Ondansetron

Drug Description

Ondansetron is an oral and parenteral serotonin (5-HT_3) receptor antagonist. It is used as an antiemetic agent for the prevention and treatment of nausea and vomiting during chemotherapy, radiation therapy, and surgery.[31266] Ondansetron has occasionally been utilized for the treatment of hyperemesis gravidarum refractory to other treatments. Novel investigational uses of ondansetron include treatment of gastrointestinal motility disorders and drug dependence (e.g., alcoholism). In the pediatric population, ondansetron is also used off-label for cyclic vomiting syndrome and gastroenteritis-induced vomiting.[52241] [52129] Ondansetron is an extremely safe and highly effective antiemetic compared to older, traditional antiemetics (e.g., metoclopramide, droperidol); however, there is a risk of dose-dependent QT-prolongation and torsade de points.[31266] [52167] When administered at optimal doses, ondansetron and other $5HT_3$ receptor antagonists (e.g., granisetron) are equally effective.[52202] The American Society of Clinical Oncology (ASCO) and the Multinational Association of Supportive Care in Cancer (MASCC) and European Society of Clinical Oncology (ESMO) guidelines both recommend combination therapy with a 5-HT_3 receptor antagonist plus a corticosteroid in children receiving chemotherapy of moderate or high emetogenic risk.[49434] [49435] The Society for Ambulatory Anesthesia (SAMBA) guidelines recommend the use of a 5-HT_3 receptor antagonist as the first choice for prophylaxis of postoperative nausea and vomiting in children.[49437] Ondansetron was originally approved for the treatment of chemotherapy-induced nausea/vomiting by the FDA in January 1991 and oral dosage forms were approved for the treatment of post-operative nausea/vomiting in April 1995. An orally disintegrating tablet, Zofran ODT, was approved by the FDA in February 1999. The FDA accepted an NDA for Zensana oral spray in August 2006. Zuplenz, an oral soluble film formulation, was FDA approved in July 2010.

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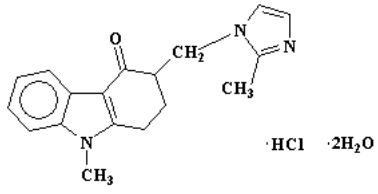
Classifications

Gastrointestinal Agents
- Antiemetics
  - Serotonin-receptor antagonists

Chemical Structures

Ondansetron Hydrochloride
$C_{18}H_{19}N_3O \cdot HCl \cdot 2H_2O$



Mechanism of Action

Mechanism of Action: Ondansetron is a 5-HT_3 receptor antagonist. Although other neurotransmitters are involved, serotonin plays an important role in the emetogenic pathways associated with chemotherapy- and radiation-induced nausea and vomiting. During the early or acute phase, the primary site of emetogenesis in chemotherapy-induced nausea and vomiting (CINV) is thought to be the gut wall. Chemotherapy is cytotoxic to enterochromaffin cells in the small intestine. Enterochromaffin cell death leads to serotonin release and therefore increased serotonin binding on nerve endings, leading to sensory input that contributes to emesis.[52167] [52168] Peripherally, ondansetron preferentially blocks the serotonin 5-hydroxytryptamine, type 3 (5-HT_3) receptors at the peripheral vagal nerve terminals in the intestines, blocking the signal transmission to the central nervous system and antagonizing the effects of serotonin. Ondansetron is also a weak antagonist of the 5-HT_{1B}, 5-HT_{1C}, alpha-adrenergic, and opioid mu receptors; the clinical implications of these actions is uncertain. It has no activity at dopamine receptors.[31266] [52167]

Much like chemotherapy-induced nausea and vomiting (CINV), postoperative nausea and vomiting (PONV) is not controlled by a single neurotransmitter, but serotonin is believed to play a major role. The process of postoperative nausea and vomiting is coordinated by the vomiting center in the central nervous system. Stimulation can be initiated centrally in areas such as the cerebral cortex and otic or vestibular nerves, or peripherally in areas such as the oropharynx, mediastinum, gastrointestinal track, renal pelvis, peritoneum, or genitalia. Stretching and inflammation that occur during or after surgery may trigger chemical stimulation that lead to nausea and vomiting. Centrally, ondansetron blocks the 5-HT_3 receptor site at the chemoreceptor trigger zone, stopping the vomiting reflex produced by the vomiting center. Because of multiple neurochemical receptor sites involved during surgery, combination antiemetic therapy with drugs of different mechanisms is often necessary.[31266] [52169]

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Pharmacokinetics

Pharmacokinetics: Ondansetron is administered orally and parenterally. It is approximately 70—76% bound to plasma protein; circulating drug also distributes into erythrocytes (approximately 36%). Animal data indicate it distributes into breast milk. Systemic exposure does not increase proportionately to the dose. Less than 5% of a dose is excreted in the urine unchanged. The mean elimination half-life in adults ranges 3.1 to 5.8 hours.[31266] [49444]

Affected cytochrome P450 isoenzymes and drug transporters: CYP3A4, CYP1A2, CYP2D6, CYP2C9, P-gp
Ondansetron undergoes extensive metabolism, mainly by hydroxylation, followed by glucuronide or sulfate conjugation. In vitro studies indicate that ondansetron is metabolized by hepatic cytochrome P450 (CYP450) drug-metabolizing enzymes, including CYP1A2, CYP2D6, and CYP3A4; with CYP3A4 playing the largest role. Because

multiple enzymes are involved in the metabolism of ondansetron, inhibition or loss of any one enzyme may not affect the overall rate of metabolism. Additionally, it is likely that inhibition or loss of one enzyme (e.g., CYP2D6 genetic deficiency) will be compensated by others and may result in little change in overall rates of ondansetron elimination.[31266] Interactions with inhibitors or inducers of these enzymes have not been reported clinically; however, the potential exists for these interactions to change the clearance and, hence, the half-life of ondansetron. On the basis of limited available data, no dosage adjustment is recommended for patients receiving CYP-interacting drugs. Ondansetron is also a substrate of P-glycoprotein.[31266] [34653] The inactive metabolites are eliminated in the urine.

