Dimension L-210 mm & W-160 mm (Auto DS)
After folding : 160 mm x 36 mm (Both side print)

Motigut® Suspension 1 mg/ml

1. NAME OF THE MEDICINAL PRODUCT: Motigut® Suspension 1 mg/ml
2. QUALITATIVE AND QUANTITATIVE COMPOSITION: Each ml oral suspension contains domperidone 1 mg.
3. PHARMACEUTICAL FORM: Suspension
Product Description: A white raspberry-banana flavored suspension having sweet taste, filled and sealed in amber color PET bottle with white color SQUARE printed cap.
4. PHARMACOLOGICAL PROPERTIES
4.1 Pharmacodynamic properties
Pharmacotherapeutic group: Propulsive
ATC Code: A03F A 03
Domperidone is a dopamine antagonist with anti-emetic properties, Domperidone does not readily cross the blood-brain barrier. In domperidone users, especially adults, extrapyramidal side effects are very rare, but domperidone promotes the release of prolactin from the pituitary. Its anti-emetic effect may be due to a combination of peripheral (gastrokinetic) effects and antagonism of dopamine receptors in the chemoreceptor trigger zone, which lies outside the blood-brain barrier in the area postrema. Animal studies, together with the low concentrations found in the brain, indicate a predominantly peripheral effect of domperidone on dopamine receptors. Studies in man have shown oral domperidone to increase lower oesophageal pressure, improve antroduodenal motility and accelerate gastric emptying. There is no effect on gastric secretion.
4.2 Pharmacokinetic properties
Absorption
In fasting subjects, domperidone is rapidly absorbed after oral administration, with peak plasma concentrations at 30 to 60 minutes. The low absolute bioavailability of oral domperidone (approximately 15%) is due to an extensive first-pass metabolism in the gut wall and liver. Although domperidone's bioavailability is enhanced in normal subjects when taken after a meal, patients with gastro-intestinal complaints should take domperidone 15-30 minutes before a meal. Reduced gastric acidity does not impair the absorption of domperidone. Oral bioavailability is not decreased by prior concomitant administration of cimetidine and sodium bicarbonate. The time of peak absorption is slightly delayed and the AUC somewhat increased when domperidone is taken after a meal.
Distribution
Oral domperidone does not appear to accumulate or to induce its own metabolism; a peak plasma level after 90 minutes of 21 ng/ml after two weeks oral administration of 30mg per day was almost the same as that of 18 ng/ml after the first dose. Domperidone is 91-93% bound to plasma proteins. Distribution studies with radiolabelled drug in animals have shown wide tissue distribution, but low brain concentration. Small amounts of drug cross the placenta in rats.
Metabolism
Domperidone undergoes rapid and extensive hepatic metabolism by hydroxylation and N-dealkylation. CYP3A4 is a major form of cytochrome P-450 involved in the N-dealkylation of domperidone, whereas CYP3A4, CYP1A2 and CYP2E1 are involved in domperidone aromatic hydroxylation.
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). The plasma half-life after a single oral dose is 7-9 hours in healthy subjects but is prolonged in patients with severe renal insufficiency.
5. CLINICAL PARTICULARS:
5.1 Therapeutic indications
Domperidone is indicated for the relief of the symptoms 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.
5.2 Recommended Dosage
It is recommended to take Motigut Suspension 15-30 minutes before meals. If taken after meals, absorption of the drug is somewhat delayed.
Adults and adolescents ≥ 12 years of age and weighing ≥ 35 kg & children <12 years of age and weighing ≥ 35 kg
The dose of Motigut 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
Tablets (10 mg/tablet)	1 tablet three to four times per day	40mg (4x10 mg tablet)
Oral suspension (1 mg/ml)	10 mL three to four times per day	40mg (40 mL of 1mg/mL oral suspension)

Adults and adolescents (≥ 12 years of age) weighing < 35 kg
The dose of Motigut should be the lowest effective dose. The total daily dose is dependent on weight (see table below).
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.

Formulation (domperidone per unit)	Dosage	Maximum dose per day
Oral suspension (1 mg/ml)	0.25 mg/kg three to four times per day	35 mg (1 mg/kg but no more than 35 mL)

Infants and children <12 years of age and weighing < 35 kg
The efficacy of Motigut 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. > 0.6 mmol/L), the dosing frequency of Motigut 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
Motigut 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.
5.3 Contraindications
Motigut 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 Warnings and Precautions).
- Co-administration with QT-prolonging drugs
- Co-administration with potent CYP3A4 inhibitors (regardless of their QTprolonging 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.

5.4 Warnings and precautions

Precautions for use

The oral suspension contains sorbitol and may be unsuitable for patients with sorbitol intolerance.

Use during lactation

The total amount of domperidone excreted in human breast milk is expected to be less than 7mg per day at the highest recommended dosing regimen. It is not known whether this is harmful to the newborn. Therefore breastfeeding is not recommended for mothers who are taking Domperidone.

