dissolution Agent ATC: A05AA02
Indications	**Adults** • The dissolution of cholesterol stones in patients: - With one or more X-ray radiolucent (X-ray negative) gallstones, preferably with a diameter of not more than 2 cm, in a well-functioning gall bladder. - Refusing a surgical procedure or in which surgical intervention is not indicated. - With whom an oversaturation of cholesterol has been shown by chemical analysis of the bile produced by duodenum drainage. • Primary Biliary Cholangitis or primary biliary cirrhosis. **Pediatrics** The safety and effectiveness in pediatric patients have not been established.
Dosage Regimen	**Adult dosing** • **Primary Biliary cirrhosis (PBC)** **Oral**: 12-16 mg/ kg body weight daily. For the first 3 months of treatment, treatment should be taken in 3 divided doses. Subsequently, the dose may be taken once daily in the evening. **Duration**: The use of ursodeoxycholic acid in PBC may be continued indefinitely. • **Dissolution of Gallstones** **Oral**: 8 to 12 mg/kg/day The daily dose can be administered either one, two, or three times after meals. A dose should be taken in the evening after the evening meal. **Duration**: usually not less than 3-4 months and up to 24 months, depending on size and composition. Treatment should be continued until 2 successive cholecystograms and/or ultrasound investigations 4-12 weeks apart demonstrate the disappearance of gallstones. **N.B.** Non-cholesterol stones account for 10-15% of radiolucent stones and may not be dissolved by bile acids. **Pediatric dosing** **Hepatobiliary disorders associated with cystic fibrosis (1 month to 18 years)** **Oral**: 20 mg/kg/day in 2-3 divided doses, with a further increase to 30 mg/kg/day if necessary.

Ursodeoxycholic

Dosage Adjustment	**Renal Impairment** No dosage adjustment needed. **Hepatic Impairment** There is no dosage adjustment needed.
Contra-indications	• Hypersensitivity to the active substance or to any of the excipients. • Acute inflammation of the gall bladder or bile ducts. • Occlusion of the biliary tract (occlusion of the common bile duct or a cystic duct). • Frequent episodes of biliary colic. • Radio-opaque calcified gallstones. • Impaired contractility of the gallbladder (Non-functioning gall bladder). • Active gastric and duodenal ulcers.
Adverse Drug Reactions	**>10%** **Gastrointestinal**: Constipation (10% to 26%), diarrhea (1% to 27%), dyspepsia (3% to 17%), nausea (5% to 17%). **Nervous system**: Dizziness (17%), headache (25%). **Neuromuscular & skeletal**: Back pain (12%). **Respiratory**: Upper respiratory tract infection (12% to 16%). **1% to 10%** **Dermatologic**: Alopecia (5%), skin rash (3%). **Endocrine and metabolic**: Increased serum glucose (1%). **Gastrointestinal**: Cholecystitis (5%), peptic ulcer (1%), vomiting (10%). **Genitourinary**: Urinary tract infection (7%). **Hematologic and oncologic**: Leukopenia (3%), thrombocytopenia (1%). **Hypersensitivity**: Hypersensitivity reaction (5%). **Neuromuscular and skeletal**: Arthritis (6%), musculoskeletal pain (6%) **Renal**: Increased serum creatinine (1%). **Respiratory**: Bronchitis (7%), cough (7%), flu-like symptoms (7%), pharyngitis (8%).
Monitoring Parameters	• **Primary biliary cholangitis**: Liver functions baseline and monthly first 3 months, then every 3 months thereafter. • **Gallstone disease:** Liver functions and ultrasonography every six months.
Drug Interactions	***Risk D: Consider therapy modification*** Aluminum Hydroxide, Bile Acid Sequestrants, Sincalide.
Pregnancy and Lactation	**Pregnancy** Limited human data. Teratogenicity appeared during the early phase of gestation in animal studies. Ursodeoxycholic acid must not be used during pregnancy, unless clearly necessary. **Lactation** Ursodeoxycholic acid levels in breast milk are extremely low, based on the few known cases of breastfeeding women, and it is unlikely that breastfed infants will have any negative side effects.

Ursodeoxycholic

Administration	**Administration: Oral** • Tablets and capsules should be taken with food. Do not chew. • Do not administer with aluminum-based antacids or bile acid sequestrants. If use is necessary, administer any of these agents 2 hours before or after ursodeoxycholic acid. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**When used for the treatment of the advanced stage of primary biliary cirrhosis** • Symptoms may worsen rarely at the start of treatment, e.g., the itching may increase. In this case, the dose should be reduced to 250 mg daily and then gradually increased to the recommended dose described. If diarrhea occurs, the dose must be reduced while in the case of persistent diarrhea, the therapy should be discontinued. • Monitor liver function periodically to evaluate response to treatment and detect early signs of potential hepatic deterioration. **When used for the dissolution of cholesterol gallstones** • Ursodeoxycholic should not be used if the gall bladder cannot be visualized on X-ray images, or in cases of calcified gallstones, impaired contractility of the gall bladder, or frequent episodes of biliary colic. • Oral cholecystography with ultrasonography 6-10 months after the beginning of treatment and at 6-month intervals is needed to assess the dissolution of gallstones and to timely identify a possible calcification of the stones. • The time required for dissolution of gallstones ranges from 6 to 24 months, depending on stone size and composition. **Hormonal contraceptives** Female patients taking ursodeoxycholic acid for dissolution of gallstones should use an effective non-hormonal contraceptive, since hormonal contraceptives may increase biliary lithiasis.
Storage	Store between 15°C and 30°C. Protect from moisture. Refer to the manufacturer's PIL if there are specific considerations.

Acid Suppressants

H2-Receptor Antagonists

Famotidine

Generic Name	Famotidine
Dosage Form/ Strengths	• **Tablets:** 20 mg, 40 mg • **Oro-dispersible Film**: 20 mg, 40 mg • **Powder for Oral Suspension**: 40 mg/5 mL • **Effervescence Powder**: 20 mg/sachet • **Effervescent Granules:** 20 mg/sachet • **Solution for IM, IV injection, and IV infusion**: 20 mg • **Concentrate for Solution for IV Injection or Infusion**: 20 mg
Route of Administration	Oral, IV, IM
Pharmacologic Category	Histamine H_2 Antagonist **ATC:** A02BA03
Indications	**Adults (oral or injection)** • Duodenal ulcers (treatment and prevention of relapse). • Benign gastric ulcers. • Treatment of pathological hypersecretory conditions (e.g., Zollinger-Ellison syndrome, multiple endocrine neoplasias). • Treatment of gastroesophageal reflux disease (GERD). **Adults and children over 12 years (oral only)** Treatment and prevention of heartburn associated with acid indigestion and sour stomach. **Pediatrics (1 year of age and older) (oral or injection)** • Treatment of peptic ulcer (duodenal or gastric ulcers). • Treatment of GERD with or without esophagitis and ulcerations. **Pediatrics (from birth to less than 1 year of age) (oral only)** Treatment of GERD
Dosage Regimen	**Adult Oral Dosing**

Active duodenal ulcers	40 mg once daily; or 20 mg twice daily (for 4-8 weeks).
Prevention of relapses of duodenal ulcer	20 mg once daily at night (for a year or as clinically indicated).
Active gastric ulcer	40 mg once daily at night (for 4-8 weeks unless earlier healing is confirmed).
Zollinger-Ellison syndrome and other Pathological Hypersecretory	20 mg every 6 hours; adjust to patient needs (up to 800 mg daily for a year).

Famotidine

Conditions	
GERD	20 mg twice daily (mild, nonerosive); or 40 mg twice daily (moderate, erosive) for 6 weeks (may extend further 6 weeks if not healed).
Heartburn	20 mg once daily (maximum 40 mg a day) for not more than 3 months, as it may be indicative of a more serious disease.

Adult Parenteral Dosing

- **Hospitalized patients with pathological hypersecretory conditions or intractable ulcers, or in patients who are unable to take oral medication,**
  IV: 20 mg every 12 hours until oral therapy can be instituted.
  In some pathological hypersecretory conditions, patients, a higher starting dose may be required.
- **GERD**
  Doses for parenteral use in patients with GERD have not been established.

Pediatric Oral Dosing

Peptic ulcer disease	**1 year to less than 17 years** **Initial**: 0.5 mg/kg once daily; or 0.25 mg/kg twice daily; may be increased to 1 mg/kg once daily at bedtime or 0.5 mg/kg twice daily. **Duration**: 8 weeks. **Maximum**: 40 mg per day.
GERD	**Birth to less than 3 months** **Initial:** 0.5 mg/kg once daily; may be increased to 1 mg/kg once daily, up to 8 weeks. **3 months to less than 1 year** **Initial**: 0.5 mg/kg twice daily; may be increased to 1 mg/kg twice daily; Maximum of 40 mg per day; up to 8 weeks. **1 year to less than 17 years** (with or without esophagitis and ulcerations) **Oral**: 0.5 mg/kg twice daily, maximum of 40 mg twice daily; for 6 to 12 weeks.

Pediatric parenteral dosing (1-16 years)

- **Peptic ulcer**
  IV: 0.25 mg/kg (up to 0.5 mg) every 12 hours. Maximum: 40 mg/day.
- **GERD**
  Doses for parenteral use in patients with GERD have not been established.

Famotidine

Dosage Adjustment	**Renal Impairment** **Oral** **CrCl ≥30 mL/minute:** No dosage adjustment is necessary. **CrCl <30 mL/minute:** Administer 50% or less of the usual dose. **Injection form** **CrCl ≥50 mL/minute:** No dosage adjustment is necessary. **CrCl <50 mL/minute:** Administer 50% or less of the usual dose **or** continue the usual dose but increase the dosing interval to every 36 to 48 hours. **Dialysis patients:** Doses should be administered after hemodialysis-on-hemodialysis days. **Hepatic Impairment** No dosage adjustments are needed.
Contra-indications	Hypersensitivity to famotidine, other H_2 antagonists, or any component of the formulation.
Adverse Drug Reactions	**>10%** **Nervous system**: Agitation (infants). **1% - 10%** **Gastrointestinal (GI):** Constipation (1%), diarrhea (2%). **Nervous system:** Dizziness (1%), headache (5%).
Monitoring Parameters	• Kidney function (before therapy). In case of long-term treatment with high dosage • Liver function • Complete blood count (CBC)
Drug Interactions	***Risk X: Avoid combination*** Cefditoren, Dasatinib, Dichlorphenamide, Levoketoconazole, Nirogacestat, Pazopanib, Posaconazole, Risedronate, Sotorasib, Sparsentan. ***Risk D: Consider therapy modification*** Acalabrutinib, Atazanavir, Bosutinib, Cefuroxime, Dacomitinib, Erlotinib, Gefitinib, Infigratinib, Itraconazole, Ketoconazole (Systemic), Ledipasvir, Neratinib, Nilotinib, Pexidartinib, Rilpivirine, Saquinavir, Secretin, Selpercatinib, Sulpiride.
Pregnancy and Lactation	**Pregnancy** No adequate and well-controlled human data. Famotidine is not recommended for use in pregnancy and should be used only if clearly needed. **Lactation** Famotidine is excreted in human milk. Because of the potential serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or discontinue the drug.
Administration	**Oral Administration** • Taken once daily before bedtime or twice daily in the morning and before bedtime.

Famotidine

	• Taken with or without food. • For prevention of heartburn: taken 10-60 minutes before food or beverages that may induce acidity. **IV Administration** • **IV push:** May be administered undiluted in adults or diluted to a total volume of either 5 mL or 10 mL with NS or 5% dextrose (and injected over at least 2 minutes. • **IV Infusion:** Dilute to 0.2 mg/mL in an appropriate diluent; in adolescents or adults, typically prepared with 100 mL NS or 5% dextrose, and infuse over 15-30 minutes. **N.B.** Refer to the manufacturer's PIL if there are specific considerations**.**
Warnings/ Precautions	**Kidney impairment** Risk of CNS adverse effects, including confusion, delirium, hallucinations, disorientation, agitation, seizures, and lethargy, and QT prolongation in patients with moderate and severe renal impairment. Reduced doses are needed. **Geriatric Use** Use the lowest effective dose for the elderly and monitor renal function. **Gastric Neoplasm** The presence of gastric malignancy should be excluded before the use of famotidine for the treatment of gastric ulcers. Symptomatic relief following treatment with famotidine does not preclude the presence of gastric malignancy. **In the case of long-standing ulcer disease** Abrupt withdrawal after symptom relief should be avoided.
Storage	• Store between 15°C and 30°C. • Protect from light, moisture, and freezing. • After reconstitution for oral suspension, store for a limited time in specific conditions. Refer to the manufacturer's PIL if there are specific considerations.

Proton Pump Inhibitors

Esomeprazole

Generic Name	Esomeprazole
Dosage Form/ Strengths	• Tablet or gastro-resistant tablet: 20 mg, 40 mg. • Enteric-coated granules for delayed-release oral suspension: 2.5 mg, 5 mg, 10 mg, 20 mg, 40 mg. • Delayed-release capsule: 20 mg, 40 mg. • Delayed-release powder for oral suspension in sachet: 20 mg, 40 mg. • Lyophilized powder for slow IV injection or infusion: 20 mg, 40 mg.
Route of Administration	Oral, IV
Pharmacologic Category	Proton Pump Inhibitor, Substituted Benzimidazole. ATC: A02BC05

Indications	**Oral**
	Adults
	• **Gastroesophageal Reflux Disease (GERD).**
	  ○ Treatment of erosive reflux esophagitis.
	  ○ Long-term management of patients with healed esophagitis to prevent relapse.
	  ○ Symptomatic treatment of GERD.
	• **In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori.**
	  ○ Healing of Helicobacter pylori-associated duodenal ulcer.
	  ○ Prevention of relapse of peptic ulcers in patients with Helicobacter pylori-associated ulcers.
	• **Patients requiring continued Nonsteroidal Anti-inflammatory drug (NSAID) therapy**
	  ○ Healing of gastric ulcers associated with NSAID therapy.
	  ○ Prevention of duodenal and gastric ulcers associated with NSAID therapy in patients at risk.
	• **Prevention of rebleeding of peptic ulcers used as prolonged treatment after injection.**
	• **Treatment of Zollinger-Ellison Syndrome.**
	
	Adolescents from the age of 12 years:
	• **Gastroesophageal Reflux Disease (GERD)**
	  ○ Treatment of erosive reflux esophagitis.
	  ○ Long-term management of patients with healed esophagitis to prevent relapse.
	  ○ Symptomatic treatment of gastroesophageal reflux disease (GERD).
	• **In combination with antibiotics in the treatment of duodenal ulcer caused by Helicobacter pylori.**

Esomeprazole

	Children 1-11 years old (granules or powder for oral suspension)
	• **Gastroesophageal Reflux Disease**
	  ○ Treatment of proven erosive reflux esophagitis (starting from 1 month of age).
	  ○ Symptomatic treatment of gastroesophageal reflux disease (GERD).
	Children over 4 years of age (granules or powder for oral suspension)
	In combination with antibiotics in the treatment of duodenal ulcer caused by Helicobacter pylori.
	
	Injection
	Adults
	• **Antisecretory when the oral route is not possible, such as:**
	  ○ GERD patients with esophagitis and/or severe symptoms.
	  ○ Healing of gastric ulcers associated with NSAIDs.
	  ○ Prevention of gastric and duodenal ulcers associated with NSAIDs, in patients at risk.
	• **Prevention of rebleeding following therapeutic endoscopy for acute bleeding gastric or duodenal ulcers.**
	
	Children and adolescents aged 1 month to 18 years for
	• **Gastric antisecretory treatment when the oral route is not possible in** Gastroesophageal reflux disease (GERD) in patients with erosive reflux esophagitis and/or severe symptoms of reflux.

Dosage Regimen	**Oral**
	Adults
	• **Gastroesophageal Reflux Disease (GERD).**
	  ○ Treatment of erosive reflux esophagitis.
	Oral: 40 mg once daily for 4 weeks.
	(Additional 4 weeks may be given if not healed or with persistent symptoms).
	  ○ Long-term management of patients with healed esophagitis to prevent relapse.
	Oral: 20 mg once daily
	  ○ Symptomatic treatment of GERD.
	Oral: 20 mg once daily in patients without esophagitis.
	• **In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori.**
	  ○ Healing of Helicobacter pylori-associated duodenal ulcer, and Prevention of relapse of peptic ulcers in patients with Helicobacter pylori-associated ulcers.
	Oral: 20 mg of esomeprazole with 1 gm amoxicillin and 500 mg clarithromycin, all twice daily for 7 days.
	• **Patients requiring continued Nonsteroidal Anti-inflammatory drug (NSAID) therapy**
	  ○ Healing of gastric ulcers associated with NSAID therapy.
	Oral: 20 mg once daily. The treatment duration is 4-8 weeks.

Esomeprazole

- Prevention of duodenal and gastric ulcers associated with NSAID therapy, in patients at risk.
  Oral: 20 mg once daily.