•Route-Specific Pharmacokinetics

Oral Route

Following oral administration, ondansetron is well absorbed from the gastrointestinal tract and undergoes first-pass metabolism. After a dose of a single 8-mg tablet, mean oral bioavailability in healthy adult subjects is 56%. The AUC from a 16 mg-tablet is 24% greater than predicted from an 8-mg tablet dose, indicating reduced first-pass metabolism at higher oral doses. Food slightly enhances tablet bioavailability, but antacids have no effect. Of note, 4- and 8-mg oral ondansetron tablets, orally disintegrating tablets (ODT), and oral solution are bioequivalent.[49444] After a single 8-mg dose of ondansetron oral soluble film in adult patients, peak plasma concentrations are achieved in 1.3 hours, and mean Cmax is 37.28 ng/mL and the mean AUC 225 n x h/mL. The Cmax and AUC of the oral soluble film is comparable to that of the same dose of ondansetron ODT. Water does not affect the exposure of ondansetron oral soluble film administration. Administration of the oral soluble film with a high-fat meal delays the Tmax by approximately 1 hour, but the AUC is unaffected.[41272]

Intravenous Route

In adults, a single 4-mg dose administered as a 5-minute intravenous (IV) infusion demonstrated a mean AUC of 156 ng x h/ml. Mean peak plasma concentrations were 42.9 ng/ml at 10 minutes after IV infusion.[31266]

•Special Populations

Hepatic Impairment

In adult patients with mild to moderate hepatic impairment, ondansetron clearance is reduced two-fold and mean half-life is increased to 11.6 hours, compared to 3—5.7 hours in patients without hepatic impairment. In adult patients with severe hepatic impairment, clearance is reduced two-fold to three-fold and volume of distribution is increased, resulting in an increase in elimination half-life to 20 hours.[31266]

Renal Impairment

A small percentage (5%) of ondansetron is renally cleared. In patients with severe renal impairment (creatinine clearance < 30 ml/min) the mean plasma clearance is reduced by approximately 40%; however, the reduction is variable and is not consistent with an increase in half-life.[31266] A dose reduction is not necessary in this population.

Pediatrics

In general, pediatric patients have a higher ondansetron clearance compared to adult patients, resulting in a shorter half-life; mean half-life is approximately 2.8 hours in pediatric cancer patients 4—15 years of age; patients older than 15 years exhibit pharmacokinetic parameters similar to adults. A pharmacokinetic study of postoperative children 3—12 years of age given a single dose of 2 or 4 mg IV demonstrated an elimination half-life of 2.5—3.5 hours. Another surgical study in infants and children 5—24 months receiving 0.1—0.2 mg/kg IV ondansetron as a single dose demonstrated an elimination half-life of 2.9 hours. Notably, during the same study, infants 1—4 months of age had a higher Vd (3.5 L/kg), longer half-life (6.7 hours), and slower clearance (0.401 L/kg/h) relative to older children.[31266] During a pharmacokinetic study in infants and children age 1—48 months, simulations showed that an intravenous dose of ondansetron 0.1 mg/kg in infants < 6 months produced exposure similar to a 0.15 mg/kg dose in older infants and young children.[52159]

Geriatric

Patients over 75 years also have a reduced clearance of ondansetron and an increased elimination half-life, however, no dosage adjustments are recommended.[31266]

Gender Differences

Gender differences exist in the disposition of single-dose ondansetron. The extent and rate of ondansetron 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 concentrations, which may in part be due to differences in body weight between men and women. It is not known if these gender-related differences are clinically important.[31266]

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Indications

Labeled

- chemotherapy-induced nausea/vomiting prophylaxis
- post-operative nausea/vomiting (PONV) prophylaxis
- radiation-induced nausea/vomiting prophylaxis

Off-Label, Recommended

- cyclic vomiting syndrome †
- ethanol dependence †
- gastroenteritis †
- hyperemesis gravidarum †
- post-operative nausea/vomiting (PONV) †
- pregnancy-induced nausea/vomiting †
- pruritus †

† Off-label indication

For chemotherapy-induced nausea/vomiting prophylaxis (CINV prophylaxis) and radiation-induced nausea/vomiting prophylaxis (RINV prophylaxis):

Intravenous dosage:

Adults: 0.15 mg/kg (150 mcg/kg) IV infused over 15 minutes beginning 30 minutes prior to the initiation of emetogenic chemotherapy. No single dose should exceed 16 mg/dose IV. Dosage may be repeated twice, administered 4 and 8 hours after the initial dose.[31266] NOTE: In June, 2012, the FDA announced that ondansetron 32 mg IV single dose regimen is no longer indicated for chemotherapy-induced nausea/vomiting (CINV) prophylaxis because of the risk of QT prolongation.[51100]

Infants 6 months and older, Children, and Adolescents: 0.15 mg/kg IV infused over 15 minutes beginning 30 minutes prior to the initiation of chemotherapy and repeat 4 and 8 hours later (3 doses total). Max: 16 mg/dose.[31266] [52202] The American Society of Clinical Oncology (ASCO) recommends 0.15 mg/kg/dose (Max: 8 mg) twice daily during chemotherapy and for 2 days after completion, or give 1 to 2 hours before each fraction of radiation and for 1 day after completion for highly emetogenic therapy.[49434] Alternatively, ondansetron has been administered every 8 hours and continued for 1 to 5 days after completion of therapy.[49435] [52191] [52192] A single dose of 0.6 mg/kg IV was as effective as standard therapy (0.15 mg/kg/dose up to 8 mg every 4 hours for 4 doses) in a prospective, double-blind study in chemotherapy-naive pediatric oncology patients; however, the maximum dose in the study was 32 mg, which is no longer recommended because of dose-dependent QT prolongation.[52188]

Oral dosage:

