Domflash®

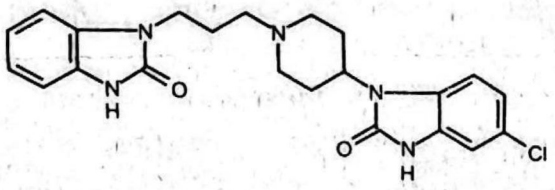
(BP Specification)
Domperidone
(BP Specification)
10mg Film Coated Tablets

COMPOSITION

Domflash 10mg Tablets: Each film coated tablet contains:
Domperidone 10mg
(BP Specification)

DESCRIPTION

DOMFLASH (Domperidone) has the following chemical structure.



$C_{22}H_{24}ClN_5O_2$ MW: 425.9 CAS Registry No.: 57808-66-9 The chemical name for **DOMFLASH** (Domperidone) is 5-Chloro-1-[1-[3-(2-oxo-2,3-dihydro-1H-benzimidazol-1-yl)propyl]piperidin-4-yl]-1,3-dihydro-2H-benzimidazol-2-one.

CLINICAL PARTICULARS

Therapeutic Indications:

1-Nausea and vomiting of functional, organic, infectious or dietetic origin or induced by radiotherapy or drug therapy.

2-A specific indication is nausea and vomiting induced by dopamine agonists, as used in Parkinson's disease (such as L- dopa and bromocriptine).

Dosage and Administration:

DOMFLASH (Domperidone) tablets should be taken by mouth.

Adults: 10 mg (1 tablet) 3 times daily, 15-30 minutes before meals and, if necessary, once more before sleep.

12 years of age and older and weighing 35 kg or more:

10 ml up to three times per day with a maximum daily dose of 30 ml per day.

Remarks: **DOMFLASH** (Domperidone) is recommended to be taken before meals. If taken after meals, absorption of the drug is somewhat delayed.

The tablets are not intended to be administered to children below the age of 5 years.

In patients with renal insufficiency, the dosing frequency should be reduced (see "Warnings and Precautions").

Contraindications:

DOMFLASH (Domperidone) is contraindicated in patients with known intolerance to the drug. **DOMFLASH** (Domperidone) should not be used whenever stimulation of gastric motility might be dangerous, e.g. in the presence of gastro-intestinal haemorrhage, mechanical obstruction or perforation **DOMFLASH** (Domperidone) is also contra-indicated In patients with a prolactin-releasing pituitary tumour (prolactinoma).

Precautions:

When antacids or antisecretory agents are used concomitantly, they should be taken after meals and not before meals, i.e. they should not be taken simultaneously with **DOMFLASH** (Domperidone).

Use in infants: Because the metabolic and blood-brain barrier functions are not fully developed during the first months of life, any drug should only be given to infants with great caution and under close medical supervision. Since the typical absence of neurological side effects with **DOMFLASH** (Domperidone) is mainly due to its poor penetration through the blood-brain barrier, the possible occurrence of such effects cannot be totally excluded in infants under 1 year of age.

Use in liver disorders: Since **DOMFLASH** (Domperidone) is highly metabolized in the liver. **DOMFLASH** (Domperidone) should be used with caution in patients with hepatic impairment.

Use in kidney disorders: In patients with severe renal insufficiency (serum creatinine > 6 mg/100 ml. i.e. > 0.6 m mol/l) the elimination half-life of **DOMFLASH** (Domperidone) was increased from 7.4 to 20.8 hours, but plasma drug levels were lower than in healthy volunteers. Since very little unchanged drug is excreted via the kidneys, it is unlikely that the dose of a single acute 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. Generally, patients on prolonged therapy should be reviewed regularly.

Drug Interactions:

Concomitant administration of anticholinergic drugs may antagonise the antidyspeptic effect of **DOMFLASH** (Domperidone). Antacids and antisecretory drugs should not be given simultaneously with **DOMFLASH** (Domperidone) orodispersible tablets as they lower its oral bioavailability (see also "warnings and precautions"). The main metabolic pathway of **DOMFLASH** (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 **DOMFLASH** (Domperidone). Examples of CYP3A4 inhibitors include the following:

- azole antifungals;
- macrolide antibiotics;
- HIV protease inhibitors;
- nefazodone.

Theoretically, since **DOMFLASH** (Domperidone) has gastrokinetic effects it could influence the absorption of concomitantly orally administered drugs, particularly those with sustained release or enteric coated formulations. However, in patients already stabilised on digoxin or paracetamol, concomitant administration of **DOMFLASH** (Domperidone) did not influence the blood levels of these drugs.

