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

PANSPED D

1. Generic Name

Pantoprazole Gastro-Resistant and Domperidone Prolonged –Release Capsules I.P.

2. Qualitative and quantitative Composition:

Each hard gelatin capsule contains:
Pantoprazole Sodium I.P. (as sesquihydrate) equivalent to Pantoprazole 40 mg (as gastro resistant tablet)
Colour: Titanium Dioxide I.P.
Domperidone Maleate I.P. equivalent to Domperidone 30 mg (as prolonged release tablet)
Colour: Red oxide of iron
Approved colours used in hard gelatin capsule shell.
The excipients used are Mannitol, Crospovidone, Sodium Carbonate Anhydrous, Hydroxypropylcellulose, Calcium Stearate, Hydroxypropylmethylcellulose, Titanium Dioxide, Propylene Glycol, Triethyl Citrate, Eudragit, Talc, Lactose, Ferric Oxide Red, Polyvinyl Pyrrolidone, Colloidal Silicon Dioxide and Magnesium Stearate.

3. Dosage form and strength

Dosage form: Hard Gelatin Capsule
Strength: Pantoprazole Sodium 40 mg and Domperidone 30 mg.

4. Clinical particulars

4.1 Therapeutic indication

For gastric ulcer, duodenal ulcer, zollinger-Ellison-syndrome and Gastro-esophageal reflux diseases.

4.2 Posology and method of administration

One capsule once daily preferably before meal or as directed by physician

Pantoprazole

Adults and adolescents 12 years of age and above

Reflux oesophagitis

One tablet of Pantoprazole per day. In individual cases the dose may be doubled (increase to 2 tablets Pantoprazole daily) especially when there has been no response to other treatment. A 4-week period is usually required for the treatment of reflux oesophagitis. If this is not sufficient, healing will usually be achieved within a further 4 weeks.

Adults

Eradication of H. pylori in combination with two appropriate antibiotics

In H. pylori positive patients with gastric and duodenal ulcers, eradication of the germ by a combination therapy should be achieved. Considerations should be given to official local guidance (e.g. national recommendations) regarding bacterial resistance and the appropriate use and prescription of antibacterial agents. Depending upon the resistance pattern, the following combinations can be recommended for the eradication of H. pylori:

a) Twice daily one tablet Pantoprazole

+ Twice daily 1000 mg amoxicillin

+ Twice daily 500 mg clarithromycin

b) Twice daily one tablet Pantoprazole

+ Twice daily 400 - 500 mg metronidazole (or 500 mg tinidazole)

+ Twice daily 250 - 500 mg clarithromycin

c) Twice daily one tablet Pantoprazole

+ Twice daily 1000 mg amoxicillin

+ Twice daily 400 - 500 mg metronidazole (or 500 mg tinidazole)

In combination therapy for eradication of H. pylori infection, the second Pantoprazole tablet should be taken 1 hour before the evening meal. The combination therapy is implemented for 7 days in general and can be prolonged for a further 7 days to a total duration of up to two weeks. If, to ensure healing of the ulcers, further treatment with pantoprazole is indicated, the dose recommendations for duodenal and gastric ulcers should be considered.

If combination therapy is not an option, e.g. if the patient has tested negative for H. pylori, the following dose guidelines apply for Pantoprazole monotherapy:

Treatment of gastric ulcer

One tablet of Pantoprazole per day. In individual cases the dose may be doubled (increase to 2 tablets Pantoprazole daily) especially when there has been no response to other treatment. A 4-week period is usually required for the treatment of gastric ulcers. If this is not sufficient, healing will usually be achieved within a further 4 weeks.

Treatment of duodenal ulcer

One tablet of Pantoprazole per day. In individual cases the dose may be doubled (increase to 2 tablets Pantoprazole daily) especially when there has been no response to other treatment. A duodenal ulcer generally heals within 2 weeks. If a 2-week period of treatment is not sufficient, healing will be achieved in almost all cases within a further 2 weeks.

Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions

For the long-term management of Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions patients should start their treatment with a daily dose of 80 mg (2 tablets of Pantoprazole 40 mg). Thereafter, the dose can be titrated up or down as needed using measurements of gastric acid secretion to guide. With doses above 80 mg daily, the dose should be divided and given twice daily. A temporary increase of the dose above 160 mg pantoprazole is possible but should not be applied longer than required for adequate acid control.