- **Prevention of rebleeding of peptic ulcers used as prolonged treatment after injection.**
  Oral: 40 mg once daily for 4 weeks after IV injection.
- **Treatment of Zollinger-Ellison Syndrome.**
  Oral: initial: 40 mg twice daily. Then the dose should be adjusted individually and continued as long as clinically needed.
  Usual doses: 80 to 160 mg daily.
  N.B. Doses above 80 mg daily should be divided and given twice daily.

Adolescents aged 12 years and above

- **Gastroesophageal Reflux Disease (GERD)**
  - Treatment of erosive reflux esophagitis.
    - **Oral**: 40 mg once daily for 4 weeks.
      (Additional 4 weeks may be given if not healed or with persistent symptoms).
    - Long-term management of patients with healed esophagitis to prevent relapse.
      Oral: 20 mg once daily.
    - Symptomatic treatment of gastroesophageal reflux disease (GERD).
      Oral: 20 mg once daily in patients without esophagitis.
- **In combination with antibiotics in the treatment of duodenal ulcer caused by Helicobacter pylori.**
  N.B. Regimen and duration (1-2 weeks) should be considered according to local guidance regarding bacterial resistance and appropriate use of antibacterials.
    - **Weight 30-40 Kg**: Twice daily the combination: Esomeprazole 20 mg, amoxicillin 750 mg, and clarithromycin 7.5 mg/kg body weight for one week.
    - **40 Kg:** Twice daily the combination: Esomeprazole 20 mg, amoxicillin 1 gm, and clarithromycin 500 mg for one week.

Children 1-11 years old (granules or powder for oral suspension)

- **Gastroesophageal Reflux Disease**
  - Treatment of endoscopically proven erosive reflux esophagitis.
    Weight ≥10<20 kg: 10 mg once daily for 8 weeks.
    Weight ≥20 kg: 10 mg or 20 mg once daily for 8 weeks.
  - Symptomatic treatment of gastroesophageal reflux disease (GERD).
    Oral: 10 mg once daily for up to 8 weeks.
    N.B. Doses over 1 mg/kg/day have not been studied.

Children over 4 years of age (granules or powder for oral suspension)
In combination with antibiotics in the treatment of duodenal ulcer caused by Helicobacter pylori.

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	N.B. Regimen and duration (1-2 weeks) should be considered according to local guidance regarding bacterial resistance and appropriate use of antibacterials. ○ **Weight < 30 kg**: Twice daily the combination: Esomeprazole 10 mg, amoxicillin 25 mg/kg, and clarithromycin 7.5 mg/kg for one week. ○ **Weight 30-40 Kg**: Twice daily the combination: Esomeprazole 20 mg, amoxicillin 750 mg, and clarithromycin 7.5 mg/kg body weight for one week. ○ **40 Kg:** Twice daily the combination: Esomeprazole 20 mg, amoxicillin 1 gm, and clarithromycin 500 mg for one week. **Injection** **Adults** **N.B.** Usually, the IV treatment duration is short and should be transferred to oral treatment as soon as possible. • **Antisecretory when the oral route is not possible** ○ GERD patients with esophagitis and/or severe symptoms. – **IV injection**: 20-40 mg once daily over not less than 3 minutes. – **Or IV infusion:** 20-40 mg once daily over 10- 30 minutes for up to 10 days. ○ Healing of gastric ulcers associated with NSAIDs. Usual dose: **IV**: 20 mg once daily. ○ Prevention of gastric and duodenal ulcers associated with NSAIDs, in patients at risk. **IV**: 20 mg once daily. • **Prevention of rebleeding following therapeutic endoscopy for acute bleeding gastric or duodenal ulcers.** **IV bolus infusion**: 80 mg over 30 minutes, followed by a continuous IV infusion of 8 mg/h given over 3 days (72 hours), followed by oral acid suppression therapy. **Children and adolescents aged 1 month to 18 years for** • **Gastric antisecretory treatment when the oral route is not possible** IV infusion over 10 to 30 minutes once daily for up to 10 days ○ 1 month to less than 1 year of age: 0.5 mg/kg once daily. ○ 1 year to 17 years – less than 55 kg: 10 mg once daily. – 55 kg or greater: 20 mg once daily.
Dosage Adjustment	**Renal impairment** • No dose adjustments required. • Severe renal insufficiency: Limited experience. Caution.

Esomeprazole

	Hepatic impairment **GERD** • Mild to moderate: No dose adjustments required. • Severe hepatic impairment: Maximum dose: 20 mg (for patients ≥12 years) or 10 mg (for patients 1-11 years age). **Bleeding ulcers** • **Mild to moderate hepatic impairment** IV infusion: 80 mg over 30 minutes, followed by a continuous infusion of 6 mg/hour for 72 hours. • **Severe hepatic impairment** IV infusion: 80 mg over 30 minutes, followed by a continuous infusion of 4 mg/hour for 72 hours.
Contra-indications	Hypersensitivity to any component of the formulation or to other substituted benzimidazole proton pump inhibitors.
Adverse Drug Reactions	**1% to 10%** **Dermatologic**: Pruritus (IV: 1%; oral: <1%). **Endocrine & metabolic**: Altered thyroid hormone levels (increased thyroxine: ≤1%), decreased serum potassium (≤1%), decreased serum sodium (≤1%), decreased thyroid hormones (thyroxine: ≤1%), increased serum potassium (≤1%), increased serum sodium (≤1%), increased thyroid stimulating hormone level (≤1%), increased uric acid (≤1%). **Gastrointestinal**: Abdominal pain (IV: 6%; oral: infants, children, adolescents, adults: 1% to 4%), acid regurgitation (infants: 1%), constipation (IV: 3%; oral: ≥1%), diarrhea (IV: 4%; oral: children, adolescents, adults: 2% to 4%), flatulence (IV: 10%; oral: ≥1%), increased gastrin (≤1%), nausea (IV: 6%; oral: adolescents, adults: 2%), vomiting (infants: ≥5%; adults: <1%), xerostomia (IV: 4%; oral: ≥1%). **Hematologic & oncologic**: Increased hemoglobin (≤1%), quantitative disorders of platelets (≤1%). **Hepatic**: Increased serum alanine aminotransferase (infants, adults: ≤1%), increased serum alkaline phosphatase (≤1%), increased serum aspartate aminotransferase (≤1%). **Local**: Injection-site reaction (IV: 2% to 4%) Nervous system: Dizziness (IV: ≤3%; oral: <1%), drowsiness (children: 2%; adults: <1%), irritability (infants: ≥5%), vertigo (IV: ≤3%; oral: <1%). **Renal**: Increased serum creatinine (≤1%). **Respiratory**: Cough (IV: 1%; oral: <1%), tachypnea (infants: 1%). **Miscellaneous**: Fever (IV: 4%; oral: <1%). **<1%** **Cardiovascular**: Chest pain, edema, flushing, hypertension, lower extremity edema, peripheral edema, substernal pain, tachycardia. **Dermatologic**: Acne vulgaris, dermatitis, diaphoresis, erythematous rash, maculopapular rash, skin rash, urticaria.

Esomeprazole

	Endocrine and metabolic: Albuminuria, goiter, hot flash, hyperuricemia, hyponatremia, increased thirst, menstrual disease, vitamin B_{12} deficiency, weight gain, weight loss. **Gastrointestinal**: Ageusia, anorexia, aphthous stomatitis, change in bowel habits, dysgeusia, dysphagia, enlargement of abdomen, eructation, exacerbation of constipation, gastroenteritis, gastrointestinal hemorrhage, hernia of abdominal cavity, hiccups, increased appetite, melena, mouth disease, pruritus ani, rectal disease, tongue disease. **Genitourinary**: Cystitis, dysmenorrhea, dysuria, erectile dysfunction, genitourinary fungal infection, glycosuria, hematuria, polyuria, urinary frequency, urine abnormality, vaginitis. **Hematologic and oncologic**: Anemia, cervical lymphadenopathy, gastrointestinal dysplasia, hypochromic anemia, leukocytosis, leukopenia, and thrombocytopenia. **Hepatic**: Hyperbilirubinemia. **Hypersensitivity**: Angioedema, facial edema, hypersensitivity reaction, tongue edema. **Infection**: Candidiasis (gastrointestinal candidiasis, genital candidiasis, and urogenital candidiasis). **Nervous system**: Altered sense of smell, apathy, asthenia, confusion, exacerbation of depression, fatigue, fibromyalgia syndrome, hypertonia, hypoesthesia, insomnia, malaise, migraine (including exacerbation of migraine headache), nervousness, pain, paresthesia, rigors, sleep disorder, tremor. **Neuromuscular and skeletal**: Arthralgia, arthropathy, back pain, exacerbation of arthritis, muscle cramps, polymyalgia rheumatica. **Ophthalmic**: Conjunctivitis, visual disturbance, visual field defect. **Otic**: Otalgia, otitis media, tinnitus. **Respiratory**: Dyspnea, epistaxis, exacerbation of asthma, flu-like symptoms, laryngeal edema, pharyngitis, pharyngitis, rhinitis, sinusitis.
Monitoring Parameters	• Magnesium level before initiation of PPI treatment and periodically, especially if taking concomitant digoxin, diuretics, or other drugs known to cause hypomagnesemia. • Calcium level baseline and periodically in patients at risk of hypocalcemia (e.g., hypoparathyroidism). • Monitor for diarrhea, rash or joint pain.
Drug Interactions	***Risk X: Avoid combination*** Acalabrutinib, Cefditoren, Clopidogrel, CYP2C19 Inducers (Strong), Dacomitinib, Dasatinib, Erlotinib, Levoketoconazole, Neratinib, Nilotinib, Nirogacestat, Pazopanib, Pexidartinib, Rilpivirine, Seladelpar, Sotorasib, Sparsentan, St John's Wort. ***Risk D: Consider therapy modification*** Atazanavir, Belumosudil, Bosutinib, Cefuroxime, Citalopram, Gefitinib, Itraconazole, Ketoconazole (Systemic), Ledipasvir, Mavacamten, Methotrexate, Nelfinavir, Palbociclib, Posaconazole, Risedronate, Secretin, Selpercatinib, Sulpiride, Technetium Tc 99m Sestamibi, Velpatasvir.

Esomeprazole

Pregnancy and Lactation	**Pregnancy** Inadequate human data. No demonstrated risk of malformities or other adverse neonatal toxicity with esomeprazole in human or animal data. **Lactation** Inadequate data. Esomeprazole should not be used during breastfeeding.
Administration	**Oral Administration** **Capsule, tablets**: Swallow whole; do not chew or crush. **Granules**: Empty the contents of a packet into a container with water and stir; leave 2 to 3 minutes to thicken. Stir and drink within 30 minutes. **Delayed-release forms** should be taken at least one hour before meals. For patients who have difficulty in swallowing • Capsule content, after opening, can be mixed with 1 half a glass of water and swallowed immediately. Do not store the mixture for future use. • Tablets can also be dispersed in half a glass of water. No other liquids should be used as the enteric coating may be dissolved. Stir until the tablets disintegrate, and the liquid should be administered with the pellets immediately or within 30 minutes. the glass is rinsed with half a glass of water and administered. The pellets must not be chewed or crushed. • Use of granules may be more appropriate for patients with difficulty in swallowing, • Administration via nasogastric tube is possible.z **IV Administration** **Preparation for administration** • Reconstitute with 5 ml 0.9% sodium chloride. • For IV infusion: The reconstituted solution should be further diluted with up to 100 ml of sodium chloride solution. • Flush the intravenous line both before and after administration. **Rate of infusion** • IV bolus injection over a period of at least 3 minutes (20 – 40mg) • IV infusion over a period of 10 to 30 minutes (20, 40 mg) or over 30 minutes (80 mg) or 8 mg/h over 72 hours. N.B. Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Gastric malignancy** • In the presence of any malignancy alarm symptoms (e.g., weight loss, dysphagia, recurrent vomiting, hematemesis, or melena) and if a gastric ulcer is suspected, malignancy should be excluded. • Relief of symptoms does not exclude the presence of a gastric malignancy, as treatment with esomeprazole may alleviate symptoms and delay diagnosis. **On-demand treatment** • Patients on on-demand treatment should be instructed to contact their physician if their symptoms change in character. • On-demand treatment is not recommended in children as it has not been investigated.

Esomeprazole

Gastrointestinal infections

- Treatment with proton pump inhibitors may lead to a slightly increased risk of gastrointestinal infections such as Clostridium difficile-associated diarrhea, Salmonella, and Campylobacter.
- Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Subacute cutaneous lupus erythematosus (SCLE)

- Proton pump inhibitors are associated with very infrequent cases of SCLE occurring within weeks to years after continuous drug therapy.
- If signs or symptoms developed (skin lesions accompanied by arthralgia), the drug should be discontinued, and the patient should be evaluated. Most patients improve on discontinuation of the PPI only in 4 to 12 weeks.

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 rarely in association with the use of PPIs.
- Patients should be informed of the signs and symptoms of this severe skin reaction. Therapy should be discontinued at the first signs or symptoms, and consider further evaluation. Re-challenge should not be undertaken.

Renal effects

- Acute tubulointerstitial nephritis (TIN) has been observed in patients taking PPIs and may occur at any point during therapy.
- Acute tubulointerstitial nephritis can progress to renal failure. If suspected, esomeprazole should be discontinued, evaluate patient and appropriate treatment should be promptly initiated.

Hypomagnesemia and Mineral Metabolism

- Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPI for at least three months.
- Serious manifestations of hypomagnesemia include fatigue, delirium, convulsions, dizziness, and arrhythmia.
- Caution in patients with prolonged treatment and patients with concomitant digoxin or medicines that may cause hypomagnesemia, e.g., diuretics.
  In these patients, measuring magnesium levels before PPI treatment and periodically during treatment is recommended.
- Hypomagnesemia may lead to hypocalcemia and/or hypokalemia. Consider monitoring magnesium and calcium levels before initiation and periodically during treatment in patients with a high risk of hypocalcemia (e.g., hypoparathyroidism). Supplements of magnesium and/or calcium or discontinuation of PPI may be needed.

Cyanocobalamin (vitamin B-12) malabsorption

- Acid-blocking medicines, including esomeprazole, may reduce the absorption of vitamin B12 (cyanocobalamin).

Esomeprazole

	• Daily long-term use (e.g., longer than 3 years) may lead to malabsorption or a deficiency of cyanocobalamin. Caution. **Risk of bone fracture** • Proton pump inhibitors, especially if used in high doses and long durations (> 1 year), may moderately increase the risk of bone fractures (by 10-40%). Some of this increase may be due to other risk factors. • Patients at risk of osteoporosis should have adequate intake of vitamin D and calcium and receive care according to current clinical guidelines. **Combination with other medicines** • Concomitant use of esomeprazole with some antiretroviral drugs (e.g., rilpivirine, atazanavir, and nelfinavir) may lead to decreased antiviral effect and promote the development of drug resistance. • Concomitant use with PPIs may elevate or prolong serum concentrations of methotrexate, possibly leading to toxicity. With high-dose methotrexate administration, consider temporary withdrawal. • Concomitant use of St. John's Wort or rifampin may lead to decreased esomeprazole serum levels by increasing its metabolism. • Avoid concomitant use with clopidogrel due to induced lower exposure to the active metabolite of clopidogrel. **Laboratory test interference** • Interference with investigations for neuroendocrine tumors may occur due to increased Chromogranin A (CgA) level that develops secondary to drug-induced decreases in gastric acidity. • To avoid this interference, esomeprazole treatment should be stopped for at least 5 days before CgA measurements.
Storage	• **Oral** solid forms: Store below 30 ° C. Protect from moisture. • **Vials**: Store below 30 ° C. Store in the original package to protect from light. • After preparation of IV solution: Solution should be used within 12 hours at 30 °C. Refer to the manufacturer's PIL if there are specific considerations.

Dexlansoprazole

Generic Name	Dexlansoprazole
Dosage Form/Strengths	**Delayed-release capsule:** 30 mg, 60 mg
Route of Administration	Oral
Pharmacologic Category	**Pharmacological category:** Proton Pump Inhibitor **ATC:** A02BC06
Indications	• Recovery from erosive esophagitis (EE) of all grades. • Maintenance of healed EE and alleviation of heartburn. • The management of non-erosive gastroesophageal reflux disease (GERD) symptoms.
Dosage Regimen	**Patients > 12 years** • **Healing of erosive esophagitis (EE):** 60 mg once daily up to 8 weeks. • **Maintenance of healed EE and relief of heartburn**: 30 mg once daily up to 6 months and in patients 12-17 years of age for 16 weeks. • **Symptomatic non-erosive GERD**: 30 mg once daily up to 4 weeks. **Pediatrics < 12 years** The efficacy and safety have not been shown.
Dosage Adjustment	**Altered kidney function** No dosage adjustment necessary. **Hepatic impairment** • **Moderate** hepatic impairment (Child-Pugh Class B): The recommended dosage is 30 mg once daily for up to 8 weeks. • **Severe** hepatic impairment (Child-Pugh Class C): Not recommended
Contra-indications	• Hypersensitivity to the active substance or to any of the excipients. • Concomitant use with products that contain rilpivirine.
Adverse Drug Reactions	**1% to 10%** • Cardiovascular: Acute myocardial infarction, angina pectoris, bradycardia, cardiac arrhythmia, chest pain, deep vein thrombosis, edema, including oral, facial edema, and pharyngeal edema, hypertension, palpitations, tachycardia. • Dermatologic: Acne vulgaris, dermatitis, erythema of skin, pruritus, skin lesion, skin rash, sunburn, urticaria • Endocrine and metabolic: Change in libido, goiter, heavy menstrual bleeding, hot flash, hypercalcemia, hypokalemia, increased serum glucose, increased serum potassium, increased serum total protein, menstrual disease, weight gain.

