**Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Chemotherapy**

**2.1 Prevention of nausea and vomiting associated with initial and repeat courses of emetogenic chemotherapy**

- Doses of ondansetron 4 mg or less, or a single 4-mg dose for patients weighing more than 40 kg. The rate of administration should not be less than 1 mg per minute.

- A second intravenous dose of 4 mg ondansetron postoperatively does not provide any additional benefit in preventing postoperative nausea and vomiting.

- For pediatric patients 6 months through 18 years of age, the intravenous dosage of ondansetron is three 0.15-mg/kg doses (0.15 mg/kg up to a maximum of 16 mg per dose) are administered 4 and 8 hours after the first dose of ondansetron. The drug is not to be administered intramuscularly or subcutaneously.

**Dosage Adjustment for Patients with Impaired Renal Function**

- For patients with creatinine clearance less than 30 mL/min, a fixed dose of ondansetron 4 mg is recommended. However, because few patients above 80 kg have been studied, the dose should be adjusted according to dose-response data if available.

**7.1 Drugs Affecting Cytochrome P-450 Enzymes**

- The coadministration of ondansetron with drugs known to reduce the clearance of ondansetron by CYP3A4, such as allopurinol, will result in increased plasma drug levels of ondansetron.

**8.4 Indications and Usage**

- **Prevention of nausea and vomiting associated with initial and repeat courses of emetogenic chemotherapy**

**11 DESCRIPTION**

- Ondansetron injection is a clear, colorless, nonpyrogenic, sterile solution for intravenous use. The pH of the injection is 5.0 to 7.5.

**12.3 Pharmacokinetics**

- Ondansetron is distributed throughout the body in a manner consistent with hepatic and peripheral blood flow. The drug is metabolized primarily in the liver by CYP3A4 and CYP2D6 enzymes. Approximately 9% of a single 32-mg intravenous dose of ondansetron is metabolized to 5-hydroxy-ondansetron, and approximately 2% is metabolized to norondansetron.

- Ondansetron is excreted in the breast milk of rats. It is not known whether ondansetron is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ondansetron is administered to a nursing mother.

**13 ADVERSE REACTIONS**

- The most frequently reported adverse reactions (incidence ≥ 1% and <10%) were:
  - Dizziness/sedation
  - Drowsiness
  - Headache
  - Fatigue
  - Nausea
  - Vomiting

**8.3 Nursing Mothers**

- Ondansetron is excreted in the breast milk of rats. It is not known whether ondansetron is excreted in human milk.

**7.6 Temazepam**

- In humans, carmustine, etoposide, and cisplatin do not affect the pharmacokinetics of ondansetron.

**10.1 Pregnancy**

- Pregnancy Category B. Reproduction studies have been performed in pregnant rats and rabbits at intravenous doses up to 50 times the recommended human intravenous dose of 0.15 mg/kg given three times daily. There was no evidence of impaired fertility or harm to the fetus due to ondansetron administration.

**7.5 Beta-Adrenergic Blocking Agents**

- In humans, ondansetron does not affect the pharmacokinetics of propranolol.

**8.2 Prolactin-Lowering Agents**

- In humans, ondansetron does not affect the pharmacokinetics of metoclopramide.

**7.2 Narcotics**

- In humans, ondansetron does not alter the pharmacokinetics of fentanyl.

**10.2 Lactation**

- Ondansetron is excreted in the breast milk of rats. It is not known whether ondansetron is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ondansetron is administered to a nursing mother.

**7.4 Other Antineoplastic Agents**

- In patients treated with potent inducers of CYP3A4 (i.e., phenytoin, carbamazepine, and rifampin), the clearance of ondansetron is increased.

**8.5 Cimetidine**

- In humans, ondansetron does not affect the pharmacokinetics of cimetidine.

**10.3 Other Antiviral and Immunosuppressive Agents**

- In humans, ondansetron does not affect the pharmacokinetics of zidovudine.

**7.3 Antihistaminics**

- In humans, ondansetron does not alter the pharmacokinetics of diphenhydramine.

**8.6 Thrombolytics**

- In patients treated with thrombolytics, ondansetron does not affect the pharmacokinetics of tirofiban.

**10.4 Anticonvulsants and Other Antiepileptics**

- In patients treated with antiepileptics, ondansetron does not affect the pharmacokinetics of lamotrigine.

**CLINICAL PHARMACOLOGY**

- Ondansetron injection should not be mixed with solutions for which physical and chemical compatibility have not been established.
Due to the very small contribution (5%) of renal clearance to the overall clearance, renal impairment was not expected to have a significant impact on ondansetron disposition. To further evaluate this, a study was performed in normal volunteers (n = 56) to evaluate the pharmacokinetics of a single 4-mg dose administered intravenously over 15 min. The study aimed to assess the impact of renal impairment on ondansetron disposition in vivo.

Ondansetron is extensively metabolized in humans, with approximately 5% of a radiolabeled dose recovered as the parent compound. The majority of the metabolites are eliminated via the feces. In the study, the pharmacokinetics of ondansetron were evaluated in a large population of cancer patients and surgery patients. The results showed that the exposure-response relationship between ondansetron concentration and ΔΔQTcF was significant, indicating that ondansetron treatment may have an impact on cardiac conduction.

The study also evaluated the treatment response of ondansetron in the prevention of postoperative nausea and vomiting. A double-blind, multicenter, placebo-controlled study was conducted in 670 pediatric patients 1 month to 24 months of age. The study found that ondansetron was more effective than placebo in preventing further episodes of nausea and vomiting. The results of the study are summarized in Table 3, which shows the median nausea scores over 24-h postoperative period and the median number of emetic episodes.

In conclusion, ondansetron is an effective antiemetic agent in the prevention of postoperative nausea and vomiting in pediatric patients. The pharmacokinetic profile of ondansetron in these patients is consistent with the established knowledge of the drug's metabolism and disposition. Further studies are needed to explore the potential cardiac effects of ondansetron and to develop strategies to minimize these effects in patients at risk.