Treatment duration in Zollinger-Ellison syndrome and other pathological hypersecretory conditions is not limited and should be adapted according to clinical needs.

Special populations

Patients with hepatic Impairment
A daily dose of 20 mg pantoprazole (1 tablet of 20 mg pantoprazole) should not be exceeded in patients with severe liver impairment. Pantoprazole must not be used in combination treatment for eradication of H. pylori in patients with moderate to severe hepatic dysfunction since currently no data are available on the efficacy and safety of Pantoprazole in combination treatment of these patients (see section 4.4).
Patients with renal Impairment
No dose adjustment is necessary in patients with impaired renal function. Pantoprazole must not be used in combination treatment for eradication of H. pylori in patients with impaired renal function since currently no data are available on the efficacy and safety of Pantoprazole in combination treatment for these patients (see section 5.2).

Older people

No dose adjustment is necessary in elderly patients (see section 5.2).

Paediatric population

Pantoprazole is not recommended for use in children below 12 years of age due to limited data on safety and efficacy in this age group.

Domperidone

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.

Hepatic Impairment

Domperidone is contraindicated in moderate or severe hepatic impairment (see section 4.3). Dose modification in mild hepatic impairment is however not needed (see section 5.2).

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 (see sections 4.4 and 5.2)

Paediatric population

The efficacy of Domperidone in children less than 12 years of age has not been established (see section 5.1).

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

Pansped D is contraindicated in following situation:

- Hypersensitivity to the active substance or to any of the excipients.
- Prolactin-releasing pituitary tumour (prolactinoma).
- When stimulation of the gastric motility could be harmful e.g. in patients with gastro-intestinal haemorrhage, 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)
- Co-administration with atazanavir.

4.4 Special warnings and precautions for use

Pantoprazole

Patients should be instructed to consult a doctor if:

• They have unintentional weight loss, anaemia, gastrointestinal bleeding, dysphagia, persistent vomiting or vomiting with blood, since it may alleviate symptoms and delay diagnosis of a severe condition. In these cases, malignancy should be excluded.

• They have had previous gastric ulcer or gastrointestinal surgery.

• They are on continuous symptomatic treatment of indigestion or heartburn for 4 or more weeks.

• They have jaundice, hepatic impairment, or liver disease.

• They have any other serious disease affecting general well-being.

• They are aged over 55 years with new or recently changed symptoms.
Patients with long-term recurrent symptoms of indigestion or heartburn should see their doctor at regular intervals. Especially, patients over 55 years taking any non-prescription indigestion or heartburn remedy on a daily basis should inform their pharmacist or doctor.
Patients should not take another proton pump inhibitor or H2 antagonist concomitantly.
Patients should consult their doctor before taking this medicinal product if they are due to have an endoscopy or urea breath test.
Patients should be advised that this medicine are not intended to provide immediate relief.
Patients may start to experience symptomatic relief after approximately one day of treatment with pantoprazole, but it might be necessary to take it for 7 days to achieve complete heartburn control.
Patients should not take pantoprazole as a preventive medicinal product.

Gastrointestinal infections caused by bacteria

Decreased gastric acidity, due to any means - including proton pump inhibitors - increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing medicinal products leads to a slightly increased risk of gastrointestinal infections such as Salmonella, Campylobacter, or Clostridium difficile.

Subacute cutaneous lupus erythematosus (SCLE)

Proton pump inhibitors are associated with very infrequent cases of SCLE. If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the health care professional should consider stopping pantoprazole Control. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Interference with Laboratory Tests

Increased Chromogranin a (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, pantoprazole Control treatment should be stopped for at least 5 days before CgA measurements. If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment

Domperidone

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 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.

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.
Renal impairment

The elimination half-life of domperidone is prolonged in severe renal impairment. The dosing frequency may also need to be reduced depending on the severity of the impairment.