DOMFLASH (Domperidone) may also be associated with:

- Neuroleptics, the action of which it does not potentiate,
- Dopaminergic agonists (bromocriptine. L-dopa), whose unwanted peripheral effects such as digestive disorders, nausea and vomiting it suppresses without counteracting their central properties.

Pregnancy and lactation

Use during pregnancy: **DOMFLASH** (Domperidone) given to animals at doses up to 160 mg/kg/day did not produce teratogenic effects. However, as most medicines, **DOMFLASH** (Domperidone) should only be used during the first trimester of pregnancy if this is justified by the anticipated therapeutic benefit. Up to now, there has been no evidence of any increase in the risk of malformations in humans.

Use during lactation: The drug is excreted in breast milk of lactating rats (mostly as metabolites: peak concentration of 40 and 800 ng/ml after oral and I.V. administration of 2.5 mg/kg respectively). In women **DOMFLASH** (Domperidone) concentrations in breast milk are 4 times lower than corresponding plasma concentrations. It is not known whether this is harmful to the newborn. Therefore nursing is not recommended for mothers who are taking **DOMFLASH** (Domperidone), unless the expected benefits outweigh any potential risk.

Adverse reactions:

Side effects are rare; exceptionally some transient intestinal cramps have been reported. Extrapyramidal phenomena are rare in young children and exceptional in adults; they reverse spontaneously and completely as soon as the treatment is stopped. As the pituitary gland is located outside the blood-brain barrier, **DOMFLASH** (Domperidone) may induce an increase in the plasma prolactin level. In rare cases this hyperprolactinaemia may give rise to neuro-endocrinological phenomena such as galactorrhoea and

gynaecomastia. When the blood-brain barrier is immature (as in infants) or impaired, the possible occurrence of neurological side effects cannot be totally excluded. Rare allergic reactions, such as rash and urticaria, have also been reported.

Overdosage symptoms:

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

Treatment: In case of overdosage, the administration of activated charcoal, and close observation of the patient are recommended. Anticholinergic, anti-parkinson drugs or antihistamines with anticholinergic properties may be helpful in controlling the extrapyramidal reactions.

CLINICAL PHARMACOLOGY

Pharmacodynamics:

DOMFLASH (Domperidone) is a dopamine antagonist with anti-emetic properties similar to those of metoclopramide and certain neuroleptic drugs. Unlike these other drugs, however, **DOMFLASH** (Domperidone) does not readily cross the blood-brain barrier. In **DOMFLASH** (Domperidone) users; especially in adults, extrapyramidal side effects are very rare, but **DOMFLASH** (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 **DOMFLASH** (Domperidone) on dopamine receptors.

Studies in man have shown **DOMFLASH** (Domperidone) to increase the duration of antral and duodenal contractions, to increase the gastric emptying of liquids and semi-solids in healthy subjects and of solids in patients in whom it was delayed, and to increase lower oesophageal sphincter pressure in healthy subjects. It has no effect on gastric secretion.

Pharmacokinetics:

In fasting subjects, Domperidone is rapidly absorbed after oral administration, with peak plasma concentrations at approximately 1 hour. 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 administration of cimetidine or sodium bicarbonate. The time of peak absorption is slightly delayed and the AUC somewhat increased when the oral drug is taken after a meal.

Oral Domperidone does not appear to accumulate or to induce its own metabolism: a peak plasma level after 90 minutes of 21 ng/ml after two weeks oral administration of 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 the drug cross the placenta in rats. Domperidone concentrations in breast milk of lactating women are 4 times lower than corresponding plasma concentrations. 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. 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.

STORAGE

Store below 30°C. Protect from light and moisture.

HOW SUPPLIED

DOMFLASH 10mg tablets: Pack of 50 film coated tablets.

TO BE SOLD ON THE PRESCRIPTION OF A REGISTERED MEDICAL PRACTITIONER ONLY.

KEEP ALL MEDICINES OUT OF THE REACH OF CHILDREN.

WARNING

Daily doses greater than 30 mg of DOMFLASH (Domperidone) may be associated with an increased risk of serious ventricular arrhythmias or sudden cardiac death, particularly patients older than 60 years of age.

Lactose & Gluten Free

ڈوم فلیش

(ڈوم پیری ڈون)

10 ملی گرام

فلم کوٹڈ گولیاں

خوراک وہدایات

ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت کی جائے۔

تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

دوا کو 30°C سے کم درجہ حرارت پر، نمی اور روشنی سے محفوظ رکھیں۔

NEXT PHARMACEUTICAL

Manufactured by:
NEXT Pharmaceutical Products (Pvt.) Ltd.
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