For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

DOMSTAL

1. Generic Name

Domperidone Tablets I.P.

2. Qualitative and quantitative composition

DOMSTAL

Each film coated tablet contains:

Domperidone Maleate I.P.

Equivalent to Domperidone 10 mg

Colours: Colours: Lake of Tartrazine and Titanium Dioxide I.P.

OTHER INACTIVE INGREDIENTS are LACTOSE , STARCH , MAGNESIUM STEARATE, POLYVINYL PYRROLIDONE, SODIUM STARCH GLYCOLLATE, COLLOIDAL SILICON DIOXIDE (AEROSIL), STARCH, LAKE OF TARTRAZINE, HYDROXY PROPYL METHYL CELU, TALC, TITANIUM DIOXIDE, PEG -6000.

3. Dosage form and strength

Dosage Form: film coated tablet

Strength: Domperidone – 10 mg

4. Clinical particulars

4.1 Therapeutic indication

Indicated in the treatment of gastric motality disorder etc.

4.2 Posology and method of administration

As directed by the Physician.

Domeperidone 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.

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.

<u>Hepatic Impairment</u>

Domperidone 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 tablets 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.

Paediatric population

The efficacy of Domperidone in children less than 12 years of age has not been established.

The efficacy of Domperidone in adolescents 12 years of age and older and weighing less than 35 kg has not been established.

4.3 Contraindications

- Known Domperidone is contraindicated in the following situations:
- 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).

  Known hypersensitivity to domperidone or any of the excipients.
- Prolactin-releasing pituitary tumour (prolactinoma.)
- When stimulation of gastric motility could be harmful e.g in patients gastro-intestinal haemorrhage, mechanical obstruction or perforation.

4.4 Special warnings and precautions for use

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. As per reported data, 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 *Undesirable effects*).

Reported epidemiological studies showed that domperidone was associated with an increased risk of serious ventricular arrhythmias or sudden cardiac death (see *Undesirable effects*). 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 adolescents 12 years of age and older.

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.

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.

4.5 Drugs interactions

The main metabolic pathway of domperidone is through CYP3A4. Reported i*n vitro* data suggest that the concomitant use of drugs that significantly inhibit this enzyme may result in increased plasma levels of domperidone.

Increased risk of occurrence of QT-interval prolongation, due to pharmacodynamic and/or pharmacokinetic interactions.

Concomitant use of the following substances is contraindicated

QTc prolonging medicinal products

- anti-arrhythmics class IA (e.g., disopyramide, hydroquinidine, quinidine)
- anti-arrhythmics class III (e.g., amiodarone, dofetilide, dronedarone, ibutilide, sotalol)
- certain anti-psychotics (e.g., haloperidol, pimozide, sertindole)
- certain anti-depressants (e.g., citalopram, escitalopram)
- certain antibiotics (e.g. , erythromycin, levofloxacin, moxifloxacin, spiramycin)
- certain antifungal agents (e.g., pentamidine)
- certain antimalarial agents (in particular halofantrine, lumefantrine)
- certain gastro-intestinal medicines (e.g., cisapride, dolasetron, prucalopride)
- certain antihistaminics (e.g., mequitazine, mizolastine)
- certain medicines used in cancer (e.g., toremifene, vandetanib, vincamine)
- certain other medicines (e.g., bepridil, diphemanil, methadone)

(see *Contraindications*)

- apomorphine, unless the benefit of the co-administration outweighs the risks, and only if the recommended precautions for co-administration are strictly fulfilled.

Potent CYP3A4 inhibitors (regardless of their QT prolonging effects), i.e.:

- protease inhibitors
- systemic azole antifungals
- some macrolides (erythromycin, clarithromycin, telithromycin) (see *Contraindications*)

Concomitant use of the following substances is not recommended

Moderate CYP3A4 inhibitors i.e. diltiazem, verapamil and some macrolides.

Concomitant use of the following substances requires caution in use

Caution with bradycardia and hypokalaemia-inducing drugs, as well as with the following macrolides involved in QT-interval prolongation: azithromycin and roxithromycin (clarithromycin is contra-indicated as it is a potent CYP3A4 inhibitor).

The above list of substances is representative and not exhaustive.

Reportedly, separate *in vivo pharmacokinetic/pharmacodynamic* interaction studies with oral ketoconazole or oral erythromycin in healthy subjects confirmed a marked inhibition of domperidone's CYP3A4 mediated first pass metabolism by these drugs.