4.5 Drugs interactions

Pantoprazole

Interactions

Pantoprazole may reduce the absorption of active substances whose bioavailability is dependent on the gastric pH (e.g. ketoconazole).
It has been shown that co-administration of atazanavir 300 mg/ritonavir 100 mg with omeprazole (40 mg once daily) or atazanavir 400 mg with lansoprazole (60 mg single dose) to healthy volunteers resulted in a substantial reduction in the bioavailability of atazanavir. The Page 4 of 22 Absorption of atazanavir is pH-dependent. Therefore, pantoprazole must not be co-administered with atazanavir.
Although no interaction during concomitant administration of phenprocoumon or warfarin has been observed in clinical pharmacokinetic studies, a few isolated cases of changes in International Normalised Ratio (INR) have been reported during concomitant treatment in the post-marketing period. Therefore, in patients treated with coumarin anticoagulants (e.g. phenprocoumon or warfarin), monitoring of prothrombin time/INR is recommended after initiation, termination or during irregular use of pantoprazole.
Concomitant use of high dose methotrexate (e.g. 300 mg) and proton-pump inhibitors has been reported to increase methotrexate levels in some patients. Therefore in settings where high-dose methotrexate is used, for example cancer and psoriasis, a temporary withdrawal of pantoprazole may need to be considered.
Pantoprazole is metabolized in the liver via the cytochrome P450 enzyme system. Interaction studies with carbamazepine, caffeine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol, naproxen, nifedipine, phenytoin, piroxicam, and theophylline and an oral contraceptive containing levonorgestrel and ethinyl oestradiol did not reveal clinically significant interactions. However, an interaction of pantoprazole with other substances which are metabolised by the same enzyme system cannot be excluded.
There were no interactions with concomitantly administered antacids.

Domperidone

The main metabolic pathway of domperidone is through CYP3A4. *In 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).
• apomorphine, unless the benefit of the co-administration outweighs the risks, and only if the recommended precautions for co-administration are strictly fulfilled. Please refer to the apomorphine SmPC.

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

• protease inhibitors
• systemic azole antifungals
• some macrolides (erythromycin, clarithromycin, telithromycin).

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.

Separate *in vivo pharmacokinetic/pharmacodynamic* interaction reported 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 Cmax 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.)

Pantoprazole

Pregnancy

A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) indicate no malformative or feto/ neonatal toxicity of Pantoprazole.
Animal studies have shown reproductive toxicity.
As a precautionary measure, it is preferable to avoid the use of pantoprazole during pregnancy.

Breast-feeding

Animal studies have shown excretion of pantoprazole in breast milk. There is insufficient information on the excretion of pantoprazole in human milk but excretion into human milk has been reported. A risk to the newborns/infants cannot be excluded. Therefore, a decision on whether to discontinue breast-feeding or to discontinue/abstain from Pantoprazole therapy
Taking into account the benefit of breast- feeding to the child and the benefit of Pantoprazole therapy to women.

Fertility

There was no evidence of impaired fertility following the administration of pantoprazole in animal studies.

Domperidone

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.

4.7 Effects on ability to drive and use machines

Pansped D has no or negligible influence on the ability to drive and use machines.
Adverse drug reactions such as dizziness and visual disturbances may occur. If affected, patients should not drive or operate machines.

4.8 Undesirable effects

Pantoprazole

Approximately 5% of patients can be expected to experience adverse reactions. The most commonly reported adverse reactions are diarrhoea and headache, both occuring in approximately 1% of patients.
Tabulated list of adverse reactions
The following adverse reactions have been reported with pantoprazole.
Within the following table, adverse reactions are ranked under the MedDRA frequency classification: 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), not known (cannot be estimated from the available data).
Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1. Adverse reactions with pantoprazole in clinical trials and post-marketing experience

Frequency	**Common**	**Uncommon**	**Rare**	**Very rare**	**Not known**
System Organ Class					
Blood and lymphatic system disorders			Agranulocytosis	Thrombocytopenia; Leukopenia; Pancytopenia	
Immune system disorders			Hypersensitivity (including anaphylactic reactions and anaphylactic shock)		
Metabolism and nutrition disorders			Hyperlipidaemias and lipid increases (triglycerides, cholesterol); Weight changes		Hyponatraemia Hypomagnesaemia. (See section 4.4); Hypocalcaemia [(1)] hypokalaemia
Psychiatric disorders		Sleep disorders	Depression (and all aggravations)	Disorientation (and all aggravations)	Hallucination; Confusion (especially in pre-disposed patients, as well as the aggravation of these symptoms in case of pre-existence)
Nervous system disorders		Headache; Dizziness	Taste disorders		Parasthesia
Eye disorders			Disturbances in vision / blurred vision		
Gastrointestinal disorders	Fundic gland polyps (benign)	Diarrhoea; Nausea / vomiting; Abdominal distension and bloating; Constipation; Dry mouth; Abdominal pain and discomfort			Microscopic colitis