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	• Gastrointestinal: Abdominal distress, abdominal pain (adolescents), abdominal tenderness, abnormal bowel sounds, abnormal stools, anorectal pain, Barrett esophagus, bezoar formation, biliary colic, change in appetite, cholelithiasis, colitis, colonic polyp, constipation, delayed gastric emptying, diarrhea, duodenitis, dysgeusia, dyspepsia, dysphagia, enteritis, eructation, esophagitis, flatulence, gastric polyp, gastritis, gastroenteritis, gastroesophageal reflux disease, gastrointestinal disease, gastrointestinal hypermotility, gastrointestinal perforation, gastrointestinal ulcer, halitosis, hematemesis, hematochezia, hemorrhoids, hiccups, increased gastrin, irritable bowel syndrome, mucosal swelling, mucus stools, oral bullae, oral herpes simplex infection, oral paresthesia, painful defecation, proctitis, rectal hemorrhage, retching, sore throat, vomiting, xerostomia. • Genitourinary: Dysmenorrhea, dyspareunia, dysuria, urinary urgency, vulvovaginal infection. • Hematologic and oncologic: Anemia, decreased platelet count, lymphadenopathy. • Hepatic: Decreased serum bilirubin, hepatomegaly, increased serum alanine aminotransferase, increased serum alkaline phosphatase, increased serum aspartate aminotransferase, increased serum bilirubin. • Hypersensitivity: Hypersensitivity reaction. • Infection: Candidiasis, influenza, viral infection. • Nervous system: Abnormal dreams, anxiety, asthenia, chills, depression, dizziness, falling, feeling abnormal, headache, insomnia, memory impairment, migraine, pain, paresthesia, procedural pain, psychomotor agitation, seizure, tremor, trigeminal neuralgia, vertigo. • Neuromuscular and skeletal: Arthralgia, arthritis, bone fracture, joint sprain, muscle cramps, musculoskeletal pain, myalgia. • Ophthalmic: Eye irritation, swelling of the eye. • Otic: Otalgia, tinnitus. • Renal: Increased serum creatinine • Respiratory: Asthma, bronchitis, cough, dyspnea, hyperventilation, nasopharyngitis, oropharyngeal pain, pharyngitis, pulmonary aspiration, respiratory congestion, sinusitis, upper respiratory tract infection. • Miscellaneous: Fever, inflammation, nodule.
Monitoring Parameters	• Magnesium (baseline and periodically thereafter; especially if taking concomitant digoxin, diuretics, or other drugs known to cause hypomagnesemia). • Calcium (baseline and periodically in patients at risk (e.g., hypoparathyroidism).
Drug Interactions	***Risk X: Avoid combination*** Acalabrutinib, Alcohol (Ethyl), Cefditoren, CYP2C19 Inducers (Strong), Dacomitinib, Dasatinib, Dafactinib, Erlotinib, Levoketoconazole, Neratinib, Nilotinib, Nirogacestat, Pazopanib, Pexidartinib, Rilpivirine, Sotorasib, Sparsentan, St John's Wort, Taletrectinib.

Dexlansoprazole

	Risk D: Consider therapy modification Atazanavir, Belumosudil, Bosutinib, Cefuroxime, Gefitinib, Itraconazole, Ketoconazole (Systemic), Ledipasvir, Methotrexate, Nelfinavir, Palbociclib, Posaconazole, Risedronate, Secretin, Selpercatinib, Sulpiride, Velpatasvir.
Pregnancy and Lactation	**Pregnancy considerations** Data about the usage of dexlansoprazole in pregnant women is scarce. it is preferable to avoid the use of dexlansoprazole when pregnant as a precaution. **Lactation considerations** Dexlansoprazole's presence in breast milk is unknown. Breastfeeding during therapy should be chosen with the mother's treatment benefits, the infant's exposure risk, and the breastfeeding benefits in mind.
Administration	**Capsules** The patient should be counselled as follows • Missed doses: If a dose is missed, administer as soon as possible. • Do not take two doses at one time to make up for a missed dose. • Take without regard to food. • Swallow whole; do not chew. • Capsules can be opened and taken with apple sauce by people who have difficulty swallowing capsules; do not chew granules, and do not save the apple sauce and granules for later use.
Warnings/ Precautions	***Concerns related to adverse effects*** • **Hypomagnesaemia:** Reported rarely, usually with prolonged PPI use of ≥3 months (most cases >1 year of therapy). In most patients, hypomagnesaemia improved after magnesium supplementation and PPI discontinuation. • **Clostridium difficile-Associated Diarrhea**: May raise the risk of diarrhea linked to Clostridium difficile, particularly in individuals who are hospitalized. If the diarrhea does not improve, this diagnosis should be taken into account. According to the condition being treated, patients should take PPI medication for the shortest amount of time and at the lowest dose possible. • **Vitamin B_{12} deficiency**: Prolonged treatment (e.g., longer than 3 years) may lead to vitamin B_{12} malabsorption and subsequent vitamin B_{12} deficiency. • **Fractures:** Increased incidence of osteoporosis-related bone fractures of the hip, spine, or wrist may occur with prolonged PPI therapy. Patients who got high-dose, or multiple daily doses, and long-term PPI medication (one year or more) had a higher risk of fracture. • **Cutaneous and Systemic Lupus Erythematosus:** Proton pump inhibitors have been linked to both new-onset and exacerbations of lupus erythematosus, mainly cutaneous (CLE). The most common type was subacute CLE (SCLE), occurring within weeks to years of continuous therapy across all age groups. If lesions develop, especially on skin areas exposed to the sun, and if accompanied by arthralgia, the patient should seek medical attention promptly and should consider stopping dexlansoprazole.

Dexlansoprazole

	• **Acute interstitial nephritis:** May occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction. Discontinue dexlansoprazole if acute interstitial nephritis develops. ***Disease-related concerns*** • **Gastric malignancy:** The presence of stomach cancer in adults is not excluded by a clinical response to dexlansoprazole therapy. ***Concurrent drug therapy issues*** • Dexlansoprazole increases the level of **Chromogranin A (CgA),** which may interfere with tests performed for the exploration of neuroendocrine tumours. Dexlansoprazole should be discontinued at least 14 days before CgA measurements. • 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
Storage	Store in a temperature not exceeding 30°C, in a dry place.

Lansoprazole

Generic Name	Lansoprazole
Dosage form/strengths	**Oro-dispersible Tablets:** 15 mg, 30 mg **Delayed-release capsule**: 15 mg, 30 mg Tablets and Capsules: Lansoprazole 30 mg (In combination with Amoxicillin 500 mg and Clarithromycin 500 mg)
Route of administration	Oral
Pharmacologic category	**Pharmacological category:** Proton Pump Inhibitor **ATC:** A02BC03
Indications	• Treatment of duodenal and gastric ulcers • Treatment & prophylaxis of reflux esophagitis • Eradication of Helicobacter pylori (H. pylori) concurrently given with appropriate antibiotic therapy • Treatment of non-steroidal anti-inflammatory drug (NSAID)-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment • Prophylaxis of NSAID-associated gastric ulcers and duodenal ulcers in patients at risk requiring continued therapy • Symptomatic gastroesophageal reflux disease • Zollinger-Ellison syndrome
Dosage Regimen	**Check the dosage regimen in the manufacturer's labelling in case of other dosage forms, strengths, or combination products available** **Adults** • **Treatment of duodenal ulcer:** 30 mg once daily up to 4 weeks • **Treatment of gastric ulcer:** 30 mg once daily up to 8 weeks • **Reflux esophagitis:** 30 mg once daily up to 8 weeks • **Prophylaxis of reflux esophagitis:** 15 mg to 30 mg once daily as necessary. • **Treatment of NSAID-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment:** 30 mg once daily up to 8 weeks. If ulcers are difficult to heal, a longer period of treatment and/or a larger dose are likely to be utilized. • **Prophylaxis of NSAID-associated gastric and duodenal ulcers in patients at risk (such as age > 65 or history of gastric or duodenal ulcer) requiring prolonged NSAID treatment:** 15 mg once daily up to 12 weeks. • **Symptomatic gastro-esophageal reflux disease:** 15 mg or 30 mg daily. If the symptoms are not relieved within 4 weeks with a daily dose of 30 mg, further examinations are recommended. • **Zollinger-Ellison syndrome:** 60 mg once daily. Treatment should be continued for as long as required, and each patient's dose should be customized up to 180 mg. If the required daily dose exceeds 120 mg, it should be given in two divided doses.

Lansoprazole

	Elderly
	Due to reduced clearance of lansoprazole in the elderly subjects, individual dose adjustment may be necessary. A daily dose of 30 mg should not be exceeded in the elderly unless there are relevant clinical indications.
	
	Pediatrics
	• Treatment of children < 1 year should be avoided.
	• Children ≤11 years:
	  ○ ≤30 kg: 15 mg once daily.
	  ○ >30 kg: 30 mg once daily.
	• Children ≥12 years and Adolescents: Oral: 15 mg once daily.

Dosage adjustment	**Altered kidney function** No dosage adjustment necessary. **Hepatic impairment** 15 mg orally daily is recommended in patients with severe liver impairment (Child Pugh C).
Contra-indications	• Hypersensitivity to the active substance or to any of the excipients.
Adverse Drug Reactions	**1% to 10%** Gastrointestinal: Abdominal pain, constipation, diarrhea, nausea. Nervous system: Dizziness, headache.
Monitoring Parameters	**Check monitoring parameters in the manufacturer's labelling in case of combination products available** • Monitor magnesium levels at baseline before treatment and periodically in patients expected to use lansoprazole for long periods, or those taking lansoprazole with other drugs that cause hypomagnesemia. • Monitor calcium levels at baseline and periodically during treatment in patients at risk for hypocalcemia. • Evaluate bone health periodically in patients taking lansoprazole for long periods.
Drug Interactions	***Risk X: Avoid combination*** Acalabrutinib, Cefditoren, CYP2C19 Inducers (Strong), Dacomitinib, Dasatinib, Dafactinib, Erlotinib, Levoketoconazole, Neratinib, Nilotinib, Nirogacestat, Pazopanib, Pexidartinib, Rilpivirine, Sotorasib, Sparsentan, St John's Wort, Taletrectinib. ***Risk D: Consider therapy modification*** Atazanavir, Belumosudil, Bosutinib, Cefuroxime, Gefitinib, Itraconazole, Ketoconazole (Systemic), Ledipasvir, Methotrexate, Nelfinavir, Palbociclib, Posaconazole, Risedronate, Secretin, Selpercatinib, Sulpiride, Technetium Tc 99m, Velpatasvir.

Lansoprazole

Pregnancy and Lactation	**Pregnancy considerations** Data about the usage of lansoprazole in pregnant women is scarce. It is preferable to avoid the use of lansoprazole when pregnant as a precaution. **Lactation considerations** Lansoprazole's presence in breast milk is unknown. Breastfeeding during therapy should be chosen with the mother's treatment benefits, the infant's exposure risk, and the breastfeeding benefits in mind.
Administration	**Oro-dispersible Tablets** • Should be taken before meals. • Do not crush or chew. • Administer as soon as possible if a dosage is missed unless the dose is due; take the subsequent dose on time, and avoid missing the missed one. Never take two doses at once to make up for one that you missed. **Capsules** • Should be taken in the morning at least 30 minutes before meals • Swallow whole with liquid; do not chew. • Capsules can be opened and administered orally or via a nasogastric tube in soft foods or liquids.
Warnings/ Precautions	**Check warnings and precautions in the manufacturer's labelling in case of combination products available** ***Concerns related to adverse effects*** • **Hypomagnesaemia** is reported rarely, usually with prolonged PPI use of ≥3 months (most cases >1 year of therapy). In most patients, hypomagnesaemia (and hypomagnesaemia-associated hypocalcaemia and/or hypokalaemia) improved after magnesium supplementation and PPI discontinuation. • **Vitamin B12 deficiency**: Prolonged treatment (several years) may lead to vitamin B_{12} malabsorption and subsequent vitamin B_{12} deficiency • **Colitis**: Very rarely, cases of colitis have been reported. lansoprazole should be discontinued in the case of severe and/or persistent diarrhea. • **Fractures**: Increased incidence of osteoporosis-related bone fractures of the hip, spine, or wrist may occur with prolonged PPI therapy. • **Subacute cutaneous lupus erythematosus (SCLE)** Proton pump inhibitors are associated with very infrequent cases of SCLE. If lesions develop, especially on skin areas exposed to the sun, and if accompanied by arthralgia, the patient should seek medical attention promptly and should consider stopping lansoprazole. • ***Clostridium Difficile*-Associated Diarrhea:** risk is increased by PPIs, especially in hospitalized patients. • **Dermatologic Reactions:** severe dermatologic reactions have been reported with the use of PPIs, including drug reaction with eosinophilia (DRESS), Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN). • **Fundic Gland Polyps:** Long-term use (more than 1 year) of PPIs increases risk.

Lansoprazole

	• **Tubulointerstitial Nephritis:** acute cases have been reported in patients using PPIs. This may occur at any time during treatment. PPIs should be discontinued if interstitial nephritis is suspected. ***Disease-related concerns*** • **Gastric malignancy:** should be ruled out because lansoprazole can mask the symptoms and delay the diagnosis. • **Gastrointestinal infection** (e.g., Salmonella, Campylobacter, and Clostridium difficile): Use of PPIs may increase the risk of these infections. • **Hepatic impairment:** Should be used with caution in patients with moderate and severe hepatic impairment. ***Dosage forms concerns*** **Sucrose:** Patients with rare hereditary problems of fructose intolerance, glucose, galactose malabsorption, or sucrase-isomaltase insufficiency should not take any lansoprazole products containing sucrose. ***Concurrent drug therapy issues*** • Concomitant administration of HIV protease inhibitors such as atazanavir and nelfinavir is not recommended due to the very significant decrease in their bioavailability. • Lansoprazole increases the level of **Chromogranin A (CgA),** which may interfere with tests performed for the exploration of neuroendocrine tumours. Lansoprazole should be discontinued at least 14 days before CgA measurements, and in case CgA levels are high after ceasing treatment with lansoprazole, consider repeating the test at the same lab for confirmation.
Storage	Store at a temperature not exceeding 30 °C, in a dry place Refer to the manufacturer's PIL if there are specific considerations

Omeprazole

Generic Name	Omeprazole
Dosage Form/ Strengths	• **Lyophilized powder for solution for IV infusion**: 40 mg • **Modified release capsule containing pellets**: 10 mg, 20 mg, 40 mg • **Enteric-coated capsules** 20 mg
Route of Administration	Oral, IV
Pharmacologic Category	Proton Pump Inhibitor, Substituted Benzimidazole. ATC: A02BC01
Indications	• Treatment of esophageal reflux disease, including reflux esophagitis. • Relief of heartburn and epigastric pain. • Treatment and prevention of relapse of duodenal and benign gastric ulcers. • Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers, and gastroduodenal erosions in patients at risk. • Relief of associated dyspeptic symptoms. • Eradication of Helicobacter pylori in peptic ulcer disease, in combination with antibiotics. • Prophylaxis of acid aspiration • Zollinger-Ellison syndrome. N.B. Intravenous use is indicated as an alternative to oral therapy.
Dosage Regimen	**Adult Oral Dosing** • **Gastroesophageal reflux disease, including reflux esophagitis** – Oral: 10-20 mg once daily. Up to 40 mg once daily in refractory cases. – Duration: 4-8 weeks. • **Treatment of Duodenal and benign gastric ulcers** – Oral: 20 mg once daily. Up to 40 mg once daily in severe or recurrent cases. – Duration: 4-8 weeks. • **Prevention of relapse of duodenal ulcer** – Oral: 10- 20 mg once daily, increasing to 20mg once daily, if symptoms return. • **Acid-related dyspepsia** – Oral: 10- 20 mg once daily – Duration: 2-4 weeks, depending on severity and persistence of symptoms. • **Treatment of NSAID-associated gastric ulcers, duodenal ulcers, or gastroduodenal erosions** – Oral: 20 mg once daily. – Duration: 4-8 weeks. • **Prophylaxis of NSAID-associated gastric ulcers, duodenal ulcers, gastroduodenal erosions, and dyspeptic symptoms in patients at risk**