With the combination of oral domperidone 10mg four times daily and ketoconazole 200mg twice daily, a mean QTc prolongation of 9.8 msec was seen over the observation period, with changes at individual time points ranging from 1.2 to 17.5 msec. With the combination of domperidone 10mg four times daily and oral erythromycin 500mg three times daily, mean QTc over the observation period was prolonged by 9.9 msec, with changes at individual time points ranging from 1.6 to 14.3 msec. Both the C_{max} and AUC of domperidone at steady state were increased approximately three-fold in each of these interaction studies. In these studies domperidone monotherapy at 10mg given orally four times daily resulted in increases in mean QTc of 1.6 msec (ketoconazole study) and 2.5 msec (erythromycin study), while ketoconazole monotherapy (200mg twice daily) led to increases in QTc of 3.8 and 4.9 msec, respectively, over the observation period.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

There are limited post-marketing data on the use of domperidone in pregnant women. Reported studies in animals have shown reproductive toxicity at maternally toxic doses (see *Animal Toxicology or Pharmacology*). 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.

4.7 Effects on ability to drive and use machines

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

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs like naproxen. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

DOMPERIDONE

Tabulated list of adverse reactions

Reportedly, the safety of domperidone was evaluated in clinical trials and in post marketing experience. The clinical trials included 1275 patients with dyspepsia, gastrooesophageal reflux disorder (GORD), Irritable Bowel Syndrome (IBS), nausea and vomiting or other related conditions in 31 double-blind, placebo-controlled studies. All patients were at least 15 years old and received at least one dose of domperidone (domperidone base). The median total daily dose was 30 mg (range 10 to 80 mg), and median duration of exposure was 28 days (range 1 to 28 days). Studies in diabetic gastroparesis or symptoms secondary to chemotherapy or parkinsonism were excluded.

The following terms and frequencies are applied: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), Where frequency can not be estimated from clinical trials data, it is recorded as "Not known".

System Organ Class	**Adverse Drug Reaction Frequency**		
	Common	**Uncommon**	**Not known**
Immune system disorders			Anaphylactic reaction (including anaphylactic shock)
Psychiatric disorders		Loss of libido Anxiety	Agitation Nervousness
Nervous system disorders		Somnolence Headache	Convulsion Extrapyramidal disorder

Eye disorders			Oculogyric crisis
Cardiac disorders			Ventricular arrhythmias Sudden cardiac death QTc prolongation Torsade de Pointes
Gastrointestinal disorders	Dry mouth	Diarrhoea	
Skin and subcutaneous tissue disorder		Rash Pruritus	Urticaria Angioedema
Renal and urinary disorders			Urinary retention
Reproductive system and breast disorders		Galactorrhoea Breast pain Breast tenderness	Gynaecomastia Amenorrhoea
General disorders and administration site conditions		Asthenia	
Investigations			Liver function test abnormal Blood prolactin increased

In 45 studies where domperidone was used at higher dosages, for longer duration and for additional indications including diabetic gastroparesis, the frequency of adverse events (apart from dry mouth) was considerably higher. This was particularly evident for pharmacologically predictable events related to increased prolactin. In addition to the reactions listed above, akathisia, breast discharge, breast enlargement, breast swelling, depression, hypersensitivity, lactation disorder, and irregular menstruation were also noted.

Reporting of suspected adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

any point of contact of Torrent Pharma available at: https://torrentpharma.com/index.php/site/info/adverse_event_reporting

By reporting side effects, you can help provide more information on the safety of this medicine

4.9 Overdose *Symptoms*

Symptoms of domperidone over dosage may include agitation, altered consciousness, convulsions, disorientation, somnolence and extrapyramidal reactions.

Symptoms following acute NSAID overdosages have been typically limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which have been generally reversible with supportive care. Gastrointestinal bleeding has occurred. Hypertension, acute renal failure, respiratory depression, and coma have occurred, but were rare (see *Special warnings and precautions for use*). Because naproxen sodium may be rapidly absorbed, high and early blood levels should be anticipated. A few patients have experienced convulsions, but it is not clear whether or not these were drug-related. It is not known what dose of the drug would be life threatening (see *Special warnings and precautions for use*).