Adults receiving moderately emetogenic chemotherapy: 8 mg PO twice daily. Give first dose 30 minutes before the start of emetogenic chemotherapy, with a subsequent dose 8 hours after the initial dose. Further doses may be given every 12 hours for 1 to 2 days after completion of chemotherapy.[49444]

Adults receiving highly emetogenic chemotherapy: 24 mg dose PO once given 30 minutes before administration of single-day highly emetogenic chemotherapy, including cisplatin 50 mg/m^2 or more. Multiday, single dose administration of ondansetron 24 mg has not been studied.[49444]

Adults receiving radiotherapy (general dosage): 8 mg PO 3 times daily.[49444]

Adults receiving total body irradiation: 8 mg PO 1 to 2 hours prior to each fraction of radiotherapy each day.[49444]

Adults receiving daily fractionated radiotherapy or single high-dose fraction radiotherapy to the abdomen: Initially, 8 mg PO 1 to 2 hours prior to radiotherapy. Then, 8 mg PO every 8 hours after the first dose for 1 to 2 days following completion of radiotherapy.[49444]

Children and Adolescents 12 years and older: 8 mg PO twice daily. Give the first dose 30 minutes prior to chemotherapy with a subsequent dose 8 hours after the initial dose. For radiation, give the first dose 1 to 2 hours prior to therapy. Further doses may be given every 8 to 12 hours for 1 to 5 days after completion of therapy.[49444] [49434] [52191] [52192] Alternatively, a single 24 mg PO dose may be given prior to chemotherapy.[52202]

Children 4 to 11 years: 4 mg PO 3 times daily. Give the first dose 30 minutes prior to chemotherapy, with subsequent doses 4 and 8 hours after the initial dose. For radiation, give the first dose 1 to 2 hours prior to therapy. Further doses may be given every 8 hours for 1 to 5 days after completion of therapy.[49444] [52191] [52192] Alternatively, a single 12 mg PO dose may be given prior to chemotherapy.[52202]

Infants† and Children less than 4 years† with a body surface area more than 1 m2: 4 mg PO 3 times daily.[52194] Give the first dose 30 minutes prior to chemotherapy or 1 to 2 hours prior to radiation.[40241] May be continued for 1 to 5 days after completion of therapy.[40241] [52191]

Infants† and Children less than 4 years† with a body surface area 0.6 to 1 m2: 3 mg PO 3 times daily.[52194] Give the first dose 30 minutes prior to chemotherapy or 1 to 2 hours prior to radiation.[40241] May be continued for 1 to 5 days after completion of therapy.[40241] [52191]

Infants† and Children less than 4 years† with a body surface area 0.3 to 0.6 m2: 2 mg PO 3 times daily.[52192] [52194] Give the first dose 30 minutes prior to chemotherapy or 1 to 2 hours prior to radiation.[40241] May be continued for 1 to 5 days after completion of therapy.[40241] [52191]

Infants† and Children less than 4 years† with a body surface area less than 0.3 m2: 1 mg PO 3 times daily.[52194] Give the first dose 30 minutes prior to chemotherapy or 1 to 2 hours prior to radiation.[40241] May be continued for 1 to 5 days after completion of therapy.[40241] [52191]

For the treatment of post-operative nausea/vomiting (PONV)†:

Intravenous dosage:

Adolescents and Adults: 4 mg IV once; the doses of 5-HT3 antagonists used for the treatment of established PONV are smaller than those used for PONV prophylaxis. A 5-HT3 antagonist is recommended if no 5-HT3 antagonist prophylaxis was given, or for those who received a prophylactic antiemetic from another drug class. Administration of a second IV dose of a 5-HT3 agent postoperatively in response to inadequate control is generally not effective; consider use of an antiemetic from another pharmacologic class.[57398]

Infants and Children: Dosing is weight based as follows:

-weight <= 40 kg: 0.05—0.1 mg/kg IV once; a 5-HT3 antagonist is recommended if no prophylaxis was given. Administration of a second IV dose postoperatively in response to inadequate control is generally not effective; consider use of an antiemetic from another pharmacologic class.[31266] [49437] Among children who had at least 2 postoperative episode of retching or vomiting within 2 hours of surgery and who had not received prophylaxis, 53% had complete control of vomiting (no emesis and no rescue 24 hours after the dose) with a single 0.1 mg/kg (max: 4 mg) IV ondansetron dose as compared with 17% of placebo recipients.[55979]

-weight > 40 kg: 4 mg IV once; a 5-HT3 antagonist is recommended if no prophylaxis was given. Administration of a second IV dose postoperatively in response to inadequate control is generally not effective; consider use of an antiemetic from another pharmacologic class.[31266] [49437]

For post-operative nausea/vomiting (PONV) prophylaxis:

Intravenous dosage:

Adults, Adolescents, and Children weighing more than 40 kg: 4 mg IV as single dose given immediately prior to or following anesthesia induction, or once postoperatively if patient experiences nausea/vomiting shortly after surgery. Administration of a second IV dose postoperatively in response to inadequate control is generally not effective; use of an antiemetic from another pharmacologic class should be considered.[31266] [57398]

Infants and Children weighing 40 kg or less: 0.05 to 0.1 mg/kg IV as single dose given immediately prior to or following anesthesia induction, or once postoperatively if patient experiences nausea/vomiting shortly after surgery. Max: 4 mg/dose. Administration of a second IV dose postoperatively in response to inadequate control is generally not effective; use of an antiemetic from another pharmacologic class should be considered.[31266] [49437] [52205]

Intramuscular dosage:

Adults and Adolescents: 4 mg IM as single dose given immediately before anesthesia induction, or once postoperatively if patient experiences nausea/vomiting shortly after surgery. Administration of a second dose postoperatively in response to inadequate control is generally not effective; use of an antiemetic from another pharmacologic class should be considered.[31266]

Oral dosage:

Adults: 16 mg PO as single dose given 1 hour before anesthesia induction.[49444] Alteratively, 8 mg ODT PO as a single dose given at the end of surgery is as effective as 4 mg IV according to clinical practice guidelines.[57398]

Infants†, Children†, and Adolescents†: 0.15 mg/kg PO as single dose, immediately prior to or after anesthesia induction, or once postoperatively if patient experiences nausea/vomiting shortly after surgery. Max: 8 mg/dose.[52220] Administration of a second dose postoperatively in response to inadequate control is generally not effective; use of an antiemetic from another pharmacologic class should be considered.[31266] [49437]

For the short-term treatment of nausea/vomiting associated with acute gastroenteritis†:

Intravenous dosage:

Adults: No data are available; not evaluated.

Infants, Children, and Adolescents: Routine use of antiemetics is not recommended in acute gastroenteritis.[52241] [52201] A single dose of 0.15—0.3 mg/kg IV has been used along with oral or IV rehydration. Maximum: 8 mg/dose IV.[27475] [52244]

Oral dosage:

Adults: No data are available; not evaluated.

Infants >=6 months, Children, and Adolescents: Routine use of antiemetics is not recommended in acute gastroenteritis.[52241] [52201] The following weight-based doses have been used along with oral or IV rehydration:
-weight < 8 kg: No data. Use not recommended.
-weight 8—15 kg: 2 mg PO as a single dose.
-weight > 15—30 kg: 4 mg PO as a single dose.
-weight > 30 kg: 6—8 mg PO as a single dose.[52245] [44904]
Infants < 6 months: Safety and efficacy have not been established.

For hyperemesis gravidarum† (severe pregnancy-induced nausea/vomiting) unresponsive to other antiemetics:
Intravenous and Oral dosage:
Adult pregnant females: Doses of 4—8 mg IV or PO given 2—3 times per day have been administered as early as 10 weeks gestation. Durations of daily treatment up to 14 days with ondansetron have been reported, and one case report exists of a patient taking 4 mg PO intermittently 1—2 times daily as needed from the 14th to 33rd week of gestation. No adverse effects on fetal outcome have been reported to date.[25505] Use of ondansetron is supported in ACOG guidelines when other agents have failed or when a patient is unresponsive to other measures and is at risk for dehydration or other adverse outcomes.[33611]

For the treatment of pruritus† secondary to cholestasis:
Intravenous and Oral dosage:
Adults: Five patients with severe pruritus secondary to cholestasis were treated with ondansetron. An initial dose of 8 mg IV was administered. Pruritus was relieved completely in 3 patients and partially in 2 with effects lasting 5—16 hours. Three patients were continued on oral therapy of 8 mg PO twice daily, with decreased severity of symptoms.[24001] Dosage should be adjusted in hepatic impairment.

For the maintenance treatment of ethanol dependence†:
NOTE: Pharmacotherapy should be used as a part of a comprehensive management program that includes psychosocial support and treatment.
Oral dosage:
Adults: A dosage of 4 mcg/kg PO twice per day, combined with weekly standardized group behavioral therapy, was effective in reducing alcohol consumption. Ondansetron was superior to placebo in increasing percentage of days abstinent and total days abstinent per study week. The results suggest that ondansetron is an effective treatment for patients with early-onset ethanol dependence, presumably by ameliorating an underlying serotonergic abnormality.[26327]

For the treatment of cyclic vomiting syndrome†:
Intravenous dosage:
Children and Adolescents 2 years and older: 0.3 to 0.4 mg/kg/dose IV infusion every 4 to 6 hours as needed.[52129] Infuse over 15 minutes. Max: 16 mg/dose.[31266]
Infants and Children less than 2 years: Safety and efficacy have not been established. A diagnosis of cyclic vomiting syndrome is difficult in this age range.[52129]

Maximum Dosage Limits
•Adults
24 mg/day PO; 0.45 mg/kg/day IV (in 3 divided doses, max single dose = 16 mg IV).
•Geriatric
24 mg/day PO; 0.45 mg/kg/day IV (in 3 divided doses, max single dose = 16 mg IV).
•Adolescents
0.15 mg/kg/dose IV (Max: 16 mg/dose IV). 16 mg/day PO.
•Children
< 4 years: 0.15 mg/kg/dose IV (Max: 16 mg/dose). Safety and efficacy have not been established for PO formulation.
4—11 years: 0.15 mg/kg/dose IV (Max: 16 mg/dose). 12 mg/day PO.
>= 12 years: 0.15 mg/kg/dose IV (Max: 16 mg/dose). 16 mg/day PO.
•Infants
1—5 months: 0.1 mg/kg IV (single dose). Safety and efficacy have not been established for PO formulation.
>= 6 months: 0.15 mg/kg/dose IV (Max: 16 mg/dose IV). Safety and efficacy have not been established for PO formulation.
•Neonates
Safety and efficacy have not been established.

Patients with Hepatic Impairment Dosing
Per the manufacturer, ondansetron dosage should not exceed 8 mg/day IV or PO in adult patients with severe hepatic impairment (Child-Pugh score >= 10). In such patients, plasma clearance is reduced, resulting in a dramatically prolonged elimination half-life.[31266] No specific pediatric recommendations are available.

Patients with Renal Impairment Dosing
No dosage adjustments are recommended. A small percentage (5%) of ondansetron is renally cleared. In patients with severe renal impairment (CrCl < 30 ml/min) the mean plasma clearance is reduced; however, the reduction is not consistent with an increase in half-life.[31266]

†Off-label indication

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Administration Information

General Administration Information
For storage information, see the specific product information within the How Supplied section.

Route-Specific Administration

Oral Administration

- All oral dosage forms are considered interchangeable.

- All oral dosage forms may be administered without regard to meals.
- Antacids do not interfere with ondansetron absorption.[49444]

Oral Solid Formulations

Oral disintegrating tablets (ODT):

- DO NOT attempt to push ODT tablets through foil backing. With dry hands, peel back the foil of 1 blister and remove the tablet.
- Place tablet on the tongue; it will dissolve in seconds. Once dissolved, the patient may swallow with saliva. Administration with liquid is not necessary.
- Wash hands after administration.[49444]

Oral Liquid Formulations

- *Oral solution:* Measure dose with a calibrated oral syringe or other calibrated container.