Hepatobiliary disorders		Liver enzymes increased (transaminases, γ-GT)	Bilirubin increased		Hepatocellular injury; Jaundice; Hepatocellular failure
Skin and sub-cutaneous tissue disorders		Rash / exanthema / eruption; Pruritus	Urticaria; Angioedema		Stevens-Johnson syndrome; Lyell syndrome; Erythema multiforme; Photosensitivity Subacute cutaneous lupus erythematosus (see section 4.4).
Musculoskeletal and connective tissue disorders		Fracture of the hip, wrist or spine (see section 4.4)	Arthralgia; Myalgia		Muscle spasm (2)
Renal and urinary disorders					Interstitial Nephritis (with possible progression to renal failure)
Reproductive system and breast disorders			Gynaecomastia		
General disorders and administration site conditions		Asthenia, fatigue and malaise	Body temperature increased; Oedema peripheral		

1. Hypocalcemia in association with hypomagnesemia

2. Muscle spasm as a consequence of electrolyte disturbance

Domperidone

Tabulated list of adverse reactions

The safety of domperidone was evaluated in clinical trials and in postmarketing experience. The clinical trials included 1275 patients with dyspepsia, gastro-oesophageal 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 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 cannot 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 disorder			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 (see section 4.4)			Ventricular arrhythmias Sudden cardiac death QTc prolongation Torsade de Pointes
Gastrointestinal disorders	Dry mouth	Diarrhoea	
Skin and subcutaneous tissue disorder		Rash Pruritus	Urticarial Angioedema
Renal and urinary disorders			Urinary retention Acute Kidney Injury
Reproductive system and breast disorders		Galactorrhoea Breast pain	Gynaecomastia Amenorrhoea

		Breast tenderness	
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.

Description of adverse reactions

Torrent Pharma available at: http://www.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

Pantoprazole

There are no known symptoms of overdose in man.

Systemic exposure with up to 240 mg administered intravenously over 2 minutes were well tolerated. As pantoprazole is extensively protein bound, it is not readily dialysable.

In the case of an overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

Domperidone

Symptoms

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.

5 Pharmacological properties

5.1 Mechanism of Action

Pantoprazole

Pantoprazole is a substituted benzimidazole which inhibits the secretion of hydrochloric acid in the stomach by specific blockade of the proton pumps of the parietal cells.

Pantoprazole is converted to its active form, a cyclic sulphenamide, in the acidic environment in the parietal cells where it inhibits the H+, K+-ATPase enzyme, i. e. the final stage in the production of hydrochloric acid in the stomach.

The inhibition is dose-dependent and affects both basal and stimulated acid secretion. In most patients, freedom from heartburn and acid reflux symptoms is achieved in 1 week. Pantoprazole reduces acidity in the stomach and thereby increases gastrin in proportion to the reduction in acidity. The increase in gastrin is reversible. Since pantoprazole binds to the enzyme distal to the receptor level, it can inhibit hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, and gastrin). The effect is the same whether the active substance is given orally or intravenously.
The fasting gastrin values increase under pantoprazole. On short-term use, in most cases they do not exceed the upper limit of normal. During long-term treatment, gastrin levels double in most cases. An excessive increase, however, occurs only in isolated cases. As a result, a mild to moderate increase in the number of specific endocrine (ECL) cells in the stomach is observed in a minority of cases during long-term treatment (simple to adenomatoid hyperplasia). However, according to the studies conducted so far, the formation of carcinoid precursors (atypical hyperplasia) or gastric carcinoids as were found in animal experiments have not been observed in humans.
During treatment with antisecretory medicinal products, serum gastrin increases in response to the decreased acid secretion. Also CgA increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours.
Available published evidence suggests that proton pump inhibitors should be discontinued between 5 days and 2 weeks prior to CgA measurements. This is to allow CgA levels that might be spuriously elevated following PPI treatment to return to reference range.

