DOMIL SUSPENSION

Description: White coloured liquid having raspberry flavour.

Composition: Each 5ml suspension contains domperidone 5mg

Actions & Pharmacology:
Domperidone is a dopamine antagonist with antiemetic properties similar to those of metoclopramide. However, domperidone does not readily cross the blood-brain barrier and is less likely than metoclopramide to produce central effects such as extrapyramidal reactions or drowsiness. Its mode of action is predominantly due to peripheral stimulation of gastrointestinal motility, as well as blockade of dopamine receptors which are located in the chemoreceptor zone outside the blood-brain barrier. Domperidone has no effect on gastric secretion. However, plasma prolactin levels may be increased. Domperidone is absorbed from the gastrointestinal tract, but its oral bioavailability is low, approximately 15%, due to an extensive first-pass metabolism in the intestinal wall and liver. Oral bioavailability is increased when domperidone is taken after a meal, and is decreased when gastric acidity is reduced, such as with prior administration of cimetidine. Domperidone is highly bound to plasma proteins. It does not readily cross the blood-brain barrier, and a small proportion is excreted in breast milk. Domperidone is rapidly and extensively metabolized in the liver, and its metabolites excreted mainly in the urine (31% of an oral dose) and faeces (66%). Only a small amount of the drug is excreted unchanged. The plasma half-life after a single oral dose is about 8 hours, but is prolonged in patients in severe renal insufficiency. 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 impairs the absorption of domperidone. Oral bioavailability is decreased by prior administration of cimetidine or sodium bicarbonate. The time of peak absorption is slightly delayed and the AUC somewhat increased when the oral drug is taken after meal.

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:
  - Radiotheraphy or drug theraphy
  - Dopamine agonists (Such as L-dopa and bromocriptine) used in the treatment of parkinson's desease.

Contraindications:
Domperidone is contraindicated in the following conditions:

- Hypersensitivity to domperidone or to any other component of the product
- Patients with a prolactin-releasing 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 warning and precautions).
- Co-administration with QT-prolonging drugs

- Co-administration with potent CYP3A4 inhibitors regardless of their QT-prolonging effects (See Section Interactions).
- Whenever stimulation of gastric motility might be dangerous, eg, in the presence of gastrointestinal haemorrhage, mechanical obstruction or perforation.
- In patients with moderate or severe hepatic impairment.

Precautions/Warnings:
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.

Hepatic impairment: Domperidone should be used with caution in patients with hepatic impairment, since the drug is extensively metabolized.

Renal impairment: In patients with severe renal impairment (serum creatinine >6mg/100ml), it is unlikely that a single dose acute administration requires adjustment. However, during prolonged or 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. Patients on prolonged therapy should be reviewed regularly.

Pregnancy and lactation:
As with all drugs, domperidone should only be used during the first trimester of pregnancy when the anticipated benefits clearly outweigh the potential risk. A small amount of domperidone is excreted in breast milk, thus, it is not recommended to be given to lactating mothers unless clearly indicated.

Use in children: 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.

Effects on the ability to drive or operate machinery:
Domperidone does not usually affect mental alertness.

Drug interactions:
Concurrent administration of domperidone with antacids and antisecretory drugs (eg cimetidine) should be avoided as this will lead to reduced oral bioavailability of domperidone. Concomitant administration with anticholinergic drugs will result in antagonism of domperidone-induced gastrointestinal motility.
The gastrokinetic effects of domperidone may affect the absorption of other concurrently administered drugs, particularly those of sustained-release or enteric-coated formulations.
However, domperidone has been found not to affect the blood levels of digoxin or paracetamol in patients who have been stabilized on the latter.
Concurrent administration with azole antifungals, macrolide antibiotics, HIV protease inhibitors and nefazodone may inhibit the metabolism of domperidone and result in enhanced plasma levels of domperidone. Domperidone may also be associated with: Neuroleptics, the action of which it does not potentiate; dopaminergic agonists (bromocriptine, L-dopa) whose unwanted peripheral effects, example digestive disorders, nausea and vomiting it suppresses without counteracting their central properties. When antacids and anti-secretory are used concomitantly, take after meals i.e. should not be taken simultaneously with domperidone suspension.
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).

Recommended dosage & administration:
It is recommended to take Domil 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 Domil suspension 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
Oral suspension (1mg/ml)	10 mL three to four times per day	40 mg (40 mL of 1 mg/mL oral suspension)

Adults and adolescents (≥12 years of age) weighing < 35 kg

The dose of Domil suspension 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	1 mg/kg but no more than 35 mL (35mg)

Infants and children < 12 years of age and weighing < 35 kg
The efficacy of Domil suspension 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 Domil suspension 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
Domil suspension 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 administration

Side effects:

Side effects occur rarely and may include transient gastrointestinal cramps, extrapyramidal effects which reverse spontaneously and completely when treatment is discontinued, and allergic reactions. Domperidone may induce secretion of prolactin from the pituitary gland, which may lead to galactorrhoea and gynaecomastia.

In patients whose blood-brain barrier may be immature (as in infants) or impaired, central neurological side-effects such as extrapyramidal reactions or drowsiness cannot be totally excluded.

Postmarketing: Cardiac Disorders

Frequency: Very rare

Ventricular arrhythmias, QTc prolongation, Torsade de Pointes, Sudden cardiac death (see Warnings and Precautions)

Overdosage & treatment:

Overdose Symptoms and signs: Overdose has been reported primarily in infants and children. Symptoms of overdose may include agitation, altered consciousness, convulsion, disorientation, somnolence and extrapyramidal reactions.

Treatment: There is no specific antidote to domperidone. Close medical supervision and supportive therapy is recommended. Anticholinergic or anti-Parkinson drugs may be helpful in controlling the extrapyramidal reactions. It is advisable to contact a poison control center to obtain the latest recommendations for the management of an overdose.

Storage condition:

Store below 30°C.

Keep container tightly closed.

Protect from light.

Keep out of reach of children.

Pack sizes :

Bottles of 60ml and 120ml

Manufactured by:

NORIPHARMA SDN. BHD.

Lot 5030, Jalan Teratai,

5 $^{1}/_{2}$ Mile Off Jalan Meru, 41050 Klang,

Selangor Darul Ehsan

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