Other Oral Formulations

Oral soluble film (Zuplenz):

- With dry hands, fold the pouch along the dotted line to expose the tear notch. While still folded, tear the pouch carefully along the edge and remove the oral soluble film just prior to dosing.
- Place the film on the tongue; it will dissolve in 4—20 seconds. Once dissolved, the patient may swallow with saliva. Administration with liquid is not necessary.
- When administering oral soluble films successively to reach a desired dose (i.e., 16 mg given as two 8 mg films) allow each film to dissolve completely before administering the next one.[41272]

Injectable Administration

- Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.

Intravenous Administration

Intravenous injection:

- Doses up to 4 mg may be administered undiluted (2 mg/ml).
- Inject IV over at least 30 seconds, and preferably over a period of 2—5 minutes.[31266]

Intermittent IV infusion:

- For chemotherapy-induced nausea and vomiting (CINV), dilute to a maximum concentration of 1 mg/ml in D_5W or NaCl 0.9%. Dilution is stable for 48 hours at room temperature.[31266] [52214]
- Infuse IV over 15 minutes.[31266]

Intramuscular Administration

- In adults, a 4 mg undiluted dose may be administered intramuscularly as a single injection.
- Use aseptic technique. Inject deeply into a well-developed muscle mass. Aspirate prior to injection to avoid injection into a blood vessel.[31266]

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Contraindications / Precautions

Absolute contraindications are italicized

- *ondansetron hypersensitivity*
- alcoholism
- bradycardia
- breast-feeding
- cardiac arrhythmias
- cardiac disease
- children
- coronary artery disease
- diabetes mellitus
- dolasetron hypersensitivity
- females
- geriatric
- GI obstruction
- granisetron hypersensitivity
- heart failure
- hepatic disease
- hepatitis
- hypertension
- hypocalcemia
- hypokalemia
- hypomagnesemia
- ileus
- infants
- long QT syndrome
- malnutrition
- myocardial infarction
- neonates
- palonosetron hypersensitivity
- phenylketonuria
- pregnancy
- QT prolongation
- thyroid disease

The fixed dose of ondansetron recommended for post-operative nausea and vomiting was established in patients weighing less than 80 kg. Patients with obesity (i.e., weight > 80 kg) have not been studied extensively.

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, reduced clearance, and subsequent toxicity.[31266]

Ondansetron should not be used in patients with a known *ondansetron hypersensitivity*. Use with caution in patients with known granisetron hypersensitivity, palonosetron hypersensitivity, dolasetron hypersensitivity, or sensitivity to related drugs.[31266] Cross-sensitivity is possible between these agents; there have been several reports of anaphylactic/anaphylactoid reactions associated with the use of drugs in this class.[23534] [52212] Antagonism at serotonin (5-HT) receptors, and the subsequent increased concentrations of serotonin, may increase the risk of developing bronchospasm and/or vasoconstriction.[52208] [52210] [52211]

Patients with phenylketonuria should be informed that ondansetron orally disintegrating tablets (ODT) contain phenylalanine (a component of aspartame). Each 4 mg and 8 mg ODT contains < 0.03 mg phenylalanine.[31266]

The use of ondansetron may mask the symptoms of adynamic ileus, GI obstruction, or gastric distention after abdominal surgery or during use to prevent chemotherapy-induced nausea and vomiting.[31266] Ondansetron is not a drug that stimulates gastric or intestinal peristalsis; it should not be used instead of nasogastric suction.[41272]

Ondansetron increases the risk of developing QT prolongation in a dose-dependent manner, which can lead to abnormal and potentially fatal heart rhythms, including torsade de pointes. Avoid ondansetron in patients with congenital long QT syndrome. Other patients at risk for developing torsade de pointes include those with underlying heart conditions, such as those who are predisposed to electrolyte imbalance and those taking other medications that lead to QT prolongation.[31266] Use ondansetron with caution in patients with cardiac disease or other conditions that may increase the risk of QT prolongation including cardiac arrhythmias, heart failure, bradycardia, myocardial infarction, hypertension, coronary artery disease, hypomagnesemia, hypokalemia, hypocalcemia, or in patients receiving medications known to cause electrolyte imbalances. Females, elderly patients, patients with diabetes mellitus, thyroid disease, malnutrition, alcoholism, or hepatic impairment may also be at increased risk for QT prolongation.[28432] [28457] [56959] [56961] [56592] [56963] In June 2012, the FDA announced preliminary results from a study suggesting that intravenous (IV) ondansetron given as a single 32 mg dose causes QT prolongation. Single IV doses should not exceed 16 mg; the 32 mg IV single-dose regimen is no longer indicated for chemotherapy-induced nausea and vomiting prophylaxis. Oral dosing recommendations have not changed and the use of single oral doses up to 24 mg may be used for the prevention of chemotherapy-induced nausea and vomiting (CINV).[51100] Electrocardiogram (ECG) monitoring is recommended in patients with hypokalemia, hypomagnesemia, congestive heart failure, significant bradycardia, or in patients taking other medications that can lead to QT prolongation.[31266]

Little information is available about dosage in children 4 years of age or younger. Furthermore, there is no experience with the use of 24 mg ondansetron tablets in pediatric patients.[31266] [49444]

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 infants 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.[31266]