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	– Oral: 20 mg once daily. • **Helicobacter pylori eradication regimens in peptic ulcer disease** – Oral: 40 mg once daily or 20mg twice daily in association with antimicrobial agents. • **Prophylaxis of acid aspiration (For patients considered to be at risk of aspiration of the gastric contents during general anesthesia)** – Oral: 40mg on the evening before surgery, followed by 40mg 2-6 hours before surgery. • **Zollinger-Ellison syndrome** – Oral: Initial: 60 mg once daily. Dose should be adjusted individually and treatment continued as long as clinically indicated. – Usual effective dose: 20-120mg daily. – Doses above 80mg daily need to be divided and given twice daily. – Duration: Treatment should be continued under specialist supervision as long as clinically indicated. **Adult IV dosing** – Use in patients where the use of oral medicinal products is inappropriate, • **Zollinger-Ellison Syndrome** – IV: 60 mg once daily. Adjust dose individually. Higher daily doses may be needed. – When doses exceed 60 mg daily, the dose should be divided and given twice daily. • **Other indications** – IV: 40 mg once daily. **Pediatric dosing** Limited data. **Severe ulcerating esophagitis** In children over 2 years Oral: 0.7-1.4 mg/kg, to a maximum of 40 mg/day, for 4- 12 weeks. Limited experience with omeprazole for IV use in children.
Dosage Adjustment	**Renal Impairment** No dose adjustment needed. **Hepatic Impairment** Oral: 10-20 mg once daily may be sufficient.
Contra-indications	Hypersensitivity to any component of the formulation or to other substituted benzimidazole proton pump inhibitors.
Adverse Drug Reactions	**>10%** **Respiratory**: Respiratory system disorder (infants: 42%; children 1 to <2 years: 75%; children ≥2 years and adolescents: 19%). **1% to 10%** **Dermatologic**: Skin rash (2%). **Gastrointestinal**: Abdominal pain (5%), constipation (2%), diarrhea (4%),

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	flatulence (3%), nausea (4%), vomiting (3%). **Nervous system**: Asthenia (1%), dizziness (2%), headache (7%). **Neuromuscular & skeletal**: Back pain (1%). **Respiratory**: Cough (1%), upper respiratory infection (2%).
Monitoring Parameters	• Magnesium level before initiation of PPI treatment and periodically, especially if taking concomitant digoxin, diuretics, or other drugs known to cause hypomagnesemia. • Calcium level baseline and periodically in patients at risk of hypocalcemia (e.g., hypoparathyroidism). • Monitor for diarrhea, rash or joint pain.
Drug Interactions	***Risk X: Avoid combination*** Acalabrutinib, Cefditoren, Clopidogrel, CYP2C19 Inducers (Strong), Dacomitinib, Dasatinib, Erlotinib, Levoketoconazole, Neratinib, Nilotinib, Nirogacestat, Pazopanib, Pexidartinib, Rilpivirine, Seladelpar, Sotorasib, Sparsentan, St John's Wort. ***Risk D: Consider therapy modification*** Atazanavir, Belumosudil, Bosutinib, Cefuroxime, Cilostazol, Citalopram, Gefitinib, Itraconazole, Ketoconazole (Systemic), Ledipasvir, Mavacamten, Methotrexate, Nelfinavir, Palbociclib, Posaconazole, Risedronate, Secretin, Selpercatinib, Sulpiride, Technetium Tc 99m Sestamibi, Velpatasvir.
Pregnancy and Lactation	**Pregnancy** Omeprazole can be used during pregnancy when clinically indicated. No evidence of adverse events of omeprazole on pregnancy or the fetus. **Lactation** Although omeprazole is excreted in breast milk, when used at therapeutic doses, it is unlikely to have an impact on the infant.
Administration	**Oral Administration** Swallowed whole with liquid before a meal; do not chew. **IV Administration** Omeprazole is to be administered in an IV infusion for 20-30 minutes. **Preparation for Administration** The powder content of the vial is to be dissolved in approximately 5 ml and then immediately diluted to 100 ml of sodium chloride (0.9%) solution or dextrose (5%) solution. N.B. Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Gastric malignancy** • In the presence of any malignancy alarm symptoms (e.g., weight loss, dysphagia, recurrent vomiting, hematemesis, or melena) and if a gastric ulcer is suspected, malignancy should be excluded. • Relief of symptoms does not exclude the presence of gastric malignancy, as treatment with omeprazole may alleviate symptoms and delay diagnosis.

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Gastrointestinal infections

- Treatment with proton pump inhibitors may lead to a slightly increased risk of gastrointestinal infections such as Clostridium difficile-associated diarrhea, Salmonella, and Campylobacter.
- Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Subacute cutaneous lupus erythematosus (SCLE)

- Proton pump inhibitors are associated with very infrequent cases of SCLE occurring within weeks to years after continuous drug therapy.
- If signs or symptoms developed (skin lesions accompanied by arthralgia), the drug should be discontinued and the patient should be evaluated. Most patients improve on discontinuation of the PPI only in 4 to 12 weeks.

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 rarely in association with the use of PPIs.
- Patients should be informed of the signs and symptoms of this severe skin reaction. Therapy should be discontinued at the first signs or symptoms, and consider further evaluation. Re-challenge should not be undertaken.

Renal effects

- Acute tubulointerstitial nephritis (TIN) has been observed in patients taking PPIs and may occur at any point during omeprazole therapy.
- Acute tubulointerstitial nephritis can progress to renal failure. If suspected, omeprazole should be discontinued, evaluate patient and appropriate treatment should be promptly initiated.

Hypomagnesemia and Mineral Metabolism

- Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPI for at least three months.
- Serious manifestations of hypomagnesemia include fatigue, delirium, convulsions, dizziness, and arrhythmia.
- Caution in patients with prolonged treatment and patients with concomitant digoxin or medicines that may cause hypomagnesemia, e.g., diuretics. In these patients, measuring magnesium levels before PPI treatment periodically during treatment is recommended.
- Hypomagnesemia may lead to hypocalcemia and/or hypokalemia. Consider monitoring magnesium and calcium levels before initiation and periodically during treatment in patients with a high risk of hypocalcemia (e.g., hypoparathyroidism). Supplements of magnesium and/or calcium or discontinuation of PPI may be needed.

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	Cyanocobalamin (vitamin B-12) malabsorption • Acid-blocking medicines, including omeprazole, may reduce the absorption of vitamin B12 (cyanocobalamin). • Daily long-term use (e.g., longer than 3 years) may lead to malabsorption or a deficiency of cyanocobalamin. Caution. **Risk of bone fracture** • Proton pump inhibitors, especially if used in high doses and long durations (> 1 year), may moderately increase the risk of bone fractures (by 10-40%). Some of this increase may be due to other risk factors. • Patients at risk of osteoporosis should have adequate intake of vitamin D and calcium and receive care according to current clinical guidelines. **Combination with other medicines** • Concomitant use of omeprazole with some antiretroviral drugs (e.g., rilpivirine, atazanavir, and nelfinavir) may lead to decreased antiviral effect and promote the development of drug resistance. • Concomitant use with PPIs may elevate or prolong serum concentrations of methotrexate, possibly leading to toxicity. With high-dose methotrexate administration, consider temporary withdrawal. • Concomitant use of St. John's Wort or rifampin may lead to decreased omeprazole serum levels by increasing its metabolism. • Avoid concomitant use with clopidogrel due to induced lower exposure to the active metabolite of clopidogrel. **Laboratory test interference** • Interference with investigations for neuroendocrine tumors may occur due to increased Chromogranin A (CgA) level that develops secondary to drug-induced decreases in gastric acidity. • To avoid this interference, omeprazole treatment should be stopped for at least 5 days before CgA measurements.
Storage	**Capsules**: Store between 15- 30 °C. Protect from light and moisture **Vial:** Store below 30 °C. Protect from light. **After aseptic reconstitution**: Use within 12 hours (sodium chloride solution) or 6 hours (dextrose solution) if left at room temperature. Use within 24 hours if stored between 2-8 ºC. Refer to the manufacturer's PIL if there are specific considerations.

Pantoprazole

Generic Name	Pantoprazole
Dosage Form /Strengths	**Enteric-coated tablet:** 20 mg, 40 mg. **Modified release tablets**: 20 mg, 40 mg. **Powder for solution for IV injection or infusion**: 40 mg.
Route of Administration	Oral, IV
Pharmacologic Category	Proton Pump Inhibitor, Substituted Benzimidazole. **ATC**: A02BC02
Indications	• Short-term treatment of reflux symptoms (e.g., heartburn, acid regurgitation) in adults. • Short-term treatment and maintenance of healing for erosive esophagitis associated with gastroesophageal reflux disease (GERD). • Long-term management and prevention of relapse in reflux esophagitis. • Zollinger-Ellison Syndrome and other pathological hypersecretory conditions. • Prevention of gastroduodenal ulcers induced by NSAIDs in patients at risk.
Dosage Regimen	**Oral** • **Short-term treatment of reflux symptoms (e.g., heartburn, acid regurgitation) in adults and adolescents** – **Oral:** 20 mg once daily. – **Duration**: 2-3 consecutive days may be needed until improvement of symptoms, then to be discontinued. Treatment should not exceed 4 weeks without consulting a doctor. • **Long-term management and prevention of relapse in reflux esophagitis in adults and adolescents** – **Oral**: 20 mg once daily, increasing to 40mg once daily if a relapse occurs. • **Short-Term Treatment of Erosive Esophagitis Associated with GERD** – **Adults and adolescents** ≥ 40 kg: oral: 40 mg once daily for up to 8 weeks. – **Children (5 years and older):** ≥ 15 kg to < 40 kg: oral: 20 mg once daily for up to 8 weeks. • **Maintenance of Healing of Erosive Esophagitis in adults** – **Oral**: 40 mg once daily. • **Zollinger-Ellison Syndrome and other pathological hypersecretory conditions in adults** – **Oral**: 40 mg twice daily. Dose should be adjusted individually and treatment continued as long as clinically indicated. – Doses above 80 mg daily should be divided and given twice daily. • **Prevention of gastroduodenal ulcers induced by NSAIDs in adult patients at risk** – **Oral:** 20 mg once daily. **Intravenous** IV route may be given up to 7 days, then switch into oral treatment as soon as the patient can tolerate oral treatment.

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	• **GERD (with history of erosive esophagitis)** **Adults** – **IV (injection or infusion)**: 40 mg once daily. **Pediatrics (3 months and older)** – Less than 12.5 kg: 0.8 mg/kg once daily. – 12.5 kg and above (up to 1-year age): 10 mg once daily. – Up to 15 kg: 10 mg once daily. – Greater than 15 kg up to 40 kg: 20 mg once daily. – Greater than 40 kg: 40 mg once daily • **Gastric and duodenal ulcer, reflux esophagitis in adults** – **IV**: 40 mg once daily • **Pathological Hypersecretion Conditions, Including Zollinger-Ellison Syndrome in adults** – **IV**: 80 mg every 12 hours by IV injection or infusion. Adjust the frequency of dosing to individual patient needs based on acid output measurements. In those patients who need a higher dosage, 80 mg intravenously every 8 hours is expected to maintain acid output below 10 mEq/h.
Dosage Adjustment	**Renal impairment** No dose adjustment is needed. **Hepatic impairment** • Mild to moderate impairment: No dosage adjustment necessary. • Severe hepatic impairment: Do not exceed a daily dose of 20 mg.
Contra-indications	Hypersensitivity to any component of the formulation or to other substituted benzimidazole proton pump inhibitors.
Adverse Drug Reactions	**>10%** **Nervous system**: Headache (children, adolescents: >4%; adults: 12%). **1% to 10%** **Cardiovascular**: Edema (≤2%), thrombophlebitis (IV: ≤2%). **Dermatologic**: Pruritus (≤2%), skin photosensitivity (≤2%), skin rash (children, adolescents: >4%; adults: ≤2%), urticaria (children, adolescents, adults: ≤4%). **Endocrine and metabolic**: Increased serum triglycerides (children, adolescents, adults: ≤4%). **Gastrointestinal**: Abdominal pain (children, adolescents: >4%), constipation (children, adolescents, adults: ≤4%), diarrhea (children, adolescents: >4%; adults: 9%), flatulence (children, adolescents: ≤4%), nausea (children, adolescents: ≤4%), vomiting (children, adolescents, adults: ≥4%), xerostomia (≤2%). **Hematologic and oncologic**: Leukopenia (≤2%), thrombocytopenia (≤2%). **Hepatic**: Hepatitis (≤2%), increased liver enzymes (children, adolescents, adults: ≤4%). **Hypersensitivity**: Facial edema (children, adolescents, adults: ≤4%), hypersensitivity reaction (children, adolescents, adults: ≤4%). **Nervous system**: Depression (≤2%), dizziness (children, adolescents, adults:

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	≤4%), vertigo (children, adolescents, adults: ≤4%). **Neuromuscular and skeletal**: Arthralgia (children, adolescents, adults: ≤4%), increased creatine phosphokinase in blood specimen (children, adolescents, adults: ≤4%), myalgia (children, adolescents, adults: ≤4%). **Ophthalmic**: Blurred vision (≤2%). **Respiratory**: Upper respiratory tract infection (children, adolescents: >4%). **Miscellaneous**: Fever (children, adolescents: >4%; adults: ≤2%). **Frequency not defined** **Miscellaneous**: Laboratory test abnormality (false-positive for THC).
Monitoring Parameters	• Magnesium level before initiation of PPI treatment and periodically, especially if taking concomitant digoxin, diuretics, or other drugs known to cause hypomagnesemia. • Calcium level baseline and periodically in patients at risk of hypocalcemia (e.g., hypoparathyroidism). • Monitor for diarrhea, rash, or joint pain. • In patients with severe liver impairment, the liver enzymes should be monitored regularly during treatment with Pantoprazole
Drug Interactions	***Risk X: Avoid combination*** Acalabrutinib, Cefditoren, Dacomitinib, Dasatinib, Erlotinib, Levoketoconazole, Neratinib, Nilotinib, Nirogacestat, Pazopanib, Pexidartinib, Rilpivirine, Sotorasib. ***Risk D: Consider therapy modification*** Atazanavir, Belumosudil, Bosutinib, Cefuroxime, Gefitinib, Itraconazole, Ketoconazole (Systemic), Ledipasvir, Methotrexate, Nelfinavir, Palbociclib, Posaconazole, Risedronate, Secretin, Selpercatinib, Sulpiride, Technetium Tc 99m Sestamibi, Velpatasvir.
Pregnancy and Lactation	**Pregnancy** Inadequate human data. Animal data have shown reproductive toxicity. Pantoprazole should not be used during pregnancy. **Lactation** Inadequate human data. Pantoprazole is present in human milk. The effect of pantoprazole on infants is unknown. Pantoprazole should not be used during breastfeeding.
Administration	**Oral Administration** The tablets should not be chewed or crushed, and should be swallowed whole with liquid with or without food. **IV Administration** • Reconstitute vial with 10 mL of 0.9% Sodium Chloride Injection. • The prepared solution may be administered directly or may be further diluted with 100 mL of sodium chloride 0.9 % solution. • The product should be administered intravenously over 2 - 15 minutes. N.B. Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Gastric malignancy** • In the presence of any malignancy alarm symptom (e.g., weight loss, dysphagia, recurrent vomiting, hematemesis, or melena) and if a gastric ulcer

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is suspected, malignancy should be excluded.

- Relief of symptoms does not exclude the presence of a gastric malignancy, as treatment with pantoprazole may alleviate symptoms and delay diagnosis.

Gastrointestinal infections

- Treatment with proton pump inhibitors may lead to a slightly increased risk of gastrointestinal infections such as Clostridium difficile-associated diarrhea, Salmonella, and Campylobacter.
- Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Subacute cutaneous lupus erythematosus (SCLE)

- Proton pump inhibitors are associated with very infrequent cases of SCLE occurring within weeks to years after continuous drug therapy.
- If signs or symptoms developed (skin lesions accompanied by arthralgia), the drug should be discontinued, and the patient should be evaluated. Most patients improve on discontinuation of the PPI only in 4 to 12 weeks.

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 rarely in association with the use of PPIs.
- Patients should be informed of the signs and symptoms of these severe skin reactions. Therapy should be discontinued at the first signs or symptoms, and consider further evaluation. Re-challenge should not be undertaken.

Renal effects

- Acute tubulointerstitial nephritis (TIN) has been observed in patients taking PPIs and may occur at any point during therapy.
- Acute tubulointerstitial nephritis can progress to renal failure. If suspected, pantoprazole should be discontinued, evaluate patient and appropriate treatment should be promptly initiated.

Hepatic impairment

In patients with severe liver impairment, the liver enzymes should be monitored regularly, particularly on long-term use. In the case of a rise in liver enzymes, the treatment should be discontinued

Hypomagnesemia and Mineral Metabolism

- Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPI for at least three months.

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- Serious manifestations of hypomagnesemia include fatigue, delirium, convulsions, dizziness, and arrhythmia.
- Caution in patients with prolonged treatment and patients with concomitant digoxin or medicines that may cause hypomagnesemia, e.g., diuretics. In these patients, measuring magnesium levels before PPI treatment and periodically during treatment is recommended.
- Hypomagnesemia may lead to hypocalcemia and/or hypokalemia. Consider monitoring magnesium and calcium levels before initiation and periodically during treatment in patients with a high risk of hypocalcemia (e.g., hypoparathyroidism). Supplements of magnesium and/or calcium or discontinuation of PPI may be needed.

Cyanocobalamin (vitamin B-12) malabsorption

- Acid-blocking medicines, including pantoprazole, may reduce the absorption of vitamin B12 (cyanocobalamin).
- Daily long-term use (e.g., longer than 3 years) may lead to malabsorption or a deficiency of cyanocobalamin. Caution.

Risk of bone fracture

- Proton pump inhibitors, especially if used in high doses and long durations (> 1 year), may moderately increase the risk of bone fractures (by 10-40%). Some of this increase may be due to other risk factors.
- Patients at risk of osteoporosis should have adequate intake of vitamin D and calcium and receive care according to current clinical guidelines.

Combination with other medicines

- Concomitant use of pantoprazole with some antiretroviral drugs (e.g., rilpivirine, atazanavir, and nelfinavir) may lead to decreased antiviral effect and promote the development of drug resistance.
- Concomitant use with PPIs may elevate or prolong serum concentrations of methotrexate, possibly leading to toxicity. With high-dose methotrexate administration, consider temporary withdrawal.
- Concomitant use of St. John's Wort or rifampin may lead to decreased PPI serum levels by increasing its metabolism.
- Concomitant use of PPIs with warfarin may increase INR and prothrombin time, which may lead to abnormal bleeding.

Laboratory test interference

- Pantoprazole sodium may produce false-positive urine screens for THC (tetrahydrocannabinol). An alternative confirmatory method should be used to verify positive results.
- Interference with investigations for neuroendocrine tumors may occur due to increased Chromogranin A (CgA) level that develops secondary to drug-

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	induced decreases in gastric acidity. • To avoid this interference, pantoprazole treatment should be stopped for at least 5 days before CgA measurements.
Storage	**Oral:** Store tablet below 30 °C. **IV** • Before reconstitution, store below 30 °C, do not freeze. Protect from light and moisture. • After reconstitution aseptically, it must be used within 12-24 hours below 25°C. Do not freeze. Refer to the manufacturer's PIL if there are specific considerations.

Rabeprazole

Generic Name	Rabeprazole
Dosage form/strengths	**Enteric-coated Tablets:** 10 mg, 20 mg
Route of administration	Oral
Pharmacologic category	**Pharmacological category:** Proton Pump Inhibitor **ATC:** A02BC04
Indications	• Active duodenal ulcer • Active benign gastric ulcer • Symptomatic erosive or ulcerative gastro-esophageal reflux disease (GERD). • Gastro-esophageal Reflux Disease Long-term Management (GERD Maintenance) • Symptomatic treatment of moderate to very severe gastro-esophageal reflux disease (symptomatic GERD) • Zollinger-Ellison syndrome • Eradication of Helicobacter pylori in combination with appropriate antibacterial therapeutic regimens.
Dosage Regimen	**Adults & Elderly** **Active Duodenal Ulcer and Active Benign Gastric Ulcer:** 20 mg once daily in the morning for 4-8 weeks. **Erosive or Ulcerative Gastro-esophageal Reflux Disease (GERD):** 20 mg once daily for 4-8 weeks. **(GERD Maintenance)**: 20 mg or 10 mg once daily can be used depending upon patient response. **Treatment of symptomatic GERD (moderate to severe)**: 20 mg once daily up to 4 weeks in patients without esophagitis. If symptom control is not obtained, the patient should undergo additional investigation. **Zollinger-Ellison Syndrome**: 60 mg once or twice a day based on individual patient needs. **Eradication of H. pylori:** Rabeprazole 20 mg twice daily + clarithromycin 500 mg twice daily and amoxicillin 1 g twice daily for 7 days is recommended. **Pediatrics** Not recommended for use in children due to a lack of data on safety and efficacy.
Dosage Adjustment	**Altered kidney function** No dosage adjustment necessary.

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	Hepatic impairment Mild-to-moderate impairment (Child-Pugh class A or B): No dosage adjustment Severe hepatic impairment (Child-Pugh class C): Use low dose 10 mg with caution as there is no clinical data on the use of rabeprazole in this setting.
Contra-indications	• Hypersensitivity to the active substance or to any of the excipients.
Adverse Drug Reactions	**> 10%** Gastrointestinal: Abdominal pain, diarrhea, vomiting. **1% to 10%:** Cardiovascular: Peripheral edema Gastrointestinal: Constipation, flatulence, nausea, xerostomia Hepatic: Hepatic encephalopathy, hepatitis, increased liver enzymes Infection: Infection Nervous system: Dizziness, headache, pain Neuromuscular & skeletal: Arthralgia, myalgia Respiratory: Pharyngitis
Monitoring Parameters	• Magnesium (baseline and periodically thereafter; especially if taking concomitant digoxin, diuretics, or other drugs known to cause hypomagnesemia); • Calcium (baseline and periodically in patients at risk of hypocalcemia [eg, hypoparathyroidism])
Drug Interactions	***Risk X: Avoid combination*** Acalabrutinib, Cefditoren, Dacomitinib, Dasatinib, Dafactinib, Erlotinib, Levoketoconazole, Neratinib, Nilotinib, Nirogacestat, PAZOPanib, Pexidartinib, Rilpivirine, Rilzabrutinib, Seladelpar, Sotorasib, Sparsentan, Taletrectinib. ***Risk D: Consider therapy modification*** Atazanavir, Belumosudil, Bosutinib, Cefuroxime, Gefitinib, Itraconazole, Ketoconazole (Systemic), Ledipasvir, Methotrexate, Nelfinavir, Palbociclib, Posaconazole, Risedronate, Secretin, Selpercatinib, Sulpiride, Technetium Tc 99m Tetrofosmin, Velpatasvir.
Pregnancy and Lactation	**Pregnancy considerations** There are no data on the safety in human pregnancy. It is preferable to avoid the use of rabeprazole when pregnant as a precaution. Rabeprazole is contraindicated during pregnancy **Lactation considerations** No studies in lactating women have been performed. So, it is recommended not to be used during breastfeeding.

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Administration	**Tablets** • Should be swallowed whole (don't chew or crush) • Should be taken in the morning, before eating; although neither the time of day nor food intake was shown to have any effect on sodium activity, this regimen will facilitate treatment compliance. • For the treatment of duodenal ulcers, rapebrazole delayed-release tablet is taken after a meal, for Helicobacter pylori eradication, rapebrazole delayed-release tablet is taken with food, and for all other indications, rapebrazole delayed-release tablets can be taken with or without food.
Warnings/ Precautions	***Concerns related to adverse effects*** • **Hypomagnesaemia** reported rarely, usually with prolonged PPI use of ≥3 months (most cases >1 year of therapy) In most patients, hypomagnesaemia (and hypomagnesaemia-associated hypocalcaemia and/or hypokalaemia) improved after magnesium supplementation and PPI discontinuation • **Vitamin B12 deficiency**: Prolonged treatment (several years) may lead to vitamin B_{12} malabsorption and subsequent vitamin B_{12} deficiency • **Clostridium difficile-Associated Diarrhea**: may increase the risk of gastrointestinal infections such as Salmonella, Campylobacter, and Clostridium difficile, so may increase the risk of Clostridium difficile-associated diarrhea, especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve. • **Fractures:** Increased incidence of osteoporosis-related bone fractures of the hip, spine, or wrist may occur with high-dose, defined as multiple daily doses, and Prolonged treatment PPI therapy. • **Subacute cutaneous lupus erythematosus (SCLE):** Proton pump inhibitors are associated with very infrequent cases of SCLE. If lesions develop, especially on skin areas exposed to the sun, and if accompanied by arthralgia, the patient should seek medical attention promptly and should consider stopping rabeprazole. • Patients on long-term treatment (particularly those treated for more than a year) should be kept under regular surveillance. • A risk of cross-hypersensitivity reactions with another proton pump inhibitor (PPI) or substituted benzimidazoles cannot be excluded. • **Fundic Gland Polyps:** Risk increases with long-term use, especially beyond one year. Use the shortest duration of therapy. ***Disease-related concerns*** • **Gastric malignancy:** should be ruled out because rabeprazole can mask symptoms and delay the diagnosis; therefore, the possibility of malignancy should be excluded before commencing treatment with Rabeprazole. • **Hepatic impairment:** Use low dose 10 mg with caution, as there is no clinical data on the use of rabeprazole in this setting. • **Acute tubulointerstitial nephritis (TIN)** may occur at any point during PPI therapy, so discontinue treatment and evaluate patients.

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	Concurrent drug therapy issues • Concomitant administration of HIV protease inhibitors such as atazanavir is not recommended. • Rabeprazole increases the level of **Chromogranin A (CgA),** which may interfere with tests performed for the exploration of neuroendocrine tumors. rabeprazole should be discontinued at least 5 days before CgA measurements. • Concomitant administration of rabeprazole with warfarin requires monitoring for increases in INR and prothrombin time. • Concomitant use of methotrexate with PPIs may elevate and/or prolong serum concentrations of methotrexate and/or its metabolite, possibly leading to methotrexate toxicity. • Daily long-term use of rabeprazole (e.g., longer than 3 years) may lead to malabsorption or a deficiency of cyanocobalamin.
Storage	Store at a temperature not exceeding 25°C, in a dry place, and protect from moisture Refer to the manufacturer's PIL if there are specific considerations

Intestinal Anti-inflammatory Agent

Mesalazine (Mesalamine)

Generic Name	Mesalazine (Mesalamine)
Dosage Form/ Strengths	**Tablet**: 500 mg **Modified release tablets**: 400 mg, 500 mg, 800 mg **Prolonged release granules:** 1 gm, 2 gm, 4 gm **Capsules Containing extended-release pellets**: 500 mg **Rectal Suppositories**: 1 gm **Rectal Suspension**: 1 gm/100mL
Route of Administration	Oral, rectal
Pharmacologic Category	5-Aminosalicylic Acid Derivative ATC: A07EC02
Indications	**Oral** **Ulcerative colitis** • Treatment and maintenance of remission for mild to moderate acute exacerbations. **Crohn's ileo-colitis** • For the maintenance of remission. **Rectal (for adults)** Treatment and maintenance of remission for mild to moderate ulcerative proctitis.
Dosage Regimen	**Adult dosing** • **Active disease** **Oral:** 1.5 gm up to 4 gm once daily or divided into 2-4 doses. **Rectal:** 1 gm once daily. • **Maintenance treatment** **Oral:** 1.2- 2 gm once daily or in divided doses. **Rectal:** 1 gm once daily at bedtime for 3 to 6 weeks. **Pediatric dosing (Children 6 years of age and older)** • **Active disease** **Oral**: 30-50 mg/kg/day in divided doses. Maximum dose: 75 mg/kg/day in divided doses. The total dose should not exceed 4 g/day. • **Maintenance treatment** **Oral**: 15-30 mg/kg/day in divided doses. Maximum dose: 2 g/day.
Dosage Adjustment	**Renal impairment** • Mild to moderate renal impairment: Extreme caution. Utilize the lowest effective dose. • Contraindicated in severe renal impairment. • Discontinue mesalamine if renal function deteriorates while on therapy.

Mesalazine (Mesalamine)

	Hepatic impairment • No dosage adjustments necessary. • Contraindicated in severe hepatic impairment.
Contra-indications	• Known hypersensitivity to mesalazine, salicylates, or any of the excipients. • Severe liver or renal impairment.
Adverse Drug Reactions	**>10%** **Gastrointestinal**: Abdominal pain (1% to 21%), constipation (≤11%), eructation (≤26%). **Nervous system**: Headache (3% to 14%). **Respiratory**: Nasopharyngitis (children and adolescents: 15%; adults: 1% to 4%). **1% to 10%** **Cardiovascular**: Hypertension (≤1%). **Dermatologic**: Acne vulgaris (≤1%), alopecia (<3%), pruritus (≤1%), skin rash (≤6%). **Endocrine & metabolic**: Increased serum triglycerides (<3%), weight loss (children and adolescents: 2%) **Gastrointestinal**: Abdominal distention (1%), anorectal pain (rectal: 1%; includes discomfort and pain on insertion of enema tip), bloody diarrhea (children and adolescents: 2%), diarrhea (2% to 8%), dyspepsia (≤4%), flatulence (≤6%), gastroenteritis (≥2%), gastrointestinal hemorrhage, hemorrhoids (≥1%), lower abdominal pain (<3%), nausea (≤4%), pancreatitis (≤2%), rectal pain (rectal: 1% to 2%), sclerosing cholangitis (children and adolescents: 2%), tenesmus (≥2%), upper abdominal pain (1% to 5%), vomiting. **Genitourinary**: Hematuria (<3%), urinary frequency. **Hematologic & oncologic**: Decreased hematocrit (<3%), decreased hemoglobin (<3%), rectal hemorrhage (<3%). **Hepatic**: Cholestatic hepatitis (<3%). **Infection**: Infection (≥2%), influenza (1% to 5%), viral infection (children and adolescents: ≥2%; including adenovirus). **Nervous system**: Dizziness (≤9%), fatigue (<3%), nervousness (≥2%), pain (<3%), paresthesia (≥2%), vertigo (<3%). **Neuromuscular & skeletal**: Arthralgia (<3%), arthropathy (≥2%), back pain (≤6%), lower extremity pain (rectal: ≤2%). **Ophthalmic**: Visual disturbance (≥2%). **Otic**: Tinnitus (<3%). **Renal**: Decreased creatinine clearance (<3%). **Respiratory**: Cough (children & adolescents: 5%; adults: ≤1%), dyspnea (<3%), flu-like symptoms (4%), rhinitis (8%), sinusitis (children and adolescents: 7%), upper respiratory tract infection (children and adolescents: ≥5%). **Miscellaneous**: Fever (≤3%), intolerance syndrome (2% to 3%).
Monitoring Parameters	• **Renal function** (before and periodically during therapy, for example: every 3 months for the first year, then every 6 months for the next 4 years, and annually thereafter). • **Liver function** (before and periodically during therapy).

Mesalazine (Mesalamine)

	• **CBC differential** (particularly in elderly patients).
Drug Interactions	***Risk D: Consider Therapy Modification*** Alcohol (Ethyl), Antacids.
Pregnancy and Lactation	**Pregnancy** • Limited human data. No increase in the overall rate of congenital malformations. • Mesalazine should only be used during pregnancy if the potential benefit outweighs the possible risk. • The underlying condition itself (Inflammatory Bowel Disease (IBD)) may increase the rate of preterm birth, stillbirth, and low birth weight. **Lactation** • Limited data. Hypersensitivity reactions like diarrhea may occur. If the infant develops diarrhea, breastfeeding should be discontinued. • Mesalamine should only be used during breastfeeding if the potential benefit outweighs the possible risk.
Administration	**Oral Administration** • Adequate amount of fluids should be administered during treatment. • Tablet, Capsule should be swallowed whole. Do not cut, break, crush, or chew. • Granules must not be chewed. • Contents of the sachet should be emptied onto the tongue and swallowed with some water or orange juice. Alternatively, the entire content of the sachet can be taken with yogurt and consumed immediately. **Rectal Administration** • A visit to the toilet is recommended before administration. • Drink an adequate amount of fluids. • Shake Enema well and use immediately. N.B. Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Mesalamine-Induced Acute Intolerance Syndrome** • Symptoms may include cramping, acute abdominal pain and bloody diarrhea, and sometimes fever, headache, malaise, pruritus, conjunctivitis, and rash. It may be challenging to differentiate symptoms from an exacerbation of ulcerative colitis. • Monitor worsening of these symptoms. If acute intolerance syndrome is suspected, treatment should be discontinued. **Renal Impairment** • Assess baseline renal function and periodically during treatment. • Treatment with mesalazine should be discontinued if renal function deteriorates. The concurrent use of other nephrotoxic agents, such as azathioprine and NSAIDs, may increase the risk of renal reactions. If dehydration develops, normal electrolyte and fluid balance should be restored as soon as possible.