Domperidone

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

Pharmacodynamic effects

Pantoprazole

Pharmacotherapeutic group: Drugs for acid related disorders, Proton pump inhibitors, ATC code: A02BC02
The inhibition of H+, K+-ATPase enzyme is dose-dependent and affects both basal and stimulated acid secretion. In most patients, freedom from heartburn and acid reflux symptoms is achieved in 1 week. Pantoprazole reduces acidity in the stomach and thereby increases gastrin in proportion to the reduction in acidity. The increase in gastrin is reversible. Since pantoprazole binds to the enzyme distal to the receptor level, it can inhibit hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, and gastrin). The effect is the same whether the active substance is given orally or intravenously.
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according to the studies conducted so far, the formation of carcinoid precursors (atypical hyperplasia) or gastric carcinoids as were found in animal experiments have not been observed in humans.
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Available published evidence suggests that proton pump inhibitors should be discontinued between 5 days and 2 weeks prior to CgA measurements. This is to allow CgA levels that might be spuriously elevated following PPI treatment to return to reference range.
In a reported retrospective analysis of 17 studies in 5960 patients with gastro-oesophageal reflux disease (GORD) who were treated with 20 mg pantoprazole monotherapy, the symptoms associated with acid reflux e.g. heartburn and acid regurgitation were evaluated according to a standardised methodology. Studies selected had to have at least one acid reflux symptom recording point at 2 weeks. GORD diagnosis in these studies was based on endoscopic assessment, with the exception of one study in which the inclusion of the patients was based on symptomatology alone. In these studies, the percentage of patients experiencing complete relief from heartburn after 7 days was between 54.0% and 80.6% in the pantoprazole group. After 14 and 28 days, complete heartburn relief was experienced in 62.9% to 88.6% and 68.1% to 92.3% of the patients, respectively.
For the complete relief from acid regurgitation, similar results were obtained as for heartburn. After 7 days the percentage of patients experiencing complete relief from acid regurgitation was between 61.5% and 84.4%, after 14 days between 67.7% and 90.4%, and after 28 days between 75.2% and 94.5%, respectively.
Pantoprazole was consistently shown to be superior to placebo and H2RA and non-inferior to other PPIs. Acid-reflux symptom relief rates were largely independent of the initial GORD stage.

Domperidone

Pharmacotherapeutic group: Propulsives, ATC code: A03F A 03
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 a reported QT study which 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

Pantoprazole

Pharmacokinetics do not vary after single or repeated administration. In the dose range of 10 to 80 mg, the plasma kinetics of pantoprazole are linear after both oral and intravenous administration.

Absorption

Pantoprazole is completely and rapidly absorbed after oral administration. The absolute bioavailability was found to be about 77 %. On average, at about 2.0 h - 2.5 h post administration (tmax) of a single 20 mg oral dose, the maximum serum concentrations (Cmax) of about 1-1.5 µg/ml are achieved, and these values remain constant after multiple administration. Concomitant intake of food had no influence on bioavailability (AUC or Cmax), but increased the variability of the lag-time (tlag).

Distribution

Volume of distribution is about 0.15 l/kg and serum protein binding is about 98%.

Biotransformation

Pantoprazole is almost exclusively metabolized in the liver.

Elimination

Clearance is about 0.1 l/h/kg, and terminal half-life (t1/2) about 1 h. There were a few cases of subjects with delayed elimination. Due to the specific binding of pantoprazole to the proton Page 13 of 22

pumps within the parietal cell, the elimination half-life does not correlate with the much longer duration of action (inhibition of acid secretion).

Renal elimination represents the major route of excretion (about 80%) for the metabolites of pantoprazole; the rest is excreted with the faeces. The main metabolite in both serum and urine is desmethylpantoprazole, which is conjugated with sulphate. The half-life of the main metabolite (about 1.5 h) is not much longer than that of pantoprazole.

Special populations

Renal impairment

No dose reduction is recommended when pantoprazole is administered to patients with impaired renal function (including patients on dialysis, which removes only negligible amounts of pantoprazole). As with healthy subjects, the half-life of pantoprazole is short. Although the main metabolite has a longer half-life (2-3h), excretion is still rapid and thus accumulation does not occur.

Hepatic impairment

After administration of pantoprazole to patients with liver impairment (Child-Pugh classes A, B and C) the half-life values increased to between 3 and 7 h and the AUC values increased by a factor of 3-6, whereas the Cmax only increased slightly by a factor of 1.3 compared with healthy subjects.

Elderly

The slight increase in AUC and Cmax in elderly volunteers compared with younger subjects was not clinically relevant.

Domperidone

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 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 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. *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 Cmax 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 Cmax 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.

Renal impairment

In subjects with severe renal insufficiency (creatinine clearance <30ml/min/1.73m2) 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

Pantoprazole

Non-clinical data reveal no special hazard for humans based on reported conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.

