DOMPER® TABLET 10 mg

Ingredient(s):
Each tablet contains:
Domperidone ..... 10 mg

Pharmacology :
Pharmacodynamics:
Domperidone is a dopamine antagonist (blocking both D1 & D2 receptors) which is structurally related to the benzimidazole. Domperidone is a potent gastrokinetic agent. Domperidone facilitates gastrointestinal smooth muscle activity by inhibiting dopamine at the D1 receptors and inhibiting the release of neural acetylcholine by blocking D2 receptors.
Domperidone binds with high affinity to the dopamine receptor. It does not cross the blood brain barrier or the placental barrier but exerts its effects at peripheral sites: the chemoreceptor trigger zone (in the brainstem) and the gastrointestinal tract. Domperidone inhibits dopamine-induced gastric relaxaton and the inhibitory effects of secretin, whose actions may be mediated by dopamine release. Finally, it stimulates phasic activity in the gastro-duodenal area and improves gastro-duodenal coordination.

Pharmacokinetics:
Absorption
Although absorption is rapid, the systemic bioavailability of domperidone is only about 13% to 17% in fasting subjects given an oral dose; this is increased when domperidone is given after food. The low bioavailability is thought to be due to first-pass hepatic and intestinal metabolism. Peak plasma concentrations are achieved 30 minutes after an oral dose.

Distribution
Domperidone is 91 - 93% bound to plasma proteins. Domperidone does not readily cross the blood-brain barrier. In humans, the apparent volume of distribution is 440 L. Small amounts of domperidone are distributed into breast milk; concentrations are 10 to 50% of those in maternal serum.

Metabolism
It undergoes rapid and extensive hepatic metabolism. The main metabolic pathways are N-dealkylation by cytochrome P450 isoenzyme CYP3A4, and aromatic hydroxylation by CYP3A4, CYP1A2, and CYP2E1.

Excretion
Urinary and faecal excretions amount to 31 and 66% of the oral dose respectively. The proportion of the drug excreted unchanged is small (10% of faecal excretion and approximately 1% of urinary excretion). Domperidone as an elimination half-life of about 7 to 9 hours, but is prolonged in patients with severe renal insufficiency.

Indication(s):
Domperidone is indicated for the symptomatic relief of nausea and vomiting.
This includes:
- Nausea and vomiting of functional, organic, infectious or dietary origin.
- Nausea and vomiting induced by:
  - radiotherapy or drug therapy
  - dopamine agonists (such as L-dopa and bromocriptine) used in the treatment of Parkinson's disease.

Dosage and Administration:
It is recommended to take this drug 15 – 30 minutes before meals. If taken after meals, absorption of the drug is somewhat delayed.

Adults and adolescents ≥ 12 years and weighing ≥ 35kg and children weighing ≥ 35kg
The dose of Domperidone should be the lowest effective dose for the individual situation (typically 30 mg/day) and can be increased if necessary to a maximum daily oral dose of 40 mg.
Usually, the maximum treatment duration should not exceed one week for the treatment of acute nausea and vomiting. If nausea and vomiting persists for longer than one week, patients should consult their physician. For other indications, the initial duration of treatment is up to four weeks. If treatment exceeds four weeks, patients should be reevaluated and the need for continued treatment reassessed.

Formulation (domperidone per unit)	Dosage	Maximum dose per day
Tablet (10 mg/tablet)	1 tablet three to four times per day	40 mg (4 x 10 mg tablet)

Adults and adolescents (≥ 12 years of age) weighing < 35 kg
The dose of Domperidone should be the lowest effective dose. The total daily dose is dependent on weight.
Usually, the maximum treatment duration should not exceed one week for the treatment of acute nausea and vomiting. For other indications, the initial duration of treatment is up to four weeks. If treatment exceeds four weeks, patients should be reevaluated and the need for continued treatment reassessed. Due to the need for accurate dosing, tablets are unsuitable for use in adults and adolescents weighing less than 35 kg.

Infants and children < 12 years of age and weighing < 35 kg
The efficacy of Domperidone has not been established in infants and children < 12 years of age and weighing < 35 kg.

Renal impairment
Since the elimination half-life of domperidone is prolonged in severe renal impairment (serum creatinine >6 mg/100 mL, i.e. >0.6mmol/L), the dosing frequency of domperidone should be reduced to once or twice daily, depending on the severity of the impairment, and the dose may need to be reduced. Patients with severe renal impairment should be reviewed regularly.

Hepatic impairment
Domperidone is contraindicated for patients with moderate (Child-Pugh 7 to 9) or severe (Child-Pugh >9) hepatic impairment. Dose adjustment is not required for patients with mild (Child-Pugh 5 to 6) hepatic impairment.

Route of Administration: Oral

Contraindication(s):
This drug is contraindicated in the following situations:
- Known hypersensitivity to domperidone or any of the excipients.
- Prolactin-releasing pituitary tumour (prolactinoma).
- In 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 (see Precautions /Warnings).
- Co-administration with QT-prolonging drugs.
- Co-administration with potent CYP3A4 inhibitors (regardless of their QT-prolonging effects).
- Whenever stimulation of gastric motility might be dangerous, e.g., in the presence of gastro-intestinal haemorrhage, mechanical obstruction or perforation.
- In patients with moderate or severe hepatic impairment.

Warnings and Precautions:
1. Use with caution in patient with renal impairment.
2. Domperidone is not recommended for chronic administration.

