Seldom Suspension / Tablet

(D o m p e r i d o n e)

سیلڈوم گولیاں/سسپنشن

(ڈوم پیری ڈون)

COMPOSITION:
SELDOM Suspension 1mg/ml
Each ml contains:
Domperidone.....1mg
(Innovator's Specifications)
SELDOM Tablet 10mg
Each tablet contains:
Domperidone (as maleate).....10mg
(BP Specifications)

DESCRIPTION:
Domperidone, is a peripherally selective dopamine D_2receptor antagonist that is used as an antiemetic, gastroprokinetic agent, and galactagogue. The drug is used to relive nausea and vomiting; to increase the transit of food through the stomach (by increasing gastrointestinal peristalsis.

MODE OF ACTION:
Domperidone is a dopamine antagonist with anti-emetic properties. Domperidone does not readily cross the blood-brain barrier. In domperidone users, especially in 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 (gastro kinetic) effects and antagonism of dopamine receptors in the chemoreceptor trigger zone, which lies outside the blood-brain barrier in the area postrema.

INDICATIONS:
SELDOM is indicated for:
- Delayed gastric emptying of functional origin with gastro-esophageal reflux and/or dyspepsia.
- Control of nausea and vomiting of central or local origin.
- As an anti-emetic in patients receiving cytostatic and radiation therapy.
- Facilitates radiological examination of the upper gastrointestinal tract.

DOSAGE & 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 tablets before meals. If taken after meals, absorption of the drug is somewhat delayed.
Patients should try to take each dose at scheduled time. 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.
Tablet Dose:
Adults and adolescents (12 years of age and older and weighing 35 kg or more)
One 10mg tablet up to three times per day with maximum dose of 30 mg per day.
Neonates, infants, children (less than 12 years of age) and adolescents weighing less than 35 kg
Due to the need for accurate dosing, Domperidone tablets are unsuitable for use in children and adolescents weighing less than 35 kg.
Suspension Dose:
Adults and adolescents (12 years of age and older and weighing 35 kg or more).
10 ml (of 1mg/ml oral suspension) up to three times per day with a maximum dose of 30ml per day.
Neonates, infants and children (under 12 years of age and weighing less than 35kg)
The dose is 0.25mg/kg. This should be given up to three times per day with a maximum dose of 0.75mg/kg per day. For example, for a child weighing 10kg, the dose is 2.5mg and this can be given three times per day to a maximum dose of 7.5mg per day.
Hepatic Impairment
Domperidone Oral Suspension/ tablet is contraindicated in moderate or severe hepatic impairment. Dose modification in mild hepatic impairment is however not needed.
Renal Impairment
Since the elimination half-life of domperidone is prolonged in severe renal impairment, on repeated administration, the dosing frequency of Domperidone Oral Suspension/ tablet 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.

PHARMACOKINETICS:
Absorption
Domperidone is rapidly absorbed after oral administration, with peak plasma concentrations occurring at approximately 1hr after dosing. The Cmax and AUC values of domperidone increased proportionately with dose in the 10mg to 20mg dose range. A 2- to 3-fold accumulation of domperidone AUC was observed with repeated four times daily (every 5 hr) dosing of domperidone for 4 days.
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 concomitant administration of cimetidine and sodium bicarbonate.
Distribution
Oral domperidone does not appear to accumulate or induce its own metabolism; a peak plasma level after 90 minutes of 21 ng/ml after two weeks oral administration of 30 mg 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.
Biotransformation
Domperidone undergoes rapid and extensive hepatic metabolism by hydroxylation and N-dealkylation. In vitro metabolism experiments with diagnostic inhibitors revealed that 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.

PRECAUTIONS:
Renal impairment:
The elimination half-life of domperidone is prolonged in severe renal impairment. For repeated administration, the dosing frequency of domperidone should be reduced to once or twice daily depending on the severity of the impairment. The dose may also need to be reduced.
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.
Epidemiological studies showed that domperidone was associated with an increased risk of serious ventricular arrhythmias or sudden cardiac death. A higher risk was observed in patients older than 60 years, patients taking daily doses greater than 30mg, 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 section 4.3). 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.

