Approved Professional Information for Medicines for Human Use

PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

VOMIGUARD 10 mg TABLETS

COMPOSITION

Each **VOMIGUARD 10 mg** tablet contains domperidone maleate equivalent to 10 mg domperidone.

Excipients: anhydrous colloidal silica, lactose monohydrate, magnesium stearate, maize starch, microcrystalline cellulose, polyvidone K30, sodium lauryl sulphate.

Contains lactose monohydrate.

CATEGORY AND CLASS

A 5.7.2 Anti-emetics and anti-vertigo preparations.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties:

Domperidone is a dopamine antagonist. It produces an anti-emetic effect through its action on the dopamine-receptor in the chemo-emetic trigger zone. Domperidone does not cross the blood-brain barrier to any significant degree and therefore exerts a relatively minor effect on cerebral dopaminergic receptors. Domperidone has been shown to increase the duration of antral and

duodenal contractions thus improving gastric emptying. Domperidone does not alter gastric secretions and has no effect on intracranial pressure or on the cardiovascular system.

Pharmacokinetic properties:

Domperidone is absorbed after oral administration in the fasting state with peak plasma concentrations at approximately 1 hour after administration. Domperidone undergoes rapid and extensive hepatic metabolism by hydroxylation and N-dealkylation. Due to this extensive first-pass hepatic and intestinal metabolism, the absolute bioavailability of oral domperidone is low (approximately 15 %).

Domperidone is 90 – 95 % bound to plasma proteins. The plasma half-life after a single oral dose is approximately 7 – 9 hours and is prolonged in patients with severe renal impairment.

Urinary and faecal excretion amount to 31 % and 66 % of the oral dose, respectively. The proportion of domperidone excreted unchanged is small (approximately 1 % of urinary and 10 % of faecal excretion).

INDICATIONS

VOMIGUARD is indicated for:

- Delayed gastric emptying of functional origin with gastro-oesophageal reflux and/or dyspepsia.
- Control of nausea and vomiting of central or local origin.
- An anti-emetic in patients receiving cytostatic and radiation therapy.
- Facilitation of radiological examination of the upper gastro-intestinal tract.
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CONTRAINDICATIONS

- Patients with known hypersensitivity to domperidone and to any of the ingredients of **VOMIGUARD**.
- Not to be used if stimulation of gastric motility is to be avoided or could be harmful, e.g. in the presence of gastrointestinal haemorrhage, obstruction or perforation.

- Patients with a prolactin-secreting or prolactin-producing pituitary tumour (prolactinoma).
- Bradycardia or heartblock.
- Pre-existing cardiac disease.
- Known congenital long QT interval or family history thereof.
- Co-administration with oral ketoconazole and other medicines inhibiting the hepatic cytochrome enzyme CYP3A4, and/or which have been shown to prolong the QT interval, such as macrolide antibiotics e.g. erythromycin, azithromycin, roxithromycin, clarithromycin, HIV protease inhibitors, azole antifungals, quinolones and amiodarone (see INTERACTIONS).
- Hypokalaemia, hypomagnesaemia.
- Moderate or severe hepatic impairment.
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WARNINGS AND SPECIAL PRECAUTIONS

Do not exceed the maximum daily dose of 40 mg.

VOMIGUARD has been associated with an increased risk of serious ventricular dysrhythmias and sudden cardiac death. The increased risk may be higher in patients older than 60 years or in patients taking oral doses greater than 30 mg per day. **VOMIGUARD** should be used with caution in these patients (see SIDE EFFECTS).

VOMIGUARD has been associated with QT interval prolongation.

Caution should be exercised in patients with renal impairment or in those at risk of fluid retention. In patients with severe renal insufficiency where the serum creatinine is more than 6 mg/100 mℓ, i.e. more than 0,6 mmol/L, the elimination half-life of **VOMIGUARD** was increased from 7,4 to 20,8 hours. The dosing frequency should be reduced to once or twice daily, depending on the severity of impairment, and the dose may need to be reduced. Patients on prolonged therapy should be monitored regularly.

VOMIGUARD should not be given to patients being treated with monoamine oxidase inhibitors. (see INTERACTIONS).

VOMIGUARD tablets contain 53,88 mg of lactose monohydrate and therefore should not be administered to patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

Effects on ability to drive and use machines

VOMIGUARD has no or negligible influence on the ability to drive and use machines, however caution should be taken as somnolence has been noted as a side effect.

INTERACTIONS

VOMIGUARD should not be used concomitantly with potent CYP3A4 inhibitors (see CONTRA-INDICATIONS). Examples of potent CYP3A4 inhibitors include macrolide antibiotics e.g. erythromycin*, azithromycin, roxithromycin, clarithromycin*, telithromycin*, HIV protease inhibitors, azole antifungals*, quinolones and amiodarone*.

(*also prolong the QT interval; see CONTRAINDICATIONS).

Concomitant use of the following medicines with **VOMIGUARD** may prolong QT interval:

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.

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

• protease inhibitors

• systemic azole antifungals

• some macrolides (erythromycin, clarithromycin, telithromycin)

Concomitant administration of anti-cholinergic medicines, antimuscarinic medicines and opioid analgesics may inhibit the action of **VOMIGUARD**.

VOMIGUARD suppresses the peripheral effects (digestive disorders, nausea and vomiting) of dopaminergic agonists.

