

# Vomena-PD

## **Introduction:**

The active ingredient in **VOMENA-PD** Oral Solution is ondansetron hydrochloride (HCl) as the dihydrate, the racemic form of ondansetron and a selective blocking agent of the serotonin 5-HT<sub>3</sub> receptor type.

Each 5 mL of **VOMENA-PD** Oral Solution contains 5 mg of ondansetron HCl dihydrate equivalent to 4 mg of ondansetron. **VOMENA-PD** Oral Solution is perfectly suited to patient requirements with strawberry flavor.

## **Clinical pharmacology:**

**Pharmacodynamics:** Ondansetron is a selective 5-HT<sub>3</sub>-receptor antagonist. Ondansetron is not a dopamine-receptor antagonist.

- \* Ondansetron may have central and/or peripheral action. Ondansetron preferentially blocks the serotonin 5-HT<sub>3</sub> receptors. 5-HT<sub>3</sub> receptors are found centrally in the chemoreceptor trigger zone and peripherally at vagal nerve terminals in the intestines.
- \* It has been established that vomiting especially due to chemotherapy and radiation therapy as well as post-operative etiology appears to be associated with the release of serotonin from enterochromaffin cells in the small intestine. By blocking these nerve endings in the intestines the signals are prevented from reaching to the central nervous system.
- \* Ondansetron has potent and highly selective antagonist properties at the 5-hydroxytryptamine 5-HT<sub>3</sub> receptor. The selectivity ratio for ondansetron on 5-HT<sub>3</sub> receptors compared with actions on other neurotransmitter receptor types is greater than 1,000. The antiemetic properties of ondansetron have been determined in ferrets against the nausea and vomiting induced by cisplatin, cyclophosphamide, and whole-body radiation.
- \* Ondansetron is also a weak antagonist of the 5-HT<sub>4</sub> receptor, and may bind to other serotonin receptors as well. Ondansetron has also been demonstrated to bind to the opioid  $\mu$  receptor.

## **Pharmacokinetics:**

- \* Mean oral availability: 56%
- \* Approximately 36% of an ondansetron dose is distributed into erythrocytes. The drug is about 70—76% bound to plasma protein.
- \* Ondansetron undergoes extensive metabolism, mainly by hydroxylation, followed by glucuronide or sulfate conjugation.
- \* For adults, the mean elimination half-life is 5.7 hours; patients under age 15 years show a shorter half-life of about 2.4 hours.

- \* The clearance of ondansetron in pediatric patients 1 to 4 months of age is slower and the half-life is roughly 2.5 fold longer than patients who are 4 to 24 months of age.
- \* Food slightly enhances bioavailability, but antacids have no effect on ondansetron bioavailability.
- \* Gender differences were shown in the disposition of ondansetron given as a single dose. The extent and rate of ondansetron's absorption is greater in women than men. Slower clearance in women, a smaller apparent volume of distribution (adjusted for weight), and higher absolute bioavailability resulted in higher plasma ondansetron levels.

**Indications:**

- Chemotherapy-induced nausea and vomiting [CINV]
- Post-operative and post-radiation nausea and vomiting [PONV]
- It is also used off-label to treat hyperemesis gravidarum in pregnant women, but there is no conclusive data available on its safety in pregnancy, especially during the first trimester.
- It is also often used to treat cyclic vomiting syndrome although there have been no formal trials to confirm efficacy, case reports suggest it can be helpful in some cases.

**Contraindications:**

- \* Ondansetron is extensively metabolized in the liver and should be used with caution in patients with hepatic disease, hepatitis, or elevated hepatic enzymes because of possible increased plasma levels and subsequent toxicity. Patients with compromised liver function should receive no more than 8 mg/day.
- \* Ondansetron should not be used in patients with known ondansetron hypersensitivity. Cross-sensitivity is possible between these agents.
- \* Furthermore, it has been hypothesized that antagonism at serotonin (5HT) receptors, and the subsequent increased concentrations of serotonin, increase the risk of developing bronchospasm and/or vasoconstriction.
- \* Data demonstrate that ECG interval changes are a class effect of the 5-HT<sub>3</sub> receptor antagonists. However, theoretical concern regarding cardiovascular adverse events with these agents is not supported by clinical experience. The clinically significant benefits of these agents appear to outweigh the theoretically small risk of meaningful cardiovascular events; however, the risks and benefits should be determined for each individual patient.
- \* **Pediatric population:**
  - Infants < 4 months of age may accumulate ondansetron and should be closely monitored for toxicity.

- Limited information is available on the use of ondansetron in neonates < 1 month of age receiving surgery or in pediatric cancer patients who are infants < 6 months of age.
- The clearance of ondansetron in pediatric patients 1 to 4 months of age is slower and the half-life is roughly 2.5-fold longer than infant patients who are 4 to 24 months of age.

✧ **Pregnancy:**

Ondansetron is classified as pregnancy category B. It should be used during pregnancy only when clearly needed. Three case reports exist where ondansetron was given during pregnancy in the first or third trimesters with no documented adverse effects on the fetus.

**Drug-drug interactions with ondansetron:**

- ✧ Ondansetron is metabolized by hepatic cytochrome P-450 enzyme, hence inducers or inhibitors like Carbamazepine, phenytoin of these enzymes may change the clearance and, hence, the half-life of ondansetron.
- ✧ Ondansetron may interact with oral chemotherapy drugs such as cyclophosphamide, cisplatin, etoposide etc.
- ✧ Oral ondansetron also interacts with anti-tubercular disease such as rifampicin.
- ✧ The co-administration of ondansetron with diuretics associated with hypokalemia could increase the risk of QT prolongation.

**Adverse effects:**

- ✧ Ondansetron is a well-tolerated drug with few side effects. Headache, constipation, and dizziness are the most commonly reported side effects associated with its use. There have been no significant drug interactions reported with this drug's use. It is broken down by the hepatic cytochrome P450 system and it has little effect on the metabolism of other drugs broken down by this system.
- ✧ Ondansetron does not have any psychosomatic adverse effect such as behavioral depression, which is associated with metoclopramide.
- ✧ Unlike metoclopramide, ondansetron will not cause extrapyramidal or other dose-limiting side effects. [Seminars in Oncology 19(4, Suppl 10): 1-8, 1992.]

**Dosage:**

Ondansetron (intravenous 0.01 to 0.1 mg/kg or subcutaneous 0.1 to 0.5 mg/kg) causes dose-dependent inhibitions of the vomiting induced by chemotherapy or surgery.

- ✧ Children 4—11 years: 4 mg PO three times per day.

- \* Children < 4 years† and BSA > 1 m<sup>2</sup>: 4 mg PO three times per day.
- \* Children < 4 years† and BSA 0.6—1 m<sup>2</sup>: 3 mg PO three times per day.
- \* Children < 4 years† and BSA 0.3—0.6 m<sup>2</sup>: 2 mg PO three times per day.
- \* Children < 4 years† and BSA < 0.3 m<sup>2</sup>: 1 mg PO three times per day.

**Presentation:**

**VOMENA-PD** is available in a glass bottle of 30ml with dropper and measuring cup.