Treatment

There is no specific antidote to domperidone and naproxen, but in the event of overdose, standard symptomatic treatment should be given immediately. Gastric lavage as well as the administration of activated charcoal (60 to 100 grams in adults, 1 to 2 grams per kg of body weight in pediatric patients) and/or osmotic cathartic in symptomatic patients seen within four hours of ingestion or in patients with a large overdosage (5 to 10 times the recommended dosage), 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.

Forced diuresis, alkalinization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding of naproxen.

5. Pharmacological properties

5.1 Mechanism of Action

Pharmacotherapeutic Group: Propulsives, ATC code: A03F A03

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 (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.

5.2 Pharmacodynamic properties

Reported studies in man have shown oral domperidone to increase lower oesophaegeal pressure, improve antroduodenal motility and accelerate gastric emptying. There is no effect on gastric secretion.

In accordance with ICH—E14 guidelines, a thorough QT study was performed. This study included a placebo, an active comparator and a positive control and was conducted in healthy subjects with up to 80 mg per day 10 or 20 mg administered 4 times a day of domperidone. This study found a maximal difference of QTc between domperidone and placebo in LS-means in the change from baseline of 3.4 msec for 20 mg domperidone administered 4 times a day on Day 4. The 2-sided 90 % CI (1.0 to 5.9 msec) did not exceed 10 msec. No clinically relevant QTc effects were observed in this study when domperidone was administered at up to 80 mg/day (i.e., more than twice the maximum recommended dosing).

However, two previous drug-drug interaction studies showed some evidence of QTc prolongation when domperidone was administered as monotherapy (10 mg 4 times a day).The largest time-matched mean difference of QTcF between domperidone and placebo was 5.4 msec (95 % CI: -1.7 to 12.4) and 7.5 msec (95 % CI: 0.6 to 14.4), respectively.

5.3 Pharmacokinetic properties

DOMPERIDONE

Absorption

Domperidone is rapidly absorbed after oral administration, with peak plasma concentrations occurring at approximately 1hr after dosing. The C_{max} and AUC values of domperidone increased proportionally with dose in the 10 mg to 20 mg 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.

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 impairs the absorption of domperidone. Oral bioavailability is decreased by prior concomitant administration of cimetidine and sodium bicarbonate. The time of peak absorption is slightly delayed and the AUC somewhat increased when the oral drug is taken after a meal.

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 9193% 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. *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.

Hepatic impairment

In subjects with moderate hepatic impairment (Pugh score 7 to 9, Child-Pugh rating B), the AUC and C_{max} of domperidone is 2.9- and 1.5-fold higher, respectively, than in healthy subjects. The unbound fraction is increased by 25%, and the terminal elimination half-life is prolonged from 15 to 23 hours. Subjects with mild hepatic impairment have a somewhat lower systemic exposure than healthy subjects based on C_{max} and AUC, with no change in protein binding or terminal half-life. Subjects with severe hepatic impairment were not studied. Domperidone is contraindicated in patients with moderate or severe hepatic impairment (see *Contraindications*).

Renal impairment

In subjects with severe renal insufficiency (creatinine clearance <30ml/min/1.73m^2) the elimination half-life of domperidone is increased from 7.4 to 20.8 hours, but plasma drug levels are lower than in healthy volunteers. Since very little unchanged drug (approximately 1%) 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.

Paediatric population

No pharmacokinetic data are available in the paediatric population.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Reportedly, electrophysiological *in vitro* and *in vivo* studies indicate an overall moderate risk of domperidone to prolong the QT interval in humans. In *in vitro* experiments on isolated cells transfected with hERG and on isolated guinea pig myocytes, exposure ratios ranged between 26- 47-fold, based on IC50 values inhibiting currents through IKr ion channels in comparison to the free plasma concentrations in humans after administration of the maximum daily dose of 10 mg administered 3 times a day. Safety margins for prolongation of action potential duration in *in vitro* experiments on isolated cardiac tissues exceeded the free plasma concentrations in humans at maximum daily dose (10 mg administered 3 times a day) by 45-fold. Safety margins in *in vitro* pro-arrhythmic models (isolated Langendorff perfused heart) exceeded the free plasma concentrations in humans at maximum daily dose (10 mg administered 3 times a day) by 9- up to 45-fold. In *in vivo* models the no effect levels for QTc prolongation in dogs and induction of arrhythmias in a rabbit model sensitized for torsade de pointes exceeded

the free plasma concentrations in humans at maximum daily dose (10 mg administered 3 times a day) by more than 22-fold and 435-fold, respectively. In the anesthetized guinea pig model following slow intravenous infusions, there were no effects on QTc at total plasma concentrations of 45.4 ng/mL, which are 3fold higher than the total plasma levels in humans at maximum daily dose (10 mg administered 3 times a day). The relevance of the latter study for humans following exposure to orally administered domperidone is uncertain.