In the 2-year carcinogenicity studies in rats, neuroendocrine neoplasms were found. In addition, squamous cell papillomas were found in the forestomach of rats in one study. The mechanism leading to the formation of gastric carcinoids by substituted benzimidazoles has been carefully investigated and allows the conclusion that it is a secondary reaction to the massively elevated serum gastrin levels occurring in the rat during chronic high-dose treatment.

In the 2-year rodent studies an increased number of liver tumors was observed in rats (in one rat study only) and in female mice and was interpreted as being due to pantoprazole's high metabolic rate in the liver.
A slight increase of neoplastic changes of the thyroid was observed in the group of rats receiving the highest dose (200 mg/kg) in one 2-year study. The occurrence of these neoplasms is associated with the pantoprazole-induced changes in the breakdown of thyroxine in the rat liver. As the therapeutic dose in man is low, no side effects on the thyroid glands are expected.
In animal studies (rats) 5 mg/kg was the observed NOAEL (No Observed Adverse Effect Level) for embryotoxicity. Investigations revealed no evidence of impaired fertility or teratogenic effects. Penetration of the placenta was investigated in the rat and was found to increase with advanced gestation. As a result, concentration of pantoprazole in the foetus is increased shortly before birth

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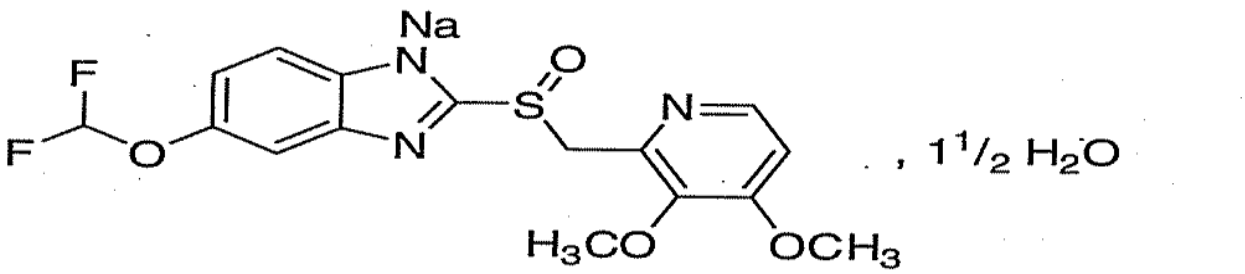
7 Description

Pantoprazole Sodium is sodium 5-(difluromethoxy) 2[[(3, 4-dimethoxy-pyridin-2-yl)methyl]sulphinyl]-benzimidazol-1-ide,sesquihydrate having molecular formula of C16H14F2N3NaO4S, 1.5 H2O molecular weight is 432.4 the chemical structure is:



Pantoprazole is a white to off white powder.
Product Description:
PANSPED D
Size '0 Elongated' Hard gelatin capsules with Blue cap having print "PANSPED D" and BLUE BODY having torrent logo (squre emblem only) containing one white to pale yellow colored, oval shaped, biconvex, gastro-resistant tablet of pantoprazole, plain on both sides and other brown red and peach colored, capsule shaped, biconvex, bilayered uncoated prolonged release tablet of Domperidone, plain on both side.

8 Pharmaceutical particulars

8.1 Incompatibilities

Not applicable

8.2 Shelf-life

Do not use later than date of expiry.

8.3 Packaging information

PANSPED D is available as strip of 10 capsules

8.4 Storage and handing instructions

Store below 25 º C, protected from light and moisture.

9 Patient Counselling Information

PANSPED D

Omeprazole Domperidone Sustained Release Capsules.
Read all of this leaflet carefully before you start taking 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 your 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
What is in this leaflet?

9.1 What PANSPED D is and what it is used for

PANSPED D Capsules contain Pantoprazole Enteric Coated and Domperidone Sustained Release Capsules with the active substance Pantoprazole Sodium 40 mg and Domperidone 30 mg respectively.
PANSPED D is used for the treatment of Gastroesophageal reflux disease (GERD).

9.2 What you need to know before you take PANSPED D

Do not take PANSPED D Capsules if

- You are allergic (hypersensitive) to pantoprazole/domperidone or any of the other ingredients. Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.
- You have a tumour of the pituitary gland (prolactinoma)
- You have a blockage or tear in your intestines
- 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 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
- You are taking HIV protease inhibitors such as atazanavir, nelfinavir (for the treatment of HIV-infection)

Do not take Pansped D if any of the above applies to you. If you are not sure, talk to your doctor before taking Pansped D.