Since **VOMIGUARD** has gastro-kinetic effects, it could influence the absorption of concomitant orally administered medicines, particularly those with sustained release or enteric coated formulations.

VOMIGUARD interferes with serum prolactin levels, thus, it may interfere with other hypoprolactaemic medicines and with some diagnostic tests.

Antacids and anti-secretory agents lower the oral bioavailability of **VOMIGUARD.**

Reduced gastric acidity impairs the absorption of **VOMIGUARD**. Oral bioavailability is decreased by prior administration of cimetidine or sodium carbonate.

VOMIGUARD should be avoided with great caution in patients taking MAOI's as it may increase the risk of cardiac reactions (arrhythmias, cardiac failure) and prolong QT interval. (See WARNINGS AND SPECIAL PRECAUTIONS).

HUMAN REPRODUCTION

Safety in pregnancy and lactation has not been established.

Administration to pregnant mothers shortly before giving birth, or during labour, may result in the newborn infant being born hypotonic, collapsed and hypoglycaemic. Domperidone is excreted in

human milk; therefore, breastfeeding is not recommended in mothers who are taking **VOMIGUARD.**

DOSAGE AND DIRECTIONS FOR USE

The dosage of **VOMIGUARD** should be the lowest effective dose for the individual situation (typically 30 mg/day) with a maximum oral dose of 40 mg.

For the treatment of acute nausea and vomiting the maximum treatment duration should not exceed one week. For other indications the initial duration of treatment is up to four weeks. If treatment exceeds four weeks, patients should be re-evaluated and the need for continued treatment reassessed.

Acute conditions (mainly nausea and vomiting):

Adults:

10 mg, 3 - 4 times per day, with a maximum of 40 mg per day orally, taken 15 to 30 minutes before meals and, if necessary, before retiring.

Children over 12 years and weighing 35 kg or more:

10 mg, 3 – 4 times per day, with a maximum of 40 mg per day orally, taken 15 to 30 minutes before meals and, if necessary, before retiring.

Tablets are not recommended for children weighing less than 35 kg.

Chronic conditions (mainly dyspepsia):

Adults:

10 mg, 3 times per day, 15 to 30 minutes before meals and, if necessary, before retiring, with a maximum of 40 mg per day orally.

Children *over 12 years old and weighing 35 kg or more:*

5 mg, 3 - 4 times per day, 15 to 30 minutes before meals and, if necessary, before retiring.

Renal insufficiency:

Since the elimination half-life of domperidone is prolonged in severe renal impairment, on repeated administration, the dosing frequency of **VOMIGUARD** 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.

SIDE EFFECTS

Psychiatric disorders:

Less frequent: depression, anxiety, libido decreased/ loss of libido

Frequency unknown: agitation (infants and children), nervousness

Nervous system disorders:

Less frequent: headache, somnolence, akathisia

Frequency unknown: dystonic reactions (extrapyramidal disorder) in young babies, where the blood brain barrier is not fully developed or is impaired, convulsions in infants and children

Gastro-intestinal disorders:

Frequent: dry mouth

Less frequent: diarrhoea, abdominal cramps

Immune system disorders:

Less frequent: hypersensitivity

Frequency unknown: anaphylactic reaction (including anaphylactic shock)

Skin and subcutaneous tissue disorders:

Less frequent: rash, pruritis

Frequency unknown: urticaria, angiodema

Reproductive system and breast disorders:

Less frequent: galactorrhoea, breast pain, breast tenderness

Frequency unknown: enlargement/gynaecomastia, amenorrhoea, breast discharge, breast swelling, lactation disorder, irregular menstruation

General disorders and administration site conditions:

Less Frequent: asthenia

Vascular disorders:

Frequency unknown: Hypertensive crisis in patients with pheochromocytoma

Cardiac disorders:

Frequency unknown: Sudden cardiac death, ventricular dysrhythmia, QTc prolongation, Torsade de Pointes

Renal and urinary disorders:

Frequency unknown: Urinary retention

Hepato-biliary disorders:

Frequency unknown: Liver function test abnormal

Blood and the lymphatic system disorders:

Frequency unknown: Blood prolactin increased, where the frequency of adverse reactions is higher including akathisia, breast discharge, breast enlargement, breast swelling, depression, hypersensitivity, lactation disorder and irregular menstruation.

KNOWN SYMPTOMS OF OVER DOSAGE AND PARTICULARS OF ITS TREATMENTS:

Symptoms of overdosage may include drowsiness, dis-orientation and extra pyramidal reactions, especially in children. Anti-cholinergic, anti-parkinson medicines or anti-histamines with anti-cholinergic properties may be helpful in controlling the extrapyramidal reactions. There is no specific antidote to **VOMIGUARD** but in the event of overdosage the administration of activated charcoal may be useful. Symptomatic and supportive measures are recommended.

IDENTIFICATION

White, round, standard, biconvex tablets, plain on both sides.

PRESENTATION

Clear PVC/Aluminium blister packs of 30 (3 x 10's) or 10 (1 x 10's) tablets in an outer cardboard carton.

White securitainers consisting of 100 tablets.

STORAGE INSTRUCTIONS

Store at or below 25 °C. Protect from light.

Keep blister in carton until required for use.

Keep the container tightly closed.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

A38/5.7.2/0620

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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DATE OF PUBLICATION OF THE PACKAGE INSERT

Date of registration certificate: 07 July 2006

Date of the most recent amendment to the professional information as approved by the Authority: