PROFESSIONAL INFORMATION FOR

ONDANSETRON CIPLA TABLETS 4 / 8

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

ONDANSETRON CIPLA TABLETS 4

ONDANSETRON CIPLA TABLETS 8

COMPOSITION:

ONDANSETRON CIPLA TABLETS 4: Each tablet contains ondansetron 4 mg (as hydrochloride dihydrate).

ONDANSETRON CIPLA TABLETS 8: Each tablet contains ondansetron 8 mg (as hydrochloride dihydrate).

Inactive ingredients include lactose monohydrate, magnesium stearate, maize starch, microcrystalline cellulose, and Opadry Y-1-7000 white (hydroxypropyl cellulose, titanium dioxide, macrogol (PEG 400)).

Contains sugar: Lactose monohydrate

ONDANSETRON CIPLA TABLETS 4: 46,00 mg.

ONDANSETRON CIPLA TABLETS 8: 92,00 mg.

PHARMACOLOGICAL CLASSIFICATION:

A 5.10 Medicines affecting autonomic functions. Serotonin antagonists.

PHARMACOLOGICAL ACTION:

Pharmacodynamics:

Ondansetron is a selective 5-HT_3 receptor-antagonist. Chemotherapeutic agents and radiotherapy may cause release of 5-HT in the small intestine initiating a vomiting reflex by activating vagal afferents via 5-HT_3 receptors. The initiation of this reflex is blocked by ondansetron. Activation of vagal afferents may also cause a release of 5-HT in the area postrema, located on the floor of the fourth ventricle, and this may also promote emesis through a central mechanism.

Thus, the effect of ondansetron in the management of the nausea and vomiting induced by chemotherapy and radiotherapy may be due to the antagonism of 5-HT_3 receptors on neurons located both in the peripheral and central nervous system.

In psychomotor testing, ondansetron does not cause sedation nor impair performance. Plasma prolactin concentrations are not altered by ondansetron.

Pharmacokinetics:

Ondansetron is rapidly absorbed following oral administration, with maximum plasma concentrations of about 30 ng/mℓ being attained approximately 1,6 hours after an 8 mg dose. The absolute oral bioavailability of ondansetron is approximately 60 %. The disposition of ondansetron following both intravenous and oral dosing is similar with a terminal elimination half-life of about 3 hours and a steady-state volume of distribution of about 140 ℓ. Plasma protein binding is 70 – 76 %. Ondansetron is cleared from the systemic circulation predominantly by metabolism with less than 5 % of a dose excreted unchanged in the urine.

Studies in healthy elderly volunteers have shown a prolonged elimination half-life (5 hrs.) and slightly increased bioavailability (65 %) for ondansetron.

As a result of reduced presystemic metabolism in patients with severe hepatic impairment, the systemic clearance of ondansetron is markedly reduced with prolonged elimination half-lives (15 – 32 hrs.) and an oral bioavailability approaching 100 %.

INDICATIONS:

ONDANSETRON CIPLA is indicated for the management of nausea and vomiting induced by chemotherapy and radiotherapy.

ONDANSETRON CIPLA is also indicated for the prevention and treatment of postoperative nausea and vomiting. Routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and vomiting will occur.

CONTRAINDICATIONS:

- **ONDANSETRON CIPLA** is contraindicated in patients known to have hypersensitivity to ondansetron or any of the ingredients of the preparation.
- The use of **ONDANSETRON CIPLA** for postoperative nausea and vomiting is contraindicated in pregnancy (see **"HUMAN REPRODUCTION"**).
- Ondansetron use is contraindicated during the first 12 weeks of pregnancy irrespective of the indication.
- Concomitant use with apomorphine is contraindicated (see **"WARNINGS AND SPECIAL PRECAUTIONS"** and **"INTERACTIONS"**).
- Congenital long QT syndrome.

WARNINGS AND SPECIAL PRECAUTIONS:

Warnings:

Patients with hepatic impairment:

In patients with moderate or severe impairment of hepatic function, clearance of **ONDANSETRON CIPLA** is significantly reduced and serum half-life significantly prolonged. In such patients, a total daily dose of 8 mg should not be exceeded (see **"DOSAGE AND DIRECTIONS FOR USE"**).

ONDANSETRON CIPLA prolongs the QT interval in a dose-dependent manner. ECG changes including QT prolongation have been reported in patients receiving ONDANSETRON CIPLA. Post-marketing cases of torsade de pointes have been reported in patients using ONDANSETRON CIPLA (see **"SIDE EFFECTS"**).

ONDANSETRON CIPLA should be administered with caution to patients who have or may develop QT prolongation. These conditions include patients with electrolyte abnormalities, with congenital long QT syndrome, or patients taking other medicinal products that could lead to QT prolongation (see **"INTERACTIONS"**).

Hypokalaemia and hypomagnesaemia should be corrected prior to **ONDANSETRON CIPLA** administration.

The use of ondansetron during the first 12 weeks of pregnancy increases the risk of developing oral cleft palate and or lip to the foetus.

Special Precautions:

Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective 5-HT_3 receptor antagonists.

Patients with signs of subacute intestinal obstructions should be monitored following administration, as **ONDANSETRON CIPLA** is known to increase large bowl transit time.

ONDANSETRON CIPLA contains lactose. Patients who are lactose intolerant and who take **ONDANSETRON CIPLA** may experience unwanted side-effects, such as nausea, cramping, bloating, diarrhoea, and flatulence. **ONDANSETRON CIPLA** should not be taken by patients with rare hereditary problems or a history of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

Effects on the ability to drive and operate machinery:

ONDANSETRON CIPLA is unlikely to affect your ability to drive or operate machinery.

INTERACTIONS:

ONDANSETRON CIPLA should be administered with caution to patients who are taking other medicines that may lead to QT prolongation and/or cause electrolyte abnormalities (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Ondansetron, as in **ONDANSETRON CIPLA**, is metabolised by multiple hepatic cytochrome P450 enzymes CYP3A4, CYP2D6 and CYP1A2. Due to the multiplicity of metabolic enzymes capable of metabolising ondansetron, enzyme inhibition or reduced activity of one enzyme (e.g. CYP2D6 genetic deficiency) is normally compensated for by other enzymes.

Apomorphine:

Cases of profound hypotension and loss of consciousness when ondansetron, as in **ONDANSETRON CIPLA**, was administered concomitantly with apomorphine hydrochloride have been reported. Concomitant use of **ONDANSETRON CIPLA** and apomorphine may intensify QT prolongation (see **"CONTRAINDICATIONS"** and **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Phenytoin, carbamazepine and rifampicin:

In patients treated with potent inducers of CYP3A4 (i.e. phenytoin, carbamazepine and rifampicin), the clearance of oral **ONDANSETRON CIPLA** was increased and ondansetron blood concentrations were decreased.

Tramadol:

ONDANSETRON CIPLA may reduce the analgesic effect of tramadol.

HUMAN REPRODUCTION:

Pregnancy:

Safety in pregnancy has not been established (see **"CONTRAINDICATIONS"**).

Lactation:

Tests have shown that ondansetron passes into the milk of lactating animals. It is therefore recommended that mothers receiving **ONDANSETRON CIPLA** should not breastfeed their babies.

DOSAGE AND DIRECTIONS FOR USE:

Chemotherapy- and radiotherapy-induced nausea and vomiting:

The emetogenic potential of cancer treatment varies according to the doses and combinations of chemotherapy and radiotherapy regimens used.

Adults:

Emetogenic chemotherapy and radiotherapy:

For most patients receiving emetogenic chemotherapy or radiotherapy **ONDANSETRON CIPLA TABLETS 8** should be administered orally 1 – 2 hours before treatment, followed by **ONDANSETRON CIPLA TABLETS 8** orally twelve hourly.

In circumstances where delayed or prolonged emesis is expected after the first 24 hours, **ONDANSETRON CIPLA** may be continued orally, 8 mg twice daily for up to five days after a course of treatment.

Highly emetogenic chemotherapy:

To protect against delayed or prolonged emesis after the first 24 hours, **ONDANSETRON CIPLA** may be continued orally, 8 mg twice daily for up to 5 days after a course of treatment.

Children:

Experience is currently limited, but ondansetron was effective and well tolerated in children over the age of 4 years, when given orally following chemotherapy in doses of **ONDANSETRON CIPLA** 4 mg every 12 hours for up to 5 days.

Elderly patients:

Efficacy and tolerance in patients aged over 65 years was similar to that seen in younger adults indicating no need to alter dosage or route of administration in the elderly.

Prevention and treatment of postoperative nausea and vomiting:

Adults:

For the prevention of postoperative nausea and vomiting, 16 mg may be given orally (two **ONDANSETRON CIPLA TABLETS 8** film-coated tablets) one hour prior to induction of anaesthesia.

Repeat dosing for patients who continue to experience nausea and/or vomiting postoperatively has not been studied. While recommended as a fixed dose for all, few patients above 80 kg or below 40 kg have been studied.

Elderly:

Safety and efficacy have not been established with the use **ONDANSETRON CIPLA** in the prevention and treatment of postoperative nausea and vomiting in the elderly.

Patients with renal / hepatic impairment:

Patients with renal impairment:

No alteration of daily dosage or frequency of dosing, or route of administration is required. There is limited information available on severely impaired renal function.

Patients with hepatic impairment:

Clearance of **ONDANSETRON CIPLA** is significantly reduced and serum half-life significantly prolonged in patients with moderate or severe impairment of hepatic function. In such patients, a total daily dose of 8 mg should not be exceeded (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

SIDE EFFECTS:

The following side-effects can occur:

Immune system disorders:

Less frequent: Immediate hypersensitivity reactions, sometimes severe (e.g. anaphylaxis, shock, angioedema, bronchospasm, shortness of breath, hypotension, urticaria) have been reported.

Nervous system disorders:

Frequent: Headache.

Less frequent: Seizures. Extrapyramidal reactions (including oculogyric crisis and dystonic reactions) have been reported without definitive evidence of persistent clinical consequences.

Cardiac disorders:

Less frequent: Dysrhythmias, bradycardia and chest pain with or without ST segment depression have been reported.

Frequency unknown: Torsade de pointes, ECG changes including QT interval prolongation.

Vascular disorders:

Frequent: Sensation of warmth or flushing.

Less frequent: Hypotension.

Respiratory, thoracic and mediastinal disorders:

Less frequent: Hiccups.

Gastrointestinal disorders:

Frequent: Increase in large bowl transit time is known to be caused by **ONDANSETRON CIPLA** which may cause constipation in some patients.

Hepatobiliary disorders:

Less frequent: Asymptomatic increases in liver function tests.

Musculoskeletal, bone and connective tissue disorders:

Less frequent: There have been rare reports of involuntary movement disorders without definitive evidence of persistent clinical sequelae.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

(See **"SIDE EFFECTS AND WARNINGS AND SPECIAL PRECAUTIONS"**). Manifestations that have been reported include severe constipation, visual disturbances, hypotension and a vasovagal episode with transient second degree AV block. In cases of suspected overdose, symptomatic and supportive therapy should be given as appropriate, as there is no specific antidote for ondansetron. Ondansetron prolongs the QT interval in a dose-dependent manner. ECG monitoring is recommended in cases of overdose.

IDENTIFICATION:

ONDANSETRON CIPLA TABLETS 4: White, circular, biconvex, film-coated tablet, marked “4” on one side and plain on the other side.

ONDANSETRON CIPLA TABLETS 8: White, circular, biconvex, film-coated tablet, marked “8” on one side and a central breakline on the other side.

PRESENTATION:

ONDANSETRON CIPLA TABLETS 4: Cartons of 10, 15 or 100 tablets blister-packed in transparent PVC/PVDC aluminium foil blister strips.

ONDANSETRON CIPLA TABLETS 8: Cartons of 10, 15 or 100 tablets blister-packed in transparent PVC/PVDC aluminium foil blister strips.

STORAGE INSTRUCTIONS:

Store at or below 25 °C

Keep the blisters in the outer carton until required for use.

REGISTRATION NUMBERS:

ONDANSETRON CIPLA TABLETS 4: A38/5.10/0435

ONDANSETRON CIPLA TABLETS 8: A38/5.10/0436

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION:

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