Warnings and precautions

Talk to your doctor or pharmacist before taking PANSPED D Capsules if

- if you have been treated for heartburn or indigestion continuously for 4 or more weeks
- if you are over 55 years old and taking non-prescription indigestion treatment on a daily basis
- if you are over 55 years old with any new or recently changed reflux symptoms
- if you have previously had a gastric ulcer or stomach surgery
- if you have liver problems or jaundice (yellowing of skin or eyes, liver function impairment or failure)
- if you regularly see your doctor for serious complaints or conditions
- if you are due to have an endoscopy or a breath test called a C-urea test.
- if you have ever had a skin reaction after treatment with a medicine similar medicine that reduces stomach acid.

- if you are due to have a specific blood test (Chromogranin A)
- if you are taking HIV protease inhibitors such as atazanivir, nelfinavir (for the treatment of HIV-infection) at the same time as pantoprazole, ask your doctor for specific advice.
- 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 this medicine less often, and your doctor may want to examine you regularly.

Pansped D may be associated with an increased risk of heart rhythm disorder and cardiac arrest. Contact your doctor if you experience heart rhythm disorders such as palpitations, trouble breathing, loss of consciousness.

Tell your doctor 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 Pansped D).

If you take Pansped D for longer periods, this may cause additional risks, such as:

- Reduced absorption of Vitamin B12, and Vitamin B12 deficiency if you already have low body stores of Vitamin B12
- Fracture of your hip, wrist or spine, especially if you already suffer from osteoporosis or if you are taking corticosteroids (which can increase the risk of osteoporosis).
- Falling magnesium levels in your blood (potential symptoms: fatigue, involuntary muscle contractions, disorientation, convulsions, dizziness, increased heart rate). Low levels of magnesium can also lead to a reduction in potassium or calcium levels in the blood. Your doctor may decide to perform regular blood tests to monitor your levels of magnesium.

Tell your doctor 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 Pansped D).

If you take Pansped D for longer periods, this may cause additional risks, such as:

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- Falling magnesium levels in your blood (potential symptoms: fatigue, involuntary muscle contractions, disorientation, convulsions, dizziness, increased heart rate). Low levels of magnesium can also lead to a reduction in potassium or calcium levels in the blood. Your doctor may decide to perform regular blood tests to monitor your levels of magnesium.

Tell your doctor immediately, before or after taking this medicine, if you notice any of the following symptoms, which could be a sign of another, more serious, disease:

- an unintentional loss of weight (not related to a diet or an exercise programme)
- vomiting, particularly if repeated
- vomiting blood; this may appear as dark coffee grounds in your vomit
- you notice blood in your stools; which may be black or tarry in appearance
- difficulty in swallowing or pain when swallowing
- you look pale and feel weak (anaemia)
- chest pain
- stomach pain
- severe and/or persistent diarrhoea, because this medicine has been associated with a small increase in infectious diarrhoea.
- if you get a rash on your skin, especially in areas exposed to the sun tell your doctor as soon as you can, as you may need to stop your treatment with Pansped D. Remember to also mention any other ill-effects like pain in your joints.

Your doctor may decide that you need some tests. If you are due to have a blood test, tell your doctor that you are taking this medicine.

You may experience relief from your acid reflux and heartburn symptoms after just one day of treatment with Pansped D, but this medicine is not meant to bring immediate relief.

You should not take it as a preventive measure.

If you have been suffering from repetitive heartburn or indigestion symptoms for some time, remember to see your doctor regularly.

Children and adolescents

PANSPED D is not intended for use in children and adolescents younger than 18 years.

Other medicines and PANSPED D

Tell your doctor if you are using, have recently used or might use any other medicines. Pansped D may stop certain other medicines from working properly. Especially medicines containing one of the following active substances:

Do not take Panspeed D with

- Other medicines which limit the amount of acid produced in your stomach, such as another proton pump inhibitor (omeprazole, lansoprazole or rabeprazole) or an H2 antagonist (e.g. ranitidine, famotidine). However, you may take Pansped D with antacids (e.g. magaldrate, alginic acid, sodium bicarbonate, aluminium hydroxide, magnesium carbonate, or combinations thereof), if needed.
- Fungal infections such as azole anti-fungals, 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)
- Warfarin and phenprocoumon (used to thin blood and prevent clots). You may need further blood tests.
- Methotrexate (used to treat rheumatoid arthritis, psoriasis, and cancer because pantoprazole can increase levels of methotrexate in the blood.