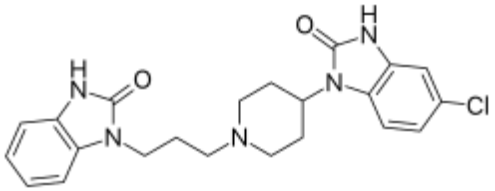
In the presence of inhibition of the metabolism via CYP3A4 free plasma concentrations of domperidone can rise up to 3-fold.

At a high, maternally toxic dose (more than 40 times the recommended human dose), teratogenic effects were seen in the rat. No teratogenicity was observed in mice and rabbits.

7. Description

Domperidone

Domperidone is 5-chloro-1-[1-[3-(2-oxo-2,3-dihydro-1H-benzimidazol-1-ylpropyl]piperidin-4-yl]-1,3-dihydro-2H-benzimidazol-2-one. Having molecular weight 425.9 and its empirical formula is $C_{22}H_{24}ClN_5O_2$. The structural formula is:



Domperidone is a white or almost white powder. Soluble in dimethylformamide, slightly soluble in ethanol(95 percent) and in methanol; practically insoluble in water.

Product Description:

Domstal Yellow coloured, biconvex, round film coated tablets.

OTHER INACTIVE INGREDIENTS are LACTOSE , STARCH , MAGNESIUM STEARATE, POLYVINYL PYRROLIDONE, SODIUM STARCH GLYCOLLATE, COLLOIDAL SILICON DIOXIDE (AEROSIL), STARCH, LAKE OF TARTRAZINE , HYDROXY PROPYL METHYL CELU, TALC, TITANIUM DIOXIDE, PEG -6000.

8. Pharmaceutical particulars

8.1 Incompatibilities

Not applicable.

8.2 Shelf-life

Do not use later than the date of expiry.

8.3 Packaging information

Domstal is available in Blister pack of 10 Tablets.

8.4 Storage and handing instructions

STORE AT A TEMPERATURE NOT EXCEEDING 30 ˚C, PROTECTED FROM LIGHT AND MOISTURE.
Keep all medicines out of reach of children.

9. Patient Counselling Information

Package leaflet: Information for the user
DOMSTAL
Domperidone Tablets I.P.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

9.1 What DOMSTALis and what it is used for

DOMSTALis consists of domperidone 10 mg. Domperidone belongs to a group of medicines called ‘dopamine antagonists’. DOMSTAL is used For the relief of post-prandial symptoms of fullness, nausea, epigastric bloating and belching that is occasionally accompanied by epigastric discomfort and heartburn and for the relief of nausea and vomiting of less than 48 hours duration.

9.2 What you need to know before you use DOMSTAL

Do Not take Domperidone Tablets if:

• You are allergic (hypersensitive) to domperidone or any of the other ingredients of Domperidone 10 mg tablets.

• You have black, tarry bowel motions (stools) or notice blood in your bowel motions. This could be a sign of bleeding in the stomach or intestines

• You have a blockage or tear in your intestines

• You have a tumour of the pituitary gland (prolactinoma).

• you have a moderate or severe liver disease

• your ECG (electrocardiogram) shows a heart problem called “prolonged QT corrected interval”

• you have or had a problem where your heart cannot pump the blood round your body as well as it should (condition called heart failure).

• you have a problem that gives you a low level of potassium or magnesium, or a high level of potassium in your blood.

• you are taking certain medicines (see "Other medicines and Domperidone tablets").

Do not take domperidone tablets if any of the above applies to you. If you are not sure, talk to your doctor or pharmacist before taking this medicine.

Warnings and precautions

Talk to your doctor or pharmacist before taking Domperidone 10mg Tablets if:

• You suffer from liver problems (liver function impairment or failure) (see "Do not take Domperidone Tablets if")

• You suffer from kidney problems (kidney function impairment or failure). It is advisable to ask your doctor for advice in case of prolonged treatment as you may need to take a lower dose or take this medicine less often, and your doctor may want to examine you regularly.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking Domperidone. Do this even if they have applied in the past.