Ondansetron is classified as FDA Pregnancy Risk Category B. According to the manufacturer, it should be used during pregnancy only when clearly needed.[31266] [40241] [41272] Available data assessing the safety of ondansetron use during pregnancy are conflicting but suggest that there may be an increased risk of certain birth defects, particularly when ondansetron is used during the first trimester. Until additional data are available, the most prudent course would be to reserve ondansetron use for cases in which safer alternatives have failed, and, if possible, avoid use during the period of organogenesis. Some studies have not shown a statistically significant increase in the risk of birth defects with the use of ondansetron [46607] [59645] [59647]; however, others have shown a possible increased risk of cleft palate and cardiovascular malformations.[59650] [59651] Ondansetron has been shown to cross the placenta in early pregnancy with a median fetal to maternal ratio of 0.41.[46606] The American College of Obstetricians and Gynecologists (ACOG) includes ondansetron as a treatment option for nausea and vomiting of pregnancy in patients who are dehydrated, require IV fluid replacement, and have failed other therapies.[29793] Since the publication of the ACOG guidelines, the off-label use of ondansetron in pregnant women has increased and several additional studies have been published evaluating the risk of birth defects when ondansetron is used during pregnancy. A cohort study that included patients from 2 medical registries in Sweden identified 1349 neonates born to mothers who were prescribed ondansetron during the first trimester. The risk of cardiovascular defects, and specifically septal defects, was statistically significantly higher in those neonates whose mothers were prescribed ondansetron (OR for cardiovascular defects 1.62, 95% CI 1.04—2.14; RR for septal defects 2.05, 95% CI 1.19-3.28). A limitation of this study, however, is that the actual ondansetron exposure is unknown because data were obtained from a combination of midwife interviews and prescription records. In addition, the authors state that the relatively wide confidence intervals may represent random variations of common risk.[59650] A case-control study using data from the National Birth Defects Prevention Study examined whether treatments of nausea and vomiting during pregnancy were associated with the most common non-cardiac birth defects (cleft lip, cleft palate, neural tube defects, and hypospadias). Ondansetron treatment during the first trimester was associated with a statistically significant increased risk of cleft palate (adjusted OR 2.37, 95% CI 1.18—4.76); however, the number of patients who received ondansetron was very small (n = 7). The authors state that due to the multiple comparisons performed in this study, the possibility exists that the findings are due to chance and warrant further research. [59651] A historical cohort study using data from medical registries in Denmark compared outcomes of neonates exposed to ondansetron to those not exposed (1:4 ratio; ondansetron exposed = 1849, not exposed = 7396). The study did not find a statistically significant increased risk of major birth defects, spontaneous abortion, stillbirth, preterm delivery, low-birth weight, or small for gestational age. However, the median time of exposure to ondansetron was 10 weeks gestation, indicating half of the patients were exposed at the end of or after the first trimester, and the study was not adequately powered to determine the risk of individual birth defects. [59647] Despite the relatively frequent use of ondansetron for the treatment of nausea and vomiting of pregnancy, the need for additional safety data remains.

It is not known whether ondansetron is excreted in human milk. However, because of its low molecular weight, transfer into breast milk should be expected.[31726] Caution should be exercised when administering ondansetron to a breast-feeding woman.

Of the total number of patients enrolled in US and foreign-controlled clinical trials for postoperative and chemotherapy-induced nausea and vomiting, for which there were subgroup analyses, 938 were 65 years of age or older. No differences in responses for safety or efficacy have been observed between geriatric and younger patients during clinical trials or other reported clinical experience. However, greater sensitivity of some older individuals can not be ruled out. The manufacturer states that no dosage adjustments are needed in elderly patients.[31266]

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Pregnancy / Breast-feeding

Ondansetron is classified as FDA Pregnancy Risk Category B. According to the manufacturer, it should be used during pregnancy only when clearly needed.[31266] [40241] [41272] Available data assessing the safety of ondansetron use during pregnancy are conflicting but suggest that there may be an increased risk of certain birth defects, particularly when ondansetron is used during the first trimester. Until additional data are available, the most prudent course would be to reserve

ondansetron use for cases in which safer alternatives have failed, and, if possible, avoid use during the period of organogenesis. Some studies have not shown a statistically significant increase in the risk of birth defects with the use of ondansetron [46607] [59645] [59647]; however, others have shown a possible increased risk of cleft palate and cardiovascular malformations.[59650] [59651] Ondansetron has been shown to cross the placenta in early pregnancy with a median fetal to maternal ratio of 0.41.[46606] The American College of Obstetricians and Gynecologists (ACOG) includes ondansetron as a treatment option for nausea and vomiting of pregnancy in patients who are dehydrated, require IV fluid replacement, and have failed other therapies.[29793] Since the publication of the ACOG guidelines, the off-label use of ondansetron in pregnant women has increased and several additional studies have been published evaluating the risk of birth defects when ondansetron is used during pregnancy. A cohort study that included patients from 2 medical registries in Sweden identified 1349 neonates born to mothers who were prescribed ondansetron during the first trimester. The risk of cardiovascular defects, and specifically septal defects, was statistically significantly higher in those neonates whose mothers were prescribed ondansetron (OR for cardiovascular defects 1.62, 95% CI 1.04—2.14; RR for septal defects 2.05, 95% CI 1.19-3.28). A limitation of this study, however, is that the actual ondansetron exposure is unknown because data were obtained from a combination of midwife interviews and prescription records. In addition, the authors state that the relatively wide confidence intervals may represent random variations of common risk.[59650] A case-control study using data from the National Birth Defects Prevention Study examined whether treatments of nausea and vomiting during pregnancy were associated with the most common non-cardiac birth defects (cleft lip, cleft palate, neural tube defects, and hypospadias). Ondansetron treatment during the first trimester was associated with a statistically significant increased risk of cleft palate (adjusted OR 2.37, 95% CI 1.18—4.76); however, the number of patients who received ondansetron was very small (n = 7). The authors state that due to the multiple comparisons performed in this study, the possibility exists that the findings are due to chance and warrant further research. [59651] A historical cohort study using data from medical registries in Denmark compared outcomes of neonates exposed to ondansetron to those not exposed (1:4 ratio; ondansetron exposed = 1849, not exposed = 7396). The study did not find a statistically significant increased risk of major birth defects, spontaneous abortion, stillbirth, preterm delivery, low-birth weight, or small for gestational age. However, the median time of exposure to ondansetron was 10 weeks gestation, indicating half of the patients were exposed at the end of or after the first trimester, and the study was not adequately powered to determine the risk of individual birth defects. [59647] Despite the relatively frequent use of ondansetron for the treatment of nausea and vomiting of pregnancy, the need for additional safety data remains.