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

Pansped D and Apomorphine

Before you use Pansped D and apomorphine, your doctor will ensure that you tolerate both medicines when used simultaneously.

Taking Pansped D with food and drink

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

Pregnancy and breast-feeding

Do not take PANSPED D Capsules.

You should not take this medicine if you are pregnant or while breast-feeding.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

If you experience side effects like dizziness or disturbed vision, you should not drive or use machines.

9.3 How to take PANSPED D

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist have told you. Check with your doctor if you are not sure.

The recommended dose is one capsule a day.

You should take this medicine for at least 2–3 consecutive days. Stop taking when you are completely symptom-free. You may experience relief from your acid reflux and heartburn symptoms after just one day of treatment with this medicine, but this medicine is not meant to bring immediate relief.

If you have no symptom-relief after taking this medicine for 2 weeks continuously, consult your doctor.

Take the capsule before a meal, at the same time every day.

You should swallow the capsule whole with some water.

Do not chew or break the capsule

If you forget to take PANSPED D

If you forget to take a dose of PANSPED D, take the next dose at the usual time. Do not take a double dose to make up for the forgotten dose.

If you stop taking PANSPED D

Should your doctor decide to stop your PANSPED D treatment, he/she will instruct you about the gradual withdrawal of PANSPED D.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you experience the following serious side effect stop taking PANSPED D capsules and seek medical help immediately:

- 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 Panspeed D.
- 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. This is more likely to happen in children. These symptoms should stop once you stop taking Pansped D.
- You have a very fast or unusual heartbeat. This could be a sign of a life-threatening heart problem.
- You have a fit (seizure).
- You get yellowing of the skin and eyes (due to severe liver damage), or kidney problems such as painful urination and lower back pain with fever

Other side effects include:

Common (affects less than 1 in 10 people)

Benign polyps in the stomach, dry mouth.

Uncommon side effects (may affect up to 1 in 100 people)

Headache; dizziness; diarrhoea; feeling sick; vomiting; bloating and flatulence (wind); constipation; dry mouth; bellyache and discomfort; skin rash or hives; itching; feeling weak,

exhausted or generally unwell; sleep disorders; increase in liver enzymes in a blood test; fracture in the hip, wrist or spine, lowering of sexual drive (libido) in men, feeling anxious, feeling drowsy, unusual production of breast milk in men and women, painful or tender breasts, general feeling of weakness.

Rare side effects:

Distortion or complete lack of the sense of taste; disturbances in vision such as blurred vision; pain in the joints; muscle pains; weight changes; raised body temperature; swelling of the extremities; depression; increased bilirubin and fat levels in blood (seen in blood test); breast enlargement in males; high fever and a sharp drop in circulating granular white blood cells (seen in blood test)

Very rare side effects (may affect up to 1 in 10,000 people):

Disorientation; reduction in the number of blood platelets, which may cause you to bleed or bruise more than normal; reduction in the number of white blood cells, which may lead to more frequent infections; coexisting abnormal reduction in the number of red and white blood cells, as well as platelets (seen in blood tests)

Frequency not known:

Acute Kidney Injury, hallucination; confusion (especially in patients with a history of these symptoms); decreased level of sodium in blood, decreased level of magnesium in blood, rash, possibly with pain in the joints, disorders of the cardiovascular system: heart rhythm disorders (rapid or irregular heart beat), 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.

Reporting of side effects

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: http://www.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 PANSPED D

Store below 25 º C, protected from light and moisture.
Keep out of reach of children.

9.6 Contents of the pack and other information

PANSPED D is available as strip of 10 capsules.

10 Details of manufacturer

Torrent Pharmaceuticals Ltd
Vill. Bhud & Makhnu Majra,
The.Baddi-173 205, Dist, Solan (H.P), INDIA

11 Details of permission or licence number with date

MNB/05/183 issued on 09.11.2011

12. Date of revision

JUNE 2020

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

Torrent House, Off Ashram Road,
Ahmedabad-380 009, INDIA

IN/PANSPED D 40, 30mg/FEB-2022/05/PI