Domperidone may be associated with an increased risk of heart rhythm disorder and cardiac arrest.

This risk may be more likely in those over 60 years old or taking doses higher than 30mg per day.

The risk also increases when domperidone is given together with some drugs.

Tell your doctor or pharmacist if you are taking drugs to treat infection (fungal infections or bacterial infection) and/or if you have heart problems or AIDS/HIV (see "Other medicines and Domperidone tablets").

Domperidone should be used at the lowest effective dose. While taking domperidone, contact your doctor if you experience heart rhythm disorders such as palpitations, trouble breathing, loss of consciousness. Treatment with domperidone should be stopped.

<u>Adolescents weighing less than 35 kg and children</u>

Domperidone should not be given to adolescents 12 years of age and older weighing less than 35 kg, or in any children less than 12 years of age, as it is not effective in these age groups.

Other medicines and Domperidone tablets

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines you can buy without a prescription, including herbal medicines. This is because Domperidone can affect the way some other medicines work. Also, some medicines can affect the way Domperidone works.

Do not take Domperidone tablet if you are taking medicine to treat:

• Fungal infections such as azole antifungals, specifically oral ketoconazole, fluconazole or voriconazole

• Bacterial infections, specifically erythromycin, clarithromycin, telithromycin, moxifloxacin, pentamidine (these are antibiotics)

• Heart problems or high blood pressure (e.g., amiodarone, dronedarone, quinidine, disopyramide, dofetilide, sotalol, diltiazem, verapamil)

• Psychoses (e.g., haloperidol, pimozide, sertindole)

• Depression (e.g., citalopram, escitalopram)

• Gastro-intestinal disorders (e.g., cisapride, dolasetron, prucalopride)

• Allergy (e.g., mequitazine, mizolastine)

• Malaria (in particular halofantrine)

• AIDS/HIV (protease inhibitors)

• Cancer (e.g., toremifene, vandetanib, vincamine)

• Certain other medicines (e.g., bepridil, diphemanil, methadone)

Tell your doctor or pharmacist if you are taking drugs to treat infection, heart problems or AIDS/HIV.

Domperidone and apomorphine

Before you use Domperidone tablet and apomorphine, your doctor will ensure that you tolerate both medicines when used simultaneously. Ask your doctor or specialist for a personalised advice. Please refer to apomorphine leaflet.

It is important to ask your doctor or pharmacist if Domperidone tablet is safe for you when you are taking any other medicines, including medicines obtained without prescription.

Taking Domperidone Tablets with food and drink

It is recommended to take Domperidone before meals, as when taken after meals the absorption of the medicine is slightly delayed.

Pregnancy and breast-feeding

Talk to your doctor or pharmacist before taking Domperidone tablets if:

• You are pregnant, might become pregnant or think you may be pregnant

• You are breast-feeding. It is best not to take Domperidone tablets if you are breast-feeding. Small amounts of Domperidone have been detected in breast milk.

Domperidone may cause unwanted side effects affecting the heart in a breast-fed baby. Domperidone should be used during breast feeding only if your physician considers this clearly necessary. Ask your doctor for advice before taking this medicine.

Driving and using machines

Domperidone does not affect your ability to drive or use machines.

Important information about some of the ingredients of Domperidone Tablets

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

9.3 How to use DOMSTAL

Always take Domperidone Tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Duration of treatment:

Your doctor will decide how long you will need to take this medicine.

Symptoms usually resolve with 3-4 days of taking this medicine. Do not take Domperidone tablets for longer than 7 days without consulting your doctor.

Taking this medicine

• Swallow the tablets whole with a drink of water.

• Take the tablets 15 to 30 minutes before a meal.

• Do not crush or chew them

The usual dose is:

Adults and adolescents <u>12 years of age and older</u> with a body weight of 35 kg or more

• The usual dose is one tablet taken up to three times per day, if possible before meals. Do not take more than three tablets per day.

• This product is not suitable for children under 12 years of age and older with a body weight of less than 35kg.

People with kidney problems

Your doctor may tell you to take a lower dose or to take the medicine less often.