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Interactions

Level 1 - Severe

- Apomorphine
- Astemizole
- Bepridil
- Bretylium
- Cisapride
- Dofetilide
- Dronedarone
- Grepafloxacin
- Halofantrine
- Levomethadyl
- Mesoridazine
- Pimozide
- Posaconazole
- Probucol
- Quinidine
- Sparfloxacin
- Terfenadine
- Thioridazine
- Voriconazole
- Ziprasidone

Level 2 - Major

- Abarelix
- Acetaminophen; Tramadol
- Alfuzosin
- Amiodarone
- Anagrelide
- Aripiprazole
- Arsenic Trioxide
- Artemether; Lumefantrine
- Asenapine
- Atomoxetine
- Azithromycin
- Bedaquiline
- Beta-agonists
- Chloroquine
- Chlorpromazine
- Ciprofloxacin
- Citalopram
- Clarithromycin
- Clozapine
- Conivaptan
- Crizotinib
- Cyclobenzaprine
- Dasabuvir; Ombitasvir; Paritaprevir; Ritonavir
- Dasatinib
- Daunorubicin
- Degarelix
- Desvenlafaxine
- Dextromethorphan; Quinidine
- Linezolid
- Lithium
- Lopinavir; Ritonavir
- Maprotiline
- Mefloquine
- Methadone
- Methylene Blue
- Mifepristone, RU-486
- Milnacipran
- Mirtazapine
- Moxifloxacin
- Nilotinib
- Norfloxacin
- Octreotide
- Ofloxacin
- Olanzapine
- Ombitasvir; Paritaprevir; Ritonavir
- Paliperidone
- Panobinostat
- Paroxetine
- Pasireotide
- Pazopanib
- Pentamidine
- Perflutren Lipid Microspheres
- Phenelzine
- Primaquine
- Procainamide
- Propafenone

- Disopyramide
- Dolasetron
- Donepezil
- Donepezil; Memantine
- Doxorubicin
- Droperidol
- Duloxetine
- Epirubicin
- Eribulin
- Erythromycin
- Escitalopram
- Ezogabine
- Fentanyl
- Fingolimod
- Flecainide
- Fluconazole
- Fluoxetine
- Fluoxetine; Olanzapine
- Fluvoxamine
- Gemifloxacin
- Granisetron
- Halogenated anesthetics
- Haloperidol
- Ibutilide
- Idarubicin
- Iloperidone
- Isocarboxazid
- Lapatinib
- Lenvatinib
- Levofloxacin
- Levomilnacipran
- Quetiapine
- Ranolazine
- Rasagiline
- Regadenoson
- Rilpivirine
- Risperidone
- Ritonavir
- Romidepsin
- Saquinavir
- Selegiline
- Selegiline, Transdermal
- Sertraline
- Solifenacin
- Sorafenib
- Sotalol
- Sunitinib
- Tacrolimus
- Telavancin
- Telithromycin
- Tetrabenazine
- Tolterodine
- Toremifene
- Tranylcypromine
- Trazodone
- Vandetanib
- Vardenafil
- Vemurafenib
- Venlafaxine
- Vilazodone
- Vorinostat

Level 3 - Moderate

- Atazanavir
- Atazanavir; Cobicistat
- Barbiturates
- Bosentan
- Carbamazepine
- Cobicistat
- Cobicistat; Elvitegravir; Emtricitabine; Tenofovir
- Cobicistat; Elvitegravir; Emtricitabine; Tenofovir Alafenamide
- Daclatasvir
- Darunavir
- Darunavir; Cobicistat
- Echinacea
- Etravirine
- Fosphenytoin
- Loop diuretics
- Mirabegron
- Phenytoin
- Rifampin
- St. John's Wort, Hypericum perforatum
- Thiazide diuretics
- Tramadol

Level 4 - Minor

- Cisplatin
- Cyclophosphamide
- Fluphenazine
- Ivacaftor
- Perphenazine
- Prochlorperazine
- Rifabutin
- Rifapentine
- Tricyclic antidepressants
- Trifluoperazine

NOTE: *In vitro* metabolism studies have shown that ondansetron is a substrate for human hepatic CYP450 drug-metabolizing enzymes (i.e., CYP1A2, CYP2D6, and CYP3A4), with CYP3A4 metabolism predominating.[7619] Because of the multiplicity of metabolic enzymes capable of metabolizing ondansetron, it is likely that inhibition or loss of one enzyme (e.g., CYP2D6 genetic deficiency) will be compensated by others and may result in little change in overall rates of ondansetron elimination.[7619] Interactions with inhibitors or inducers of these enzymes have not been reported clinically; however, the potential exists for these interactions to change the clearance and, hence, the half-life of ondansetron. On the basis of limited available data, no dosage adjustment is recommended for patients receiving CYP-interacting drugs. Ondansetron is also a substrate of P-glycoprotein.[7619] [11512]

Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP).[31266] Among 42 patients receiving a 4 mg bolus dose of intravenous ondansetron for the treatment of postoperative nausea and vomiting, the mean maximal QTc interval prolongation was 20 +/- 13 msec at the third minute after antiemetic administration ($p < 0.0001$).[9564] Because of the potential for TdP, use of the following drugs with ondansetron is contraindicated: astemizole [28400], bepridil [4953], bretylium [6159], cisapride [47221], dofetilide [28221], grepafloxacin [29117], halofantrine [4968], levomethadyl [5079], mesoridazine [29096], pimozide [43463], probucol [5145], sparfloxacin [28232], terfenadine [141] [231], thioridazine [43069], and ziprasidone [28233].

Concomitant use of dronedarone and ondansetron is contraindicated. Dronedarone is an inhibitor of CYP2D6, CYP3A, and P-gp. Ondansetron is a substrate for CYP2D6, CYP3A4, and P-gp. Coadministration of dronedarone and ondansetron may result in elevated plasma concentrations of ondansetron. In addition, ondansetron has been established to have a possible risk of QT prolongation and torsade de pointes (TdP).[31266] Dronedarone is associated with dose-related increases in the QTc interval.