Use in infants

Neurological side effects are rare. Since metabolic functions and the blood-brain barrier are not fully developed in the first months of life the risk of neurological side effects is higher in young children. Therefore, it is recommended that the dose be determined accurately and followed strictly in neonates, infants, toddlers and small children. Overdosing may cause extrapyramidal symptoms in children, but other causes should be taken into consideration.

Use in liver disorders

Since domperidone is highly metabolised in the liver, Domperidone should be not be used in patients with hepatic impairment.

Renal insufficiency

In patients with severe renal insufficiency (serum creatinine> 6 mg/100 ml, i.e.> 0.6 m mol/l) the elimination halflife of domperidone was increased from 7.4 to 20.8 hours, but plasma drug levels were lower than in healthy volunteers. Since very little unchanged drug is excreted via the kidneys, it is unlikely that the dose of a single administration needs to be adjusted in patients with renal insufficiency. However, on repeated administration, the dosing frequency should be reduced to once or twice daily depending on the severity of the impairment, and the dose may need to be reduced. Such patients on prolonged therapy should be reviewed regularly.

Use with ketoconazole

A slight increase of QT interval (mean less than 10msec) was reported in a drug-drug interaction study with oral ketoconazole. Even if the significance of this study is not fully clear, alternative therapeutic options should be considered if antifungal treatment is required.

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.

5.5 Interaction with other medicinal products and other forms of interaction

The main metabolic pathway of domperidone is through CYP3A4. In vitro and human data show that the concomitant use of drugs that significantly inhibit this enzyme may result in increased plasma levels of domperidone. Co-administration of domperidone with potent CYP3A4 inhibitors which have been shown to cause QT interval prolongation is contraindicated. (See section Contraindications)

5.6 Pregnancy and lactation

The potential risk for humans is unknown. Therefore, domperidone should only be used during pregnancy when justified by the anticipated therapeutic benefit. Domperidone concentrations in breast milk of lactating women are 10 to 50% of the corresponding plasma concentrations and expected not to exceed 10ng/ml. The total amount of domperidone excreted in human breast milk is expected to be less than 7mg per day at the highest recommended dosing regimen. It is not known whether this is harmful to the newborn. Therefore breast-feeding is not recommended for mothers who are taking domperidone.

5.7 Effects on ability to drive and use machines

Motigut has no or negligible influence on the ability to drive and use machines.

5.8 Undesirable effects

At the dosages and duration recommended here domperidone is generally very well tolerated with few undesirable effects. Immune system disorder: Very rare; allergic reaction.

Endocrine disorder: Rare; increased prolactin levels.

Nervous system disorders: Very rare; extrapyramidal side effects.

Gastrointestinal disorders: Rare; gastrointestinal disorders, including very rare transient intestinal cramps.

Skin and subcutaneous tissue disorders: Very rare; urticaria.

Reproductive system and breast disorders: Rare; galactorrhoea, gynaecomastia, amenorrhoea.

As the hypophysis is outside the blood brain barrier, domperidone may cause an increase in prolactin levels. In rare cases, this hyperprolactinaemia may lead to neuro endocrinological side effects such as galactorrhoea, gynaecomastia and amenorrhoea.

Extrapyramidal side effects are very rare in neonates and infants, and exceptional in adults. These side effects reverse spontaneously and completely as soon as the treatment is stopped.

Post marketing

Cardiac Disorders

Frequency: Very rare

Ventricular arrhythmias, QTc prolongation, Torsadede Pointes, Sudden cardiac death (see Warnings and Precautions).

5.9 Overdose

Symptoms: Symptoms of overdosage may include drowsiness, disorientation and extrapyramidal reactions, especially in children.

Treatment: There is no specific antidote to domperidone, but in the event of overdose, gastric lavage as well as the administration of activated charcoal, may be useful. Close medical supervision and supportive therapy is recommended.

Anticholinergic, anti-parkinson drugs may be helpful in controlling the extrapyramidal reactions.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Liquid Sorbitol (Non-Crystalizing), Sodium Methyl Hydroxybenzoate, Dispersible Cellulose (Avicel RC 591), Sodium Propyl Hydroxybenzoate, Saccharin Sodium, Carmellose Sodium (Tylopur C600), Polysorbate 60 (Tween 60), Anhydrous Citric Acid, Sodium Hydroxide, Raspberry Liquid Essence No. 1, Banana Liquid Essence, Purified Water

6.2 Incompatibilities: Not applicable.

6.3 Special precautions for storage: Store below 30°C. Protect from light. Keep out of children's' reach.
Jauhkan dari kanak-kanak

6.4 Nature and contents of container: Each amber colored PET bottle contains 60 ml oral suspension.

Mfg. Lic. No. : 33 & 114

Manufactured by :
SQUARE PHARMACEUTICALS PLC.
Square Road, Salgaria, Pabna 6600, Bangladesh

® Registered Trade Mark
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