If you take more Domperidone Tablets than you should

• If you have used or taken too many Domperidone tablets, contact your doctor, pharmacist, or the poisons centre at your nearest hospital casualty department immediately. Take the carton and any tablets left with you. This is so the doctors know what you have taken.In the events of overdose, symptomatic treatment could be implemented. An ECG monitoring could be undertaken, because of the possibility of heart problem called prolonged QT interval.

• The signs of taking more than you should include feeling sleepy, confused, uncontrolled movements which include unusual eye movements, unusual movements of the tongue or abnormal posture (such as a twisted neck).

If you forget to take Domperidone Tablets

• If you forgot to take Domperidone, take it as soon as you remember.

• However If it is almost time for your next dose, wait until that is due and continue as normal.

• Do not take a double dose to make up for a forgotten dose.

9.4 Possible Side Effects

Like all medicines, Domperidone Tablets can have side effects, although not everybody gets them.

Stop taking Domperidone and see your doctor or go to a hospital straightaway if:

• You get swelling of the hands, feet, ankles, face, lips or throat which may cause difficulty in swallowing or breathing. You could also notice an itchy, lumpy rash (hives) or nettle rash (urticaria). This may mean you are having an allergic reaction to Domperidone.

• You notice any uncontrolled movements. These include irregular eye movements, unusual movements of the tongue, and abnormal posture such as a twisted neck, trembling and muscle stiffness. These symptoms should stop once you stop taking Domperidone.

• You have a very fast or unusual heartbeat. This could be a sign of a life-threatening heart problem.

• You have a fit (seizure).

Other side effects include:

Common (may affect up to 1 in 10 people):

• Dry mouth

Uncommon (may affect up to 1 in 100 people):

• Lowering of sexual drive (libido) in men

• Feeling anxious

• Feeling drowsy

• Headaches

• Diarrhoea

• Itchy skin. You may also have a rash

• Unusual production of breast milk in men and women

• Painful or tender breasts

• A general feeling of weakness

Not known *(Frequency cannot be estimated from the available data):*

• Disorders of the cardiovascular system: heart rhythm disorders (rapid or irregular heart beat) have been reported; if this happens, you should stop the treatment immediately. Domperidone may be associated with an increased risk of heart rhythm disorder and cardiac arrest. This risk may be more likely in those over 60 years old or taking doses higher than 30 mg per day. Domperidone should be used at the lowest effective dose.

• Feeling agitated or irritable

• Feeling more nervous than usual

• Abnormal eye movements

• Inability to urinate

• Breast enlargement in men

• In women, menstrual periods may be irregular or stop

• A blood test shows changes in the way your liver is working.

Some patients who have used Domperidone for conditions and dosages requiring longer term medical supervision have experienced the following unwanted effects:

Restlessness; swollen or enlarged breasts, unusual discharge from breasts, irregular menstrual periods in women, difficulty breastfeeding, depression, hypersensitivity.

Reporting of suspected adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://torrentpharma.com/index.php/site/info/adverse_event_reporting

By reporting side effects, you can help provide more information on the safety of this medicine

9.5 How to store DOMSTAL

STORE AT A TEMPERATURE NOT EXCEEDING 30 ˚C, PROTECTED FROM LIGHT AND MOISTURE.

Keep all medicines out of reach of children.

9.6 Contents of the pack and other information What

DOMSTAL contains:

The active substance is domperidone.

OTHER INACTIVE INGREDIENTS are LACTOSE , STARCH , MAGNESIUM STEARATE, POLYVINYL PYRROLIDONE, SODIUM STARCH GLYCOLLATE, COLLOIDAL SILICON DIOXIDE (AEROSIL), STARCH, LAKE OF TARTRAZINE, HYDROXY PROPYL METHYL CELU, TALC, TITANIUM DIOXIDE, PEG -6000.

Domstal is available in Blister pack of 10 Tablets.

10. Details of manufacturer

Manufactured by:

Torrent Pharmaceuticals Ltd

32 No.Middle camp, NH-10,

East District, Gangtok, Sikkim-737 135

OR

Windlas Healthcare (P) Limited

Plot No. 183 & 192,

Mohabewala Industrial Area,

Dehradun-248110, Uttarakhand.

11. Details of permission or licence number with date

Torrent Pharmaceuticals Ltd
Mfg. Lic. No. M/563/2010 issued on 23.12.2016
OR
Mfg. Lic. No. 47/UA/2009 issued on 14.09.2020

12. Date of revision

APRIL-2022

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/DOMSTAL 10/APRIL-2022/03/PI