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.

Use with Potent CYP3A4 Inhibitors:
Co-administration with oral ketoconazole, erythromycin or other potent CYP3A4 inhibitors that prolong the QTc interval should be avoided.

Co-administration of levodopa:
Although no dosage adjustment of levodopa is necessary, an increase of plasma levodopa concentration (max 30-40%) has been observed when domperidone was taken concomitantly with levodopa.

Use with apomorphine:
Domperidone is contra-indicated with QT prolonging drugs including apomorphine, unless the benefit of the co-administration with apomorphine outweighs the risks.

Pregnancy
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 women. Caution should be exercised in case of QTc prolongation risk factor in breast-fed infants.

SIDE EFFECTS:
Immune system disorders
- Anaphylactic reaction (including anaphylactic shock)

Psychiatric disorders
- Loss of libido
- Anxiety
- Agitation
- Nervousness

Nervous system disorders
- Somnolence
- Headache
- Convulsion
- Extrapyramidal disorder
- Restless leg syndrome

Eye disorders
- Oculogyric crisis

Cardiac disorders
- Ventricular arrhythmias
- QTc prolongation
- Torsades de Pointes
- Sudden cardiac death

Gastrointestinal disorders
- Dry mouth
- Diarrhea

Skin and subcutaneous tissue disorder
- Rash
- Pruritus
- Urticaria
- Angioedema

Renal and urinary disorders
- Urinary retention

Reproductive system and breast disorders
- Galactorrhea
- Breast pain
- Breast tenderness
- Gynecomastia
- Amenorrhea

General disorders and administration site conditions
- Asthenia

Investigations
- Liver function test abnormal
- Blood prolactin increased

DRUG INTERACTIONS:
Concomitant administration of anti-cholinergic drugs may inhibit the anti-dyspeptic effects of SELDOM.
Anti-muscarinic agents and opioid analgesics may antagonise the effect of SELDOM.
SELDOM suppresses the peripheral effects (digestive disorders, nausea and vomiting) of dopaminergic agonists. Since SELDOM has gastro-kinetic effects, it could influence the absorption of concomitant orally administered medicines, particularly those with sustained release or enteric coated formulations.
As SELDOM interferes with serum prolactin levels, it may interfere with other hyperprolactinemic agents and with some diagnostic tests.
Antacids and anti-secretory agents lower the oral bioavailability of domperidone. They should be taken after meals and not before meals, i.e. they should not be taken simultaneously with SELDOM.
Reduced gastric acidity impairs the absorption of domperidone. Oral bioavailability is decreased by prior administration of cimetidine or sodium carbonate.
The main metabolic pathway of domperidone is through CYP3A4. In vitro data suggests that the concomitant use of drugs that significantly inhibit this enzyme may result in increased plasma levels of domperidone. Examples of CYP3A4 inhibitors include the following:
- azole antifungals
- macrolide antibiotics
- HIV protease inhibitors
- nefazodone.

CONTRAINDICATIONS:
- Domperidone is contraindicated in the following situations:
- Known hypersensitivity to domperidone or any of the excipients
- Prolactin-releasing pituitary tumor (prolactinoma).
- When stimulation of the gastric motility could be harmful, e.g. in patients with gastro-intestinal hemorrhage, mechanical obstruction or perforation.
- In patients with moderate or severe hepatic impairment.
- 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
- Co-administration with QT-prolonging drugs, at the exception of apomorphine
- Co-administration with potent CYP3A4 inhibitors (regardless of their QT prolonging effects)

STORAGE & INSTRUCTIONS:
Store between 15-25°C.
Protect from heat, sunlight and moisture. Do not freeze.
Keep away from the reach of children.
To be sold on the prescription of a registered medical practitioner only.

HOW SUPPLIED:
SELDOM Suspension 1mg/ml
120 ml glass bottle.
SELDOM Tablet 10mg
50's tablets.

خوراک وطریقہ استعمال:
ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:
دوا کو ۱۵۔۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔
دھوپ، گرمی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

Manufactured by:
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PRIVATE LIMITED
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