3. When antacids or antisecretory agents are used concomitantly, they should not be taken simultaneously with oral formulations of Domperidone; i.e. they should be taken after meals and not before meals.
4. Cardiovascular effects:
   Domperidone has been associated with prolongation of the QT interval on the electrocardiogram. During post-marketing surveillance, there have been very rare cases of QT-prolongation and torsades de pointes in patients taking domperidone. These reports included patients with confounding risk factors, electrolyte abnormalities and concomitant treatment which may have been contributing factors (see Adverse Reactions).
   Epidemiological studies showed that domperidone was associated with an increased risk of serious ventricular arrhythmias or sudden cardiac death (see Adverse Reactions). A higher risk was observed in patients older than 60 years, patients taking daily doses greater than 30 mg, and patients concurrently taking QT-prolonging drugs or CYP3A4 inhibitors.
   Domperidone should be used at the lowest effective dose in adults and children.
   Domperidone is contraindicated in patients with known existing prolongation of cardiac conduction intervals, particularly QTc, in patients with significant electrolyte disturbances (hypokalaemia, hyperkalaemia, hypomagnesaemia), or bradycardia, or in patients with underlying cardiac diseases such as congestive heart failure due to increased risk of ventricular arrhythmia (see Contraindications).
   Electrolyte disturbances (hypokalaemia, hyperkalaemia, hypomagnesaemia) or bradycardia are known to be conditions increasing the proarrythmic risk.
   Treatment with domperidone should be stopped if signs or symptoms occur that may be associated with cardiac arrhythmia, and the patients should consult their physician.
   Patients should be advised to promptly report any cardiac symptoms.
5. Effects on Ability to Drive and Use Machines: Domperidone has no or negligible influence on the ability to drive or use machinery.
6. Use in infants: Although neurological side effects are rare, the risk of neurological side effects is higher in young children since metabolic functions and the blood-brain barrier are not fully developed in the first months of life. Overdosing may cause extrapyramidal symptoms in children, but other causes should be taken into consideration.

Interaction with Medicaments:
1. Co-administration with anticholinergic drugs may compromise the beneficial effect of Domperidone.
2. Care should be exercised when Domperidone is administered in combination with MAO inhibitors.
3. In vitro data suggest that the concomitant use of drugs that significantly inhibit CYP3A4 may result in increased plasma levels of domperidone. Examples of CYP3A4 inhibitors include Azole antifungals, macrolide antibiotics, HIV protease inhibitors and nefazodone.
4. Concomitant use of QT-prolonging medicinal products such as anti-arrhythmics class IA and class III, anti-pyschotics, anti-depressants, antibiotics, antifungal agents, antimalarial agents, gastro-intestinal medicines, antihistaminics, due to increased risk of occurrence of QT-interval prolongation.
5. Caution in concomitant use with bradycardia and hypokalaemia-inducing drugs.
6. A QTc prolongation was observed in an interaction study for the combination of Domperidone (10 mg qid) and ketoconazole (200 mg bid) or erythromycin (500mg tds).

Pregnancy and Lactation:

Pregnancy

There are limited post-marketing data on the use of domperidone in pregnant women. Studies in animals have shown reproductive toxicity at maternally toxic doses. Domperidone should only be used during pregnancy when justified by the anticipated therapeutic benefit.

Breast-feeding

Domperidone is excreted in human milk and breast-fed infants receive less than 0.1 % of the maternal weight-adjusted dose. Occurrence of adverse effects, in particular cardiac effects cannot be excluded after exposure via breast milk. A decision should be made whether to discontinue breast-feeding or to discontinue/abstain from domperidone therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. Caution should be exercised in case of QTc prolongation risk factors in breast-fed infants.

Side Effects/Adverse Reactions:

Domperidone is well tolerated. The side effects which have been reported are as follows:
CNS: dry mouth, headache, insomnia, dizziness, thirst.
Gastrointestinal: transient mild abdominal cramps, diarrhoea.
Endrocrinologic: Domperidone may elevate prolactin level, which may lead to mastalgia, galactorrhoea or gynecomastia.
Postmarketing: Cardiovascular : Frequency: very rare
: edema, palpitations, ventricular arrhythmias, QTc prolongation, *Torsade de Pointes*, sudden cardiac death (see Warnings and Precautions).
Paediatric population: Extrapyramidal disorder occurs primarily in neonates and infants. Other central nervous system-related effects of convulsion and agitation also are primarily reported in infants and children.

Symptoms and Treatment of Overdose:

Symptoms

Overdose has been reported primarily in infants and children. Symptoms of overdosage may include agitation, altered consciousness, convulsions,disorientation, somnolence and extrapyramidal reactions.

Treatment

There is no specific antidote to domperidone, but in the event of overdose, standard symptomatic treatment should be given immediately. Gastric lavage as well as the administration of activated charcoal, may be useful. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation. Close medical supervision and supportive therapy is recommended.
Anticholinergic, anti-parkinson drugs may be helpful in controlling the extrapyramidal reactions.

Product Description:

A white color tablet, one side with a score " ⊖ ", and the other side impressed with a mark " (R) ".

Shelf Life:

3 Years from the date of manufacture

Storage Condition(s):

Store at temperature below 30°C. Protect from light and moisture.

Dosage forms and packaging available

Tablets in Blister packing of 10's x 10, 10's x 50 and 10's x 100.

Y. S. P.®
Manufacturer and Product Registration Holder:
Y.S.P. INDUSTRIES (M) SDN. BHD. (199001001034)
Lot 3, 5, 7, 12 & 14, Jalan P/7, Section 13,
Kawasan Perindustrian Bandar Baru Bangi,
43000 Kajang, Selangor, Malaysia.
Ordering Line: 1 800 88 3027
Product Info: 1 800 88 3679

Date of revision: 13 Dec 2024