Mesalazine (Mesalamine)

	• Evaluate the risks and benefits in patients with known renal impairment or taking nephrotoxic drugs. • Nephrolithiasis: Mesalamine-containing stones may occur and are undetectable by standard radiography or computed tomography (CT). Ensure adequate fluid intake during treatment. **Hypersensitivity Reactions** • Reactions may include severe cutaneous reactions, myocarditis, pericarditis, nephritis, hepatitis, pneumonitis, and hematologic abnormalities. • At the first signs or symptoms, evaluate patients immediately and discontinue if no other etiology. **Blood disorders** • Serious blood dyscrasias have been reported very rarely with mesalazine. • Differential blood count is recommended in geriatrics before and during treatment. Also, azathioprine or 6-mercaptopurine increases the risk of blood disorders. • Treatment should be discontinued on suspicion or evidence of these adverse reactions. **Hepatic Failure** Hepatic failure has been reported in patients with pre-existing liver disease. Evaluate the risks and benefits in patients with known liver impairment. **Photosensitivity** Advise patients with pre-existing skin conditions to avoid sun exposure and use a broad-spectrum sunscreen when outdoors. **Respiratory disorders** Patients with pulmonary disease, in particular asthma, should be very carefully monitored during a course of treatment due to possible adverse effects. **Elderly population** Use in the elderly with caution. The product should only be prescribed to patients having a normal or non-severely impaired liver and renal function.
Storage	**Oral forms:** Store between 15°C and 30°C. Protect from light and moisture. **Rectal forms:** Store at 15°C to 25°C. Protect from light, moisture, and freezing. Refer to the manufacturer's PIL if there are specific considerations.

Sulfasalazine

Generic Name	Sulfasalazine
Dosage Form/ Strengths	**Tablet**: 500 mg
Route of Administration	Oral
Pharmacologic Category	5-Aminosalicylic Acid Derivative; Antirheumatic, Disease Modifying. ATC: A07EC01
Indications	• Treatment and maintenance of remission of ulcerative colitis. • Treatment of active Crohn's disease (including distal proctocolitis). • Rheumatoid arthritis, which has failed to respond to non-steroidal anti-inflammatory drugs (NSAIDs).
Dosage Regimen	The dose should be adjusted according to the patient's severity of the disease and tolerance. **Adult dosing** **Ulcerative Colitis** • **Initial or attacks: Oral**: 1-2 gm daily up to 1-2 gm four times daily in evenly divided doses with dose intervals not exceeding 8 hours. It may be combined with steroids for intensive management. • **Maintenance: Oral:** 2 gm daily continued indefinitely to avoid relapse. **Crohn's Disease** **Attacks: Oral**: 1-2 gm daily up to 1-2 gm four times daily in evenly divided doses with dose intervals not exceeding 8 hours. It may be combined with steroids for intensive management. **Rheumatoid Arthritis** • **Initial: Oral:** 0.5 gm daily for one week, increased by 0.5 gm weekly until 0.5 gm four times daily or 1 gm three times daily. Maximum: 3 gm daily. • If the patient experiences nausea, the dose should be reduced to a previously tolerated dose for one week and then increased. **Pediatric dosing** **Ulcerative Colitis (children over 2 years of age)** • **Initial or attacks: Oral**: 40 to 60 mg/kg daily, divided into 3 to 6 doses. • **Maintenance: Oral:** 20- 30 mg/kg daily, divided into 4 doses.
Dosage Adjustment	**Renal Impairment** • Baseline renal impairment: Use should only be initiated if the benefits are considered to outweigh the risk. • Deterioration of renal function: Treatment should be discontinued. **Hepatic Impairment** • Baseline hepatic impairment: Use should only be initiated if the benefits are considered to outweigh the risk.

Sulfasalazine

	Dosing adjustments
	• **Ulcerative colitis**
	  ○ When the disease improves (evidenced by endoscopic examination), the dose may be reduced to a maintenance level.
	  ○ If symptoms of gastric intolerance (anorexia, nausea, vomiting, etc.) occur after the first few doses, the daily dose should be decreased by half and subsequently increased gradually over several days. If gastric intolerance continues, the drug should be stopped for 5 to 7 days, then reintroduced at a lower daily dose.
	• **Rheumatoid Arthritis**
	If the patient experiences nausea, the dose should be reduced to a previously tolerated dose for one week and then increased.

Contra-indications	• Known hypersensitivity to sulfasalazine, its metabolites (as well as salicylates or sulfonamides), or any of the excipients. • Patients with porphyria. • Children under the age of 2 years.
Adverse Drug Reactions	**>10%** **Dermatologic**: Skin rash (rheumatoid arthritis: 13%; ulcerative colitis: ≤3%). **Gastrointestinal**: Anorexia (ulcerative colitis: 33%), dyspepsia (rheumatoid arthritis: 13%), gastric distress (ulcerative colitis: 33%), nausea (rheumatoid arthritis: 19%; ulcerative colitis: 33%), vomiting (rheumatoid arthritis: 8%; ulcerative colitis: 33%). **Genitourinary**: Oligospermia (reversible; ulcerative colitis: 33%). **Nervous system**: Headache (rheumatoid arthritis: 9%; ulcerative colitis: 33%). **1% to 10%** **Dermatologic**: Pruritus (≤4%), urticaria (ulcerative colitis: ≤3%). **Gastrointestinal**: Abdominal pain (rheumatoid arthritis: 8%), stomatitis (rheumatoid arthritis: 4%). **Hematologic & oncologic**: Acquired Heinz body anemia (ulcerative colitis: ≤3%), hemolytic anemia (ulcerative colitis: ≤3%), leukopenia (rheumatoid arthritis: 3%), thrombocytopenia (rheumatoid arthritis: 1%). **Hepatic**: Abnormal hepatic function tests (rheumatoid arthritis: 4%). **Nervous system**: Dizziness (rheumatoid arthritis: 4%). **Respiratory**: Cyanosis (ulcerative colitis: ≤3%). **Miscellaneous**: Fever (≤5%).
Monitoring Parameters	• Renal function (including urinalysis): initially and at least at monthly intervals for a minimum of the first three months of treatment and periodically during treatment. • CBC (differential) and liver function test: Before use, and every second week during the first three months of therapy. Then once monthly during the second three months, thereafter once every three months, and as clinically indicated.
Drug Interactions	***Risk X: Avoid combination*** Bulevirtide, Leniolisib, Methenamine, Sparsentan, Taurursodiol, Voxilaprevir.

Sulfasalazine

	Risk D: Consider therapy modification Belumosudil, COVID-19 Vaccines, Riluzole, Vimseltinib.
Pregnancy and Lactation	**Pregnancy** Inadequate human data. No evidence of teratogenic hazards. sulfasalazine should be used during pregnancy only if clearly needed. **Lactation** Patients should avoid breastfeeding while taking this medicine. There have been reports of bloody stools or diarrhea in infants who were breastfed by mothers on sulfasalazine and resolved after discontinuation. **Fertility** Oligospermia and infertility may occur in men treated with sulfasalazine. Discontinuation of the drug appears to reverse these effects within 2 to 3 months.
Administration	**Oral Administration** Taken in evenly divided doses, preferably after meals. N.B. Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Renal Impairment** • Assess baseline renal function and periodically during treatment. • Treatment with sulfasalazine should be discontinued if renal function deteriorates. • Evaluate the risks and benefits in patients with known renal impairment. • Because sulfasalazine causes crystalluria and kidney stone formation, adequate fluid intake should be ensured during treatment. **Hypersensitivity Reactions** • Reactions may include severe cutaneous reactions, myocarditis, pericarditis, nephritis, hepatitis, pneumonitis, and hematologic abnormalities. • At the first signs or symptoms, evaluate patients immediately and discontinue if no other etiology. **Blood disorders** • Since sulfasalazine may cause hemolytic anemia, patients with G-6-PD deficiency should be monitored closely. • Folic acid deficiency may occur due to the inhibition of absorption and metabolism of folic acid by sulfasalazine. This may potentially result in serious blood disorders (e.g., macrocytosis and pancytopenia), and can be normalized by administration of folic acid (leucovorin). **Infections** • Serious infections associated with myelosuppression, including sepsis and pneumonia, have been reported. Monitor closely if infection has been developed. • Patient should report immediately sore throat and fever.

Sulfasalazine

	• Patient with blood dyscrasias should not be initiated unless the potential benefit outweighs the risk. **Toxicities** • The presence of clinical signs such as sore throat, fever, pallor, purpura, or jaundice may be an indication of serious blood disorders or hepatotoxicity. • Patients should be counselled to report immediately any of these signs or unexpected non-specific illness during sulfasalazine treatment. **Respiratory disorders** Sulfasalazine should be given with caution to patients with severe allergies or bronchial asthma.
Storage	Store between 15°C and 30°C. Protect from moisture. Refer to the manufacturer's PIL if there are specific considerations.

Methotrexate: Refer to the conventional anti-cancer formulary

You can access it through the following link

https://www.edaegypt.gov.eg/media/hskb4dm3/3-new-code-conventional-anticancers-egyptian-national-formulary-2024_4.pdf

Laxatives

Osmotic

Glycerin

Generic Name	Glycerin
Dosage Form/ Strengths	• Rectal Suppositories: 1.4 gm, 1.47 gm, 1.61 gm. 70% w/w • Infantile rectal suppository: 0.7gm
Route of Administration	Rectal
Pharmacologic Category	Laxative, Osmotic ATC: A06AX01
Indications	• For occasional use as a stimulant laxative for the treatment of constipation.
Dosage Regimen	**Adolescents, adults, and the elderly** Rectal: 1-2 adults suppositories as needed. **Children** Rectal: One suppository (1.4 gm) as needed. **Infants** Rectal**:** One suppository (0.7 gm) as needed.
Dosage Adjustment	No adjustments needed.
Contra-indications	• Hypersensitivity to the active ingredient or any of the excipients. • Intestinal obstruction or blockage.
Adverse Drug Reactions	**Frequency not defined** **Gastrointestinal**: Abdominal cramps, rectal irritation.
Monitoring Parameters	No monitoring data needed.
Drug Interactions	There are no known significant interactions.
Pregnancy and Lactation	**Pregnancy and Lactation** • All medicines should be avoided if possible during pregnancy and lactation. • No evidence of harmful effects. • Use only under a doctor's instruction in these conditions.
Administration	• The suppository tip should be moistened with water before use to aid insertion. • Not to be swallowed. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.

Glycerin

Warnings/ Precautions	• Adults' suppositories are not suitable for use by children and infants. • For occasional use only. Prolonged or excessive use of the product is not recommended. • Use of this product may interfere with glucose control in diabetic patients. If symptoms persist, consult a doctor.
Storage	Store at 15°- 30° C. Do not exceed 30° C. Protect from moisture. N.B. Refer to the manufacturer's PIL if there are specific considerations.

Lactulose

Generic Name	Lactulose
Dosage Form/ Strengths	**Syrup or oral solution**: 3.35 gm/5 mL **Granules in sachet for oral solution**: 6 gm/ sachet **Powder for oral solution:** 10 gm/sachet
Route of Administration	Oral
Pharmacologic Category	Ammonium Detoxicant; Laxative, Osmotic ATC: A06AD11
Indications	• Treatment of constipation. • Treatment of hepatic encephalopathy and hepatic coma in adults.
Dosage Regimen	• **Constipation** N.B. Lactulose may be given as a single daily dose or in two divided doses. N.B. Adjust dose to the maintenance dose after 2-3 days based upon response. **Adults and adolescents** Starting dose: 10-30 gm lactulose (15 – 45 mL/day of oral solution). Maintenance dose: 10-20 gm (15 – 30 ml/day of oral solution). **Pediatrics** **Children (7 – 14 years)** Starting dose: 10 gm (15 mL of oral solution). Maintenance dose: 7-10 gm (10 – 15 mL of oral solution). **Children (1 – 6 years)** Starting and maintenance dose: 3-7 gm (5 – 10 mL of oral solution). **Infants < 1 year** Starting and maintenance dose: 3 gm (up to 5 mL). • **Hepatic encephalopathy** **Adults** Initial: 60 -100 gm (30 – 45 mL) 3 – 4 times/day. Adjust the dose to pass soft stools 2 – 3 times/day. **Pediatrics** The safety and efficacy of lactulose for the treatment of hepatic encephalopathy have not been established in children.
Dosage Adjustment	**Renal Impairment** There is no dosage adjustment needed. **Hepatic Impairment** There is no dosage adjustment needed.
Contra-indications	• Hypersensitivity to the active substance or any of the excipients. • Galactosemia. • Gastrointestinal obstruction. • Digestive-perforation or risk of digestive perforation.

Lactulose

Adverse Drug Reactions	**≥ 10%** **Gastrointestinal**: Diarrhea. **1-10%** **Gastrointestinal**: Abdominal pain, flatulence, nausea, vomiting.
Monitoring Parameters	• Serum electrolytes (chronic use can cause electrolyte disturbance from fluid loss). • Bowel movement frequency.
Drug Interactions	No significant *Risk X or D* drug interactions.
Pregnancy and Lactation	**Pregnancy** Inadequate data. Lactulose can be used during pregnancy as it is poorly absorbed after oral administration, and the systemic exposure is so low. **Lactation** Lactulose can be used for lactating mothers as it is poorly absorbed after oral administration.
Administration	**Oral Administration** • Lactulose solution can be administered with or without dilution. • Lactulose may be mixed with water, milk, or fruit juice. • It is recommended to drink enough fluids (1.5–2 liters) during the day during therapy with laxatives. • In case of single daily dosing, the dose should be taken at the same time of the day. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Abdominal symptoms** • In case of painful abdominal symptoms, an undiagnosed digestive perforation or obstruction should be excluded. • Flatulence occurs within the first few days of treatment and resolves after a few days. **Diabetic patients** The doses used for constipation should not cause a problem for diabetics. However, doses used for hepatic encephalopathy are much larger and should be considered when managing diabetic patients due to the presence of sugars such as lactose, galactose, and fructose in the product. **Chronic use** • Misuse and chronic use of unadjusted doses can lead to diarrhea and disturbance of electrolyte balance. • It should be considered that the defecation reflex could be disturbed during the treatment.

Lactulose

	Proper use • After several days of insufficient therapeutic effect, adjustment of dose and/or additional measures should be reconsidered. • Patients who are galactose or lactose intolerant should be given lactulose with caution. **Pediatric patients** • Children should only use laxatives under medical supervision.
Storage	Store between 15-30°C. Powder and granules should be kept in a dry place. Refer to the manufacturer's PIL if there are specific considerations.

Polyethylene glycol 3350 (macrogol)

Generic Name	Polyethylene glycol 3350 (macrogol)
Dosage Form/Strengths	Powder for oral suspension (in combinations): • 6.563 grams per sachet. • 13.125 grams per sachet. • 100 grams per pouch.
Route of Administration	Oral
Pharmacologic Category	Laxative, Osmotic **ATC:** A06AD65
Indications	**Products containing 6.563 grams per sachet:** 1. For the treatment of chronic constipation in children 2 to 11 years of age. 2. For the treatment of fecal impaction in children from the age of five years, defined as refractory constipation with fecal loading of the rectum and/or colon. 3. For the prevention of re-impaction after successful dis-impaction in children 2 to 11 years of age. **Products containing 13.125 grams per sachet:** 4. Treatment of chronic constipation in adults (products containing 13.125 grams per sachet). **Products containing 100 grams per pouch:** 5. Osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults (products containing 100 grams per pouch).
Dosage Regimen	**Cleansing the colon in preparation for colonoscopy in adults and the elderly:** • Macrogol products for cleansing the bowel before colonoscopy are marketed in Egypt in packs containing 4 pouches: 2 large pouches containing macrogol and electrolytes (pouch A), and 2 small pouches containing ascorbic acid and electrolytes (pouch B). • A dose is prepared by mixing the contents of 1 pouch A and 1 pouch B with 1 liter of water. • A course of treatment consists of two liters of the product (2 doses). • This course of treatment can be taken either as divided or as single doses, and the timing differs based on whether anesthesia is used:

	With General Anesthesia	Without General Anesthesia
Single Dose Regimen	• 2 liters taken over 2 – 4 hours either: – In the evening of the day before the procedure, or – In the morning of the day of the procedure. • The intake of the macrogol	• 2 liters taken over 2 – 4 hours either: – In the evening of the day before the procedure, or – In the morning of the day of the procedure. • The intake of the macrogol

Polyethylene glycol 3350 (macrogol)

	product and any other clear fluids should be stopped at least **2 hours** before the procedure.	product should be stopped at least **2 hours** before the procedure. • The intake of any other clear fluids should be finished at least **1 hour** before the procedure.
Divided Doses Regimen	• 1 liter taken over 1 – 2 hours in the evening of the day before the procedure, and 1 liter taken over 1 – 2 hours in the morning of the day of the procedure. • The intake of the macrogol product and any other clear fluids should be stopped at least **2 hours** before the operation.	• 1 liter taken over 1 – 2 hours in the evening of the day before the procedure, and 1 liter taken over 1 – 2 hours in the morning of the day of the procedure. • The intake of the macrogol product and any other clear fluids should be finished at least **1 hour** before the procedure.

- One liter should be consumed over a course of 1 – 2 hours; drinking a glassful every 10 – 15 minutes.
- The use of macrogol products for cleansing the colon before colonoscopy was not studied in pediatrics (patients below 18 years of age) and is not recommended.

Treatment of chronic constipation in adults and the elderly:

Note: Doses for the treatment of chronic constipation in adults are based on sachets containing 13.125 grams of macrogol.

	Regular Treatment Course	Extended Use
Dose	1 – 3 sachets daily in divided doses.	1 – 2 sachets daily in divided doses.
Course	Not for more than 2 weeks.	Started after the regular course and continued as needed.
When to use	Initial treatment of chronic constipation.	• Severe chronic constipation. • Resistant Constipation. • Constipation secondary to multiple sclerosis or Parkinson's disease. • Constipation secondary to drugs such as opioids or anti-muscarinics.

Treatment of chronic constipation in pediatrics:

Note: Pediatric doses are based on products containing 6.563 grams of macrogol per sachet.

- The usual starting dose is 1 sachet daily for children aged 2 to 6 years, and 2 sachets daily for children aged 7 – 11 years.

Polyethylene glycol 3350 (macrogol)

	• The dose should be adjusted up or down as required to produce regular soft stools. • If the dose needs increasing, this is best done every second day. • The maximum dose is 4 sachets a day. • Treatment of children with chronic constipation needs to be for a prolonged period (at least 6 – 12 months). However, its safety and efficacy have only been proven for a period of up to three months. • Treatment should be stopped gradually and resumed if constipation recurs. **Treatment of fecal impaction and prevention against re-impaction in pediatrics:** • A course of treatment for fecal impaction is for up to 7 days as follows: – Day 1: 4 sachets. – Day 2: 6 sachets. – Day 3: 8 sachets. – Day 4: 10 sachets. – Days 5, 6, and 7: 12 sachets. • The daily number of sachets should be taken in divided doses; all consumed within 12 hours. • The above dosage regimen should be stopped once disimpaction has occurred. • An indicator of disimpaction is the passage of a large volume of stools. • After disimpaction, it is recommended that the child follow an appropriate bowel management program to prevent reimpaction (dosing for prevention of re-impaction should be as for patients with chronic constipation; see above). Notes: • Macrogol products are not recommended for the treatment of chronic constipation in children below 2 years of age. • Macrogol products are not recommended for the treatment of fecal impaction in children below 5 years of age. • The use of macrogol products for the treatment of fecal impaction in pediatrics with impaired renal or cardiovascular function is not supported by clinical evidence; and therefore, is not recommended.
Dosage Adjustment	**Altered kidney function:** • No dosage adjustment necessary for any degree of kidney dysfunction (systemic absorption limited). • Administered with caution in renal impairment or patients taking concomitant medications that affect renal function. • Advise these patients of the importance of adequate hydration before, during, and after therapy, and consider performing pre-dose and post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients. **Hepatic impairment:** There are no dosage adjustments.
Contra-indications	• Hypersensitivity to the active substances or to any of the excipients. • Gastrointestinal obstruction or perforation. • Disorders of gastric emptying (e.g., gastroparesis). • Ileus.

Polyethylene glycol 3350 (macrogol)

	• Glucose-6-phosphate dehydrogenase deficiency (due to presence of ascorbate) (in 100 gm product only). • Phenylketonuria (for products containing aspartame). • Toxic megacolon, which complicates very severe inflammatory conditions of the intestinal tract, including Crohn's disease and ulcerative colitis. • Do not use in unconscious patients.
Adverse Drug Reactions	• **Gastrointestinal:** Gastrointestinal signs and symptoms (including abdominal cramps, abdominal distention, abdominal pain, bloating, diarrhea, dyspepsia, eructation, flatulence, frequent bowel movements, loose stools, nausea, rectal hemorrhage, stomach discomfort). • **Hypersensitivity:** Anaphylactic shock, anaphylaxis, hypersensitivity reaction, type I hypersensitivity reaction.
Monitoring Parameters	• Pre-dose and post-colonoscopy renal laboratory tests (electrolytes, creatinine, and BUN). • The elderly are more likely to show CNS signs of dehydration and electrolyte loss than younger adults. Therefore, monitor closely for fluid and electrolyte loss with chronic use. • If patients develop any symptoms indicating arrhythmia or shifts of fluid/electrolytes (e.g., oedema, shortness of breath, increasing fatigue, cardiac failure), plasma electrolytes should be measured, ECG monitored, treatment stopped, and any abnormality treated appropriately.
Drug Interactions	No serious interactions.
Pregnancy and Lactation	**Pregnancy considerations** • Adverse effects are not expected because systemic exposure to macrogol 3350 is minimal. • Macrogol products can be used in pregnant women after careful risk-benefit assessment since clinical evidence on their use is limited. **Breastfeeding Considerations** • There are limited data on the secretion of macrogol in human breast milk, the effects of macrogol products on human infants, or human breast milk production. • Infant exposure and adverse effects are not expected due to the large molecular weight of macrogol. • Macrogol can be used during lactation after risk-benefit assessment.
Administration	**Products containing 6.563 grams per pouch:** • Each sachet should be dissolved in 62.5 mL of water. • The correct number of sachets may be reconstituted in advance and kept covered and refrigerated for up to 24 hours. For example, for use in fecal impaction, 12 sachets can be made up into 750 ml of water.

Polyethylene glycol 3350 (macrogol)

	Products Containing 13.125 grams per pouch: • The contents of each pouch should be dissolved in 125 mL of water. Products containing 100 grams per pouch: • The reconstituted solution should be drunk over a period of one to two hours. • Make sure you finish dose 2 at least 2 hours before your colonoscopy. • Do not add any other ingredients to the preparation. • Do not mix the preparation with starch-based thickeners. • The preparation must be mixed with water. • Instruct patients to drink clear liquids before, during, and after they take the preparation, up until 2 hours before their colonoscopy, to help prevent fluid loss (dehydration) and changes in blood salt (electrolyte) levels. Examples of clear liquids include water, clear broth soups, herbal tea, black tea or coffee, watered down (diluted) (from concentrate) clear fruit juices (without pulp) including apple juice or white grape juice, clear soda, gelatin (without added fruit or topping), popsicles (without pieces of fruit or fruit pulp), strained limeade or lemonade. • Instruct patients not to eat or drink alcohol, milk, anything colored red or purple, or any foods that have pulp. • Instruct patients not to eat on the morning of the colonoscopy procedure. • Instruct patients not to take other laxatives while taking the preparation. • Instruct patients that, if they need to take any other medicines by mouth, they should take those medicines at least 1 hour before starting each dose of the preparation. • Instruct patients not to eat solid food while taking the preparation until after their colonoscopy. • For the Two-Day Split Dosage Schedule: – Instruct patients that they should have a light breakfast and a light lunch on the day before the colonoscopy operation. – Patients must finish eating lunch at least 3 hours before they start taking the preparation. – After starting the preparation, patients can only drink clear liquids. • For the One-Day Morning Dosage Schedule: – On the day before the colonoscopy procedure, patients can eat a light breakfast followed by a light lunch. – For dinner, patients may have clear broth soup or plain yogurt. – Patients should finish dinner by about 8 pm. – After patients start taking the preparation, they can only drink clear liquids. **Refer to the manufacturer's PIL product-specific administration instructions.**
Warnings/ Precautions	**Serious Fluid and Electrolyte Abnormalities:** • Advise patients to hydrate adequately before, during, and after the use of the preparation. • If a patient develops significant vomiting or signs of dehydration after taking the preparation, consider performing post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN).

Polyethylene glycol 3350 (macrogol)

- Bowel preparations can cause fluid and electrolyte disturbances, which can lead to serious adverse reactions, including cardiac arrhythmias, seizures, and renal impairment.
- Correct fluid and electrolyte abnormalities before treatment.
- The preparation should be used with caution in patients using concomitant medications that increase the risk of electrolyte abnormalities [such as diuretics, angiotensin converting enzyme (ACE) inhibitors, or angiotensin receptor blockers (ARBs)].

Cardiac Arrhythmias:

- There have been rare reports of serious arrhythmias (including atrial fibrillation) associated with the use of ionic osmotic laxative products for bowel preparation.
- These occur predominantly in patients with underlying cardiac risk factors and electrolyte disturbances.
- When macrogol is used to prepare for colonoscopy in patients with underlying cardiac risks, caution should be exercised. Also, baseline and post-colonoscopy ECG should be considered.

Seizures:

- There have been rare reports of generalized tonic-clonic seizures and/or loss of consciousness associated with the use of bowel preparation products in patients with no prior history of seizures.
- The seizure cases were associated with electrolyte abnormalities and low serum osmolality, and were resolved by correction.
- Use caution when prescribing that preparation for patients with a history of seizures and in patients at increased risk of seizure, such as patients taking medications that lower the seizure threshold (e.g., tricyclic antidepressants), patients withdrawing from alcohol or benzodiazepines, or patients with known or suspected hyponatremia.

Use in Patients with Renal Impairment:

- Use the preparation with caution in patients with renal impairment or patients taking concomitant medications that affect renal function (such as diuretics, ACE inhibitors, angiotensin receptor blockers, or nonsteroidal anti-inflammatory drugs).
- These patients may be at risk for renal injury.
- Advise these patients of the importance of adequate hydration before, during, and after the use of the preparation, and consider performing pre-dose and post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients.

Colonic Mucosal Ulceration, Ischemic Colitis, and Ulcerative Colitis:

- Osmotic laxatives may produce colonic mucosal aphthous ulcerations, and there have been reports of more serious cases of ischemic colitis requiring hospitalization.

Polyethylene glycol 3350 (macrogol)

- Concurrent use of stimulant laxatives and that preparation may increase the risk and is not recommended.
- Consider the potential for mucosal ulcerations resulting from the bowel preparation when interpreting colonoscopy findings in patients with known or suspected inflammatory bowel disease.

Use in Patients with Significant Gastrointestinal Disease:

- If gastrointestinal obstruction or perforation is suspected, perform appropriate diagnostic studies to rule out these conditions before administering that preparation.

Aspiration:

- Patients with impaired gag reflex or other swallowing abnormalities are at risk for regurgitation or aspiration of the preparation.
- Use with caution in these patients.
- Do not combine that preparation with starch-based thickeners. Polyethylene glycol (PEG), a component of that preparation, when mixed with starch-thickened liquids, reduces the viscosity of the starch-thickened liquid in patients with dysphagia. Thinning of the liquid occurred, and cases of choking and potential aspiration were reported.

Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency:

- Since some preparation contains sodium ascorbate and ascorbic acid, it should be used with caution, especially in G6PD deficiency patients with an active infection, with a history of hemolysis, or taking concomitant medications known to precipitate hemolytic reactions.

Hypersensitivity Reactions:

- It may cause serious hypersensitivity reactions, including anaphylaxis, angioedema, rash, urticaria, and pruritus.
- Inform patients of the signs and symptoms of anaphylaxis, and instruct them to seek immediate medical care should signs and symptoms occur.

Oesophageal Rupture:

- Cases of oesophageal rupture (Boerhaave syndrome) associated with excessive vomiting after intake of macrogol 3350 with electrolytes for bowel preparation have been reported post-marketing, mostly in elderly patients.
- Advise patients to stop administration and seek immediate medical assistance if they experience intractable vomiting and subsequent chest, neck, abdominal pain, dysphagia, hematemesis, or dyspnoea.

Phenylketonuria:

- Some macrogol products contain aspartame, which can be harmful to patients with phenylketonuria.

Other Warnings/ Precautions:

- Macrogol compound powder for oral solution is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

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	• Diagnosis of impaction/fecal loading of the rectum should be confirmed by physical or radiological examination of the abdomen and rectum before use for fecal impaction. • The absorption of other medicinal products could transiently be reduced due to an increase in gastrointestinal transit rate induced by Macrogol compound powder for oral solutions. • Potassium content should be taken into consideration if the patient takes more than one sachet daily and has reduced kidney function or is on a controlled potassium diet.
Storage	Before reconstitution: Store at a temperature not exceeding 30 °C in a dry place. After reconstitution: Cover the solution and store in the refrigerator (2 – 8 °C) for a maximum of 24 hours. Refer to the manufacturer's PIL if there are product-specific instructions on storage.

Stimulant

Bisacodyl

Generic Name	Bisacodyl
Dosage Form/ Strengths	**Enteric-coated tablet**: 5 mg, 10 mg **Suppository**: 5 mg, 10 mg **Enema**: 10 mg/30 mL
Route of Administration	Oral, Rectal
Pharmacologic Category	Laxative, Stimulant ATC: A06AG02
Indications	• Short-term relief of occasional constipation whenever a stimulant laxative is required. • Bowel clearance before surgery or radiological investigation ~~(rectal combined with oral).~~
Dosage Regimen	**Dosing: Adult** **Constipation (Short-term treatment)** • **Oral**: 5 to 10 mg once daily before bedtime. • **Rectal**: 10 mg once daily for immediate effect. **For the preparation of diagnostic procedures and preoperatively** **Adults and children over 10 years:** 10 mg tablet in the morning and 10 mg tablet in the evening, and 10 mg on the following morning. **Dosing: Pediatric** **Constipation (Short-term treatment)** • **Oral:** Children over 12 years: 5 - 10 mg once daily before bedtime. • **Rectal:** Children 4 – 10 years: 5 mg daily for immediate effect. **For the preparation of diagnostic procedures and preoperatively** **Children aged 4 -10 years of age:** 5 mg tablet in the evening and 5 mg suppository on the following morning.
Dosage Adjustment	**Renal Impairment** There are no dosage adjustments available. Caution **Hepatic Impairment** There are no dosage adjustments available.
Contra-indications	• Hypersensitivity to bisacodyl or any other ingredients in the product. • Ileus or intestinal obstruction. • Acute abdominal conditions, including appendicitis. • Acute inflammatory bowel diseases. • Severe abdominal pain associated with nausea and vomiting. • Patients with severe dehydration.

Bisacodyl

	• Bisacodyl Suppositories should not be used when anal fissures or ulcerative proctitis with mucosal damage are present.
Adverse Drug Reactions	**1% - 10%** **Gastrointestinal**: Abdominal cramps, abdominal pain, diarrhea, nausea.
Monitoring Parameters	No monitoring data needed.
Drug Interactions	***Risk X: Avoid combination*** Sodium Sulfate. ***Risk D: Consider therapy modification*** Antacids, Polyethylene Glycol.
Pregnancy and Lactation	**Pregnancy** Limited human data. Long experience showed no undesirable or damaging effects. Use is not recommended, particularly in the first trimester, unless the benefit-to-risk ratio is favorable and only on medical advice. **Lactation** Use is not recommended unless the benefit-to-risk ratio is favorable and only on medical advice.
Administration	**Administration: Oral** • Administer with an adequate amount of fluid. Swallow the tablet whole; do not break, chew, or crush • Do not administer within 1 hour of antacids, milk, or dairy products in order not to prematurely dissolve the enteric coating. **Administration: Rectal** Suppositories should be unwrapped and inserted into the rectum pointed end first. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Use and duration** • Bisacodyl should not be taken continuously for more than five days without investigating the cause of constipation to avoid harming the intestinal function. This product should only be used if the effect cannot be achieved by a change of diet or the administration of bulk-forming agents. Stimulant laxatives do not help with weight loss. • Prolonged or excessive use may lead to impaired function of the intestine, dependence on laxatives, electrolyte imbalance, and hypokalemia.

Bisacodyl

	Dehydration • Intestinal loss of fluids can promote dehydration. Symptoms may include thirst and oliguria. • In renal insufficient or elderly patients suffering from fluid loss, bisacodyl should be discontinued and only be restarted under medical supervision. **Caution** • Patients may experience hematochezia (blood in stool) that is generally mild and self-limiting. • Reports of abdominal pain and bloody diarrhea. Some cases are associated with colonic mucosal ischemia.
Storage	**Oral**: Store below 30 °C; protect from humidity. **Rectal**: Store below 25°C. Protect from humidity and light. N.B.: Refer to the manufacturer's PIL if there are specific considerations**.**

Sodium Picosulfate

Generic Name	Sodium Picosulfate
Dosage Form /Strengths	**Oral drops** 7.5 mg/mL **Tablets**: 5 mg
Route of Administration	Oral
Pharmacologic Category	Osmotic Laxative; Stimulant Laxative ATC: A06AB08
Indications	**Tablets:** Symptomatic treatment of constipation. **Oral drops:** All forms of temporary constipation. Relief of evacuation in cases such as hemorrhoids and anal fissures. In surgical patients preparing for abdominal radiological examination.
Dosage Regimen	**Adults dosing** **Oral**: 5 -10 mg per day. Dose should be reduced or discontinued once regularity is achieved. **N.B**. As with all laxatives, sodium picosulfate should not be taken continuously every day for longer than five days without determining the cause of constipation. **Pediatrics** Should not be used in children and adolescents under the age of 18 years.
Dosage Adjustment	**Renal Impairment** There are no dosage adjustments available. Use with caution. **Hepatic Impairment** There are no dosage adjustments available. Use with caution.
Contra-Indications	• Hypersensitivity to sodium picosulfate or any component of the product. • Ileus, intestinal obstruction. • Acute abdominal conditions like acute appendicitis, acute inflammatory bowel diseases, and severe abdominal pain associated with nausea and vomiting. • Severe dehydration.
Adverse Drug Reactions	**>10%** **Gastrointestinal**: Diarrhea. **1% to 10%** **Gastrointestinal**: Abdominal discomfort, abdominal pain, abdominal cramps.
Monitoring Parameters	• Bowel movement patterns. • Monitor for signs of dehydration or electrolyte imbalance.
Drug Interactions	***Risk D: Consider therapy modification*** Antibiotics, adreno-corticosteroids, cardiac glycosides, and diuretics.

Sodium Picosulfate

Pregnancy and Lactation	**Pregnancy** • No adequate human data. No reports of undesirable or damaging effects during pregnancy. • Medicines should not be used in pregnancy, especially in the first trimester, unless considering benefits are considered and any possible risks to the fetus. **Lactation** Not excreted in breast milk. Nevertheless, use is not recommended during lactation unless considering the benefit and any possible risk to the fetus.
Administration	**Oral Administration** • Administer with adequate fluid intake to prevent dehydration. • Liquid formulation may be diluted with purified water. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Use and duration** • Sodium picosulfate should not be taken continuously without investigating the cause of constipation to avoid harming the intestinal function. This product should only be used if the effect cannot be achieved by a change of diet or the administration of bulk-forming agents. Stimulant laxatives do not help with weight loss. • Prolonged or excessive use may lead to impaired function of the intestine, dependence on laxatives, electrolyte imbalance, and hypokalemia. • Overuse of laxatives can cause a need for larger doses to produce bowel movements. • Should not be used in children and adolescents under the age of 18 years. **Dehydration** • Prolonged or excessive use may lead to electrolyte imbalance (sodium, potassium, magnesium, and phosphorus), which may disturb functions of nerves and muscles, including those of the colon and heart. • May cause intestinal loss of fluids, which may result in dehydration. Renal insufficient or elderly patients should only be used under medical supervision. • Severe dehydration may cause tremors, blurred vision, fainting, or kidney damage. Dehydration often needs medical treatment.
Storage	• Store oral drops between 15°C and 30°C. • Store tablets between 15-30°C. Protect from moisture. Refer to the manufacturer's PIL if there are specific considerations.

Stool Softener

Docusate Sodium

Generic Name	Docusate sodium
Dosage Form/ Strengths	**Oral solution or syrup:** 12.5 mg/5 mL, 20 mg/5 mL, 50 mg/5 mL **Capsules:** 100 mg **Rectal micro enema:** 120 mg/10 gm **Ear drops (wax):** 5 gm/100 mL
Route of Administration	Oral, Rectal, Otic
Pharmacologic Category	Laxative, Stimulant; Stool Softener **Oral ATC**: A06AA02
Indications	**Oral** • To prevent and treat chronic constipation by softening stool. • As an adjunct in abdominal radiological procedures. **Rectal** • Symptomatic treatment of constipation. • Preparation of the colon and rectum for endoscopic examination. **Otic** • For the softening of earwax to facilitate its removal.
Dosage Regimen	**Dosing: Adult** **Rectal enema** **Adults and children 12 years and over** - Use one micro-enema. If required, a second micro-enema may be used on the same or the next day. - Rectal micro enema is usually effective in 5 to 20 minutes. **Oral** **N.B.** Doses should be started in high doses, then reduced as the patient's condition improves. Maximum dose: 500 mg. **Capsule:** Up to 500 mg should be taken daily in divided doses. **Solution:** 100 to 150mg three times daily, followed by plenty of water or a flavored drink. **For barium meals**: 400 mg with the meal. **Otic solution** 4 drops twice daily to be instilled into the affected ear (or ears) for 2-3 days.

Docusate Sodium

	Dosing: Pediatric **Oral solution** **Infants ≥6 months:** 12.5 mg three times daily. **Children:** 12.5 mg – 25 mg three times daily. **For barium meals**: 75 mg to be taken with a meal. Dilute the medicine in a glass of flavored drink, e.g., fruit juice or milk. Drink the diluted medicine within 30 minutes of preparation. **Otic solution** **Children**: The number of drops instilled may be reduced to the level required to fill the ear with solution.
Dosage Adjustment	**Renal Impairment** There are no dosage adjustments. **Hepatic Impairment** There are no dosage adjustments.
Contra-indications	Hypersensitivity to the active ingredient or to any of the excipients. **Oral and Rectal suppository** Abdominal pain, intestinal obstruction, nausea, and vomiting. **Enema** Hemorrhoids, anal fissures, rectocolitis, anal bleeding, abdominal pain, intestinal obstruction, nausea, vomiting, inflammatory bowel disease, and ileus. **Otic solution** Perforation of the eardrum, inflammation of the ear.
Adverse Drug Reactions	**Rectal, Oral** **≤ 0.1%** **Gastrointestinal disorders**: diarrhea, nausea, abdominal cramps. **Otic** **Frequency not known** Otitis externa, hypersensitivity/allergic reactions, dizziness, hypoacusis, ear pain, ear discomfort, allergic skin reactions, contact dermatitis, application site reactions (e.g., irritation, pruritus, exfoliation, inflammation, pain, erythema).
Monitoring Parameters	No monitoring data needed.
Drug Interactions	Docusate sodium should not be taken concurrently with mineral oil.
Pregnancy and Lactation	**Oral, rectal** **Pregnancy** Inadequate data. Use in pregnancy only if the benefits outweigh the risks. **Lactation** Docusate sodium is excreted in breast milk. A decision on whether to continue or discontinue lactation or therapy should be made. Caution.

Docusate Sodium

	Otic solution No evidence that it should not be used in pregnancy and Lactation.
Administration	**Oral Administration** • Ensure enough fluid intake. • Liquid dosage forms may be diluted in a glass of flavored drink, e.g., fruit juice or milk, and should be taken within 30 minutes of preparation. **Rectal Administration** • The applicator is inserted into the rectum after removing the protective cap, squeezing gently until the tube is empty. A drop of the gel may be used as a lubricant if required. • The laxative effect occurs in 5-20 minutes. **Otic solution** Drops to be instilled into the ears. The head should be inclined with the affected ear uppermost. The ear can be plugged with cotton wool, soaked in ear wax remover drops if necessary. After 2-3 days, the wax should be easy to remove. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Oral: Use and duration** • This product should only be used if the effect cannot be achieved by a change of diet or the administration of bulk-forming agents. Stimulant laxatives do not help with weight loss. • Docusate sodium should not be taken continuously without investigating the cause of constipation to avoid harming the intestinal function. Prolonged or excessive use may lead to impaired function of the intestine, dependence on laxatives, electrolyte imbalance, and hypokalemia. • If laxatives are needed every day, or if there is persistent abdominal pain, consult your doctor. **Otic** If pain or inflammation is experienced, treatment should be discontinued.
Storage	Store at 15-30 ºC. Protect capsules from moisture. Refer to the manufacturer's PIL if there are specific considerations.

Herbal Medicines: Refer to the Egyptian Herbal Monograph

Senna

Psyllium

You can access it through the following link

https://www.edaegypt.gov.eg/ar/%D8%A5%D8%B5%D8%AF%D8%A7%D8%B1%D8%A7%D8%AA-%D8%A7%D9%84%D9%87%D9%8A%D8%A6%D8%A9/%D9%85%D9%88%D9%86%D9%88%D8%AC%D8%B1%D8%A7%D9%81%D8%A7%D8%AA/

Miscellaneous

Lubiprostone

Generic Name	Lubiprostone
Dosage Form/ Strengths	**Capsule**: 8 mcg, 24 mcg
Route of Administration	Oral
Pharmacologic Category	Chloride Channel Activator; Gastrointestinal Agent, Miscellaneous ATC: A06AX03
Indications	Treatment of • Chronic idiopathic constipation in adults. • Opioid-induced constipation in adult patients with chronic non-cancer pain who do not require frequent (e.g. weekly) opioid dosage escalation. • Irritable bowel syndrome with constipation in women ≥18 years old.
Dosage Regimen	• **Chronic idiopathic constipation or Opioid-induced constipation in adults** **Oral**: 24 mcg twice daily. • **Irritable bowel syndrome with constipation** **Oral:** 8 mcg twice daily. **N.B.** Assess periodically the need for continuous therapy.
Dosage Adjustment	**Renal Impairment** No adjustments needed. **Hepatic Impairment** • **Chronic idiopathic constipation** – Moderate Impairment: 16 mcg twice daily. – Severe Impairment: 8 mcg twice daily. • **Irritable bowel syndrome with constipation** – Moderate Impairment: No adjustment necessary. – Severe Impairment: 8 mcg once daily. **N.B.** If the dose is tolerated, doses can then be escalated to full dosing if needed with appropriate monitoring.
Contra-indications	Known or suspected mechanical gastrointestinal obstruction.
Adverse Drug Reactions	**>10%** **Gastrointestinal**: Diarrhea (7% to 12%; severe diarrhea: ≤2%), nausea (8% to 29%, incidence lower in males; older adults: 19%; severe nausea: 1% to 4%). **Nervous system**: Headache (2% to 11%). **1% to 10%** **Cardiovascular**: Chest discomfort (≤2%), chest pain (≤2%), edema (3%), peripheral edema (1%)

Lubiprostone

	Gastrointestinal: Abdominal distention (3% to 6%), abdominal distress (3%), abdominal pain (4% to 8%), dyspepsia (2%), flatulence (4% to 6%), loose stools (3%), vomiting (3%), xerostomia (1%) **Nervous system**: Dizziness (3%), fatigue (2%) **Respiratory**: Dyspnea (2% to 3%)
Monitoring Parameters	Liver functions.
Drug Interactions	***Risk C: Monitor therapy*** Levomethadone, Methadone.
Pregnancy and Lactation	**Pregnancy** Limited human data. Animal data show possible fetal risk. **Lactation** No human data. Not present in animal milk. Monitor infants for diarrhea while their mother is on therapy.
Administration	**Oral administration** • Capsules should be swallowed whole with food and water. • Concomitant administration of food may reduce nausea symptoms. **N.B.** Refer to the manufacturer's PIL if there are specific considerations.
Warnings/ Precautions	**Diarrhea** Avoid use in patients with severe diarrhea. If severe diarrhea occurs during treatment, therapy should be discontinued and the patient should consult their healthcare provider. **Syncope and Hypotension** May occur after taking the first dose or with subsequent doses. Generally, resolves before the next dose, but may recur with repeat dosing. The patient should consult their healthcare provider if symptoms occur. **Dyspnea** May occur within an hour of the first dose. Generally, resolves within hours, but may recur with repeat dosing. The patient should consult their healthcare provider if symptoms occur. **Bowel Obstruction** Evaluate patients with symptoms suggestive of mechanical gastrointestinal obstruction before initiating treatment.
Storage	Store between 15° to 30°C. Protect from light and extreme temperatures. Refer to the manufacturer's PIL if there are specific considerations.

Bismuth subcitrate

Generic Name	Bismuth subcitrate
Dosage Form/Strengths	**Film-coated tablet:**295.1 mg equivalent to 120 mg bismuth oxide. **Capsule**: 140 mg of bismuth subcitrate potassium, in combination with 125 mg of metronidazole, and 125 mg of tetracycline hydrochloride.
Route of Administration	Oral
Pharmacologic Category	**Pharmacological category** Gastrointestinal Agent, Miscellaneous **ATC** A02BX05
Indications	• In combination with the eradication of Helicobacter pylori in patients with active duodenal ulcer or history of duodenal ulcer disease (active or history of within the past 5 years). • Bismuth oxide is indicated in the treatment of: ○ Chronic gastritis associated with Helicobacter pylori • Gastric and duodenal ulcer Refer to the manufacturer's labeling if there are specific considerations for the combination.
Dosage Regimen	(Refer to manufacturer labeling if there are specific considerations for the combination) **<u>For bismuth subcitrate, 295.1 mg is equivalent to 120 mg bismuth oxide</u>** **Adults:** 240 mg (2 tablets), 2 times a day. As an alternative dose for adults: 120 mg (1 tablet), 4 times a day. **Elderly patients**: 240 mg (2 tablets), 2 times a day. As an alternative dose for the elderly: 120 mg (1 tablet), 4 times a day. **<u>140 mg of bismuth subcitrate potassium, in combination with 125 mg of metronidazole, and 125 mg of tetracycline hydrochloride</u>** Administer three capsules 4 times a day (after meals and at bedtime) for 10 days. One omeprazole 20mg capsule should be taken twice a day with a bismuth capsule after the morning and evening meal for 10 days
Dosage Adjustment	(Refer to manufacturer labeling if there are specific considerations for the combination) **<u>Dosing: Altered kidney function: Adult/Pediatrics</u>** Use is contraindicated. **<u>Dosing: Hepatic impairment: Adults/Pediatrics</u>** There are no dosage adjustments.

Bismuth subcitrate

Contra-indications	(Refer to manufacturer labeling if there are specific considerations for the combination) • • Bismuth oxide is contraindicated in children under 12 years of age, and is not recommended in patients aged 12 to 18 years. • Severe kidney impairment. • Pregnancy • A combination of bismuth subcitrate potassium, with metronidazole, and tetracycline hydrochloride is contraindicated with methoxyflurane, as concurrent use of tetracycline hydrochloride with methoxyflurane has been reported to result in fatal renal toxicity. • A combination of bismuth subcitrate potassium, with metronidazole, and tetracycline is contraindicated in patients who have taken disulfiram within the last two weeks. Psychotic reactions have been reported in alcoholic patients who are using metronidazole and disulfiram concurrently.
Adverse Drug Reactions	(Refer to manufacturer labeling if there are specific considerations for the combination) • Gastrointestinal: Burning sensation of the gastrointestinal tract, darkening of stools, fecal discoloration, nausea, stomach pain, vomiting. • Skin: Rash and irritation • Combination of bismuth subcitrate potassium, with metronidazole, and tetracycline hydrochloride: has the adverse drug reactions of tetracycline and metronidazole
Monitoring Parameters	(Refer to manufacturer labeling if there are specific considerations for the combination) H. pylori eradication confirmation, when indicated.
Drug Interactions	(Refer to manufacturer labeling if there are specific considerations for the combination) ***Risk D: Consider therapy modification:*** Antacids and Tetracyclines. N.B., Combination of bismuth subcitrate potassium, with metronidazole, and tetracycline hydrochloride: has the interactions of tetracycline and metronidazole
Pregnancy and Lactation	(Refer to manufacturer labeling if there are specific considerations for the combination) **Pregnancy considerations** Avoid use in pregnancy. **Breastfeeding Considerations** It is not known if bismuth subcitrate is present in breast milk. Avoid use in breastfeeding.

Bismuth subcitrate

Administration	• The film-coated tablets should be swallowed with some still water and not chewed. • The capsules should be swallowed whole with a full glass of water. Ingestion of adequate amounts of fluid, particularly with the bedtime dose, is recommended to reduce the risk of esophageal irritation and ulceration by tetracycline hydrochloride. • The film-coated tablets: Administer on an empty stomach. • The film-coated tablets: Administer 30 minutes before three main meals and 2 hours after the last meal of the day (four times daily regimen) or administer 30 minutes before morning and evening meals (twice daily regimen). • Capsules: Administer after meals and at bedtime **Refer to the manufacturer's PIL if there are specific considerations**
Warnings/ Precautions	(Refer to manufacturer labeling if there are specific considerations for the combination) • The maximum duration of a course of treatment is 2 months. • For the treatment of gastric or duodenal ulcer, the duration of a course of treatment is 4 to 8 weeks. • For the eradication of Helicobacter pylori, the selection of a combination therapy and a treatment duration of 7 to 14 days, taking into account the individual drug tolerance of each patient and according to regional resistance patterns and treatment guidelines. • Prolonged administration of the drug is not advisable, nor as maintenance treatment. • Drinking alcoholic beverages is also not recommended, since bismuth subcitrate is a potent inhibitor of alcohol dehydrogenase, an enzyme that prevents bacterial oxidation of ethanol to acetaldehyde. Typical symptoms of this excess acetaldehyde include skin rash, tachycardia. shortness of breath, nausea, and vomiting (antabus effect). • Bismuth may cause temporary darkening of the tongue and/or black stools; generally reversible within several days after treatment is discontinued. • This medicinal product contains 36.8 mg of potassium per tablet, which should be taken into account in the treatment of patients with renal insufficiency or with a diet low in potassium.
Storage	Store below 30 °C in a dry place. Refer to the manufacturer's PIL if there are specific considerations

Rifaximin: Refer to antimicrobial formulary
https://edaegypt.gov.eg/media/gubjjcgl/1-new-code-antimicrobial-egyptian-national-formulary_c.pdf

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