[36101] Although there are no studies examining the effects of dronedarone in patients receiving other QT prolonging drugs, coadministration of such drugs may result in additive QT prolongation; concomitant use is contraindicated.[36101]

Concomitant administration of posaconazole and drugs that both prolong the QT interval and are CYP3A4 substrates is contraindicated according to the FDA-approved product labeling.[31266] [32723] The exact risk for QT prolongation when posaconazole and ondansetron are administered together has not been clearly defined. If ondansetron and posaconazole are administered together, extreme caution and careful monitoring is advised, especially if higher doses are used or if other drugs that may affect CYP1A2 or CYP2D6 are also given.[31266] [57433] Posaconazole is a strong CYP3A4 inhibitor.[32723] Ondansetron is metabolized by CYP3A, CYP1A2, and CYP2D6. *In vivo* microsomal inhibition data has suggested that no single isoenzyme dominates ondansetron's metabolism thereby making clinically significant interactions due to inhibition of a single isoenzyme unlikely [57434]; however, since the publication of this data, ondansetron has been found to produce concentration-dependent QT prolongation.[31266] It is not clear what degree of enzyme inhibition or increased concentration is required to increase the risk of QT prolongation.

Concomitant administration of fluconazole and drugs that both prolong the QT interval and are CYP3A4 substrates is contraindicated according to the FDA-approved product labeling.[28674] [31266] The exact risk for QT prolongation when fluconazole and ondansetron are administered together has not been clearly defined. If ondansetron and fluconazole are administered together, extreme caution and careful monitoring is advised, especially if higher doses are used or if other drugs that may affect CYP1A2 or CYP2D6 are also given.[29036] [31266] [57433] Fluconazole is a CYP3A4 inhibitor.[34447] Ondansetron is metabolized by CYP3A, CYP1A2, and CYP2D6. *In vivo* microsomal inhibition data has suggested that no single isoenzyme dominates ondansetron's metabolism thereby making clinically significant interactions due to inhibition of a single isoenzyme unlikely [57434]; however, since the publication of this data, ondansetron has been found to produce concentration-dependent QT prolongation.[31266] It is not clear what degree of enzyme inhibition or increased concentration is required to increase the risk of QT prolongation. Inhibition of CYP3A isoenzymes is likely to increase with higher fluconazole doses (>= 200 mg/day in adults).[29036] [31266] [57433]

Both quinidine and dextromethorphan; quinidine are contraindicated in patients receiving drugs that both prolong the QT interval and are metabolized by CYP2D6, such as ondansetron. Quinidine inhibits CYP2D6 and has QT-prolonging actions; therefore, the effects on the QT interval may be increased during concurrent use of these agents.[42280] [47357] [31266]

Subcutaneous apomorphine administration is associated with a high risk of nausea and vomiting; however, certain antiemetic therapies should not be used to circumvent this effect.[28661] The concurrent use of apomorphine and serotonin-receptor antagonists, such as ondansetron, is contraindicated due to the possibility of an excessive lowering of blood pressure and unconsciousness.[5392] Additionally, ondansetron may also lengthen the QT interval.[31266] Limited data indicate that QT prolongation is possible with apomorphine administration; the change in QTc interval is not significant in most patients receiving dosages within the manufacturer's guidelines. Alternative anti-emetics, such as trimethobenzamide, are recommended for prophylaxis of apomorphine-induced nausea and vomiting.[5387]

Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP).[31266] Among 42 patients receiving a 4 mg bolus dose of intravenous ondansetron for the treatment of postoperative nausea and vomiting, the mean maximal QTc interval prolongation was 20 +/- 13 msec at the third minute after antiemetic administration ($p < 0.0001$).[9564] Risk for QT prolongation increases with increased dosage, and a 32 mg IV dose must no longer be used for prevention of chemotherapy induced emesis.[31266] If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended.[31266] Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with ondansetron include: abarelix [28406], alfuzosin [28261], amiodarone [28224], aripiprazole [42845], arsenic trioxide [28226] [28432] [28457], artemether; lumefantrine [35401], asenapine [36343], atomoxetine [28405] [59321], azithromycin [28855] [43974], bedaquiline [52746], beta-agonists [28318] [33925] [41231], chloroquine [28229] [28230] [28231], chlorpromazine [28415] [24817] [43065], ofloxacin [30738], clarithromycin [28238], clozapine [28262], crizotinib [45458], cyclobenzaprine [28425], dasatinib [32387], degarelix [35023], disopyramide [28228], dolasetron [42844], donepezil [59321] [59322], donepezil; memantine [59321] [59322], droperidol [28235] [28236] [28737] [51289], eribulin [42449], erythromycin [43258], ezogabine [44800], fingolimod [41823], flecainide [42297], fluphenazine [28415], gemifloxacin [28424], halogenated anesthetics [28457] [28458] [28754] [28755] [28756], haloperidol [28307], ibutilide [41830], iloperidone [36146], lapatinib [33192], levofloxacin [28421], ritonavir [28315], lopinavir; ritonavir [28341], maprotiline [28759], mefloquine [28301], methadone [28319] [28320] [28321] [28322] [33136], mifepristone, RU-486 [48697], moxifloxacin [28423], norfloxacin [29818], octreotide [15238], olanzapine [28785], paliperidone [40936], pasireotide [52611], pazopanib [37098], systemic pentamidine [23620] [23778] [28419] [28879], perflutren lipid microspheres [46931], perphenazine [28415], primaquine [41984], procainamide [28250], prochlorperazine [28415], propafenone [28287], quetiapine [29118] [33068] [33072] [33074], ranolazine [31938], regadenoson [33906], rilpivirine [44376], risperidone [28414], romidepsin [37292], solifenacin [30515], sorafenib [31832], sotalol [28234], sunitinib [31970], tacrolimus [28611], telavancin [36615], telithromycin [28156], tetrabenazine [11246], tolterodine [31112], toremifene [28822], trazodone [38831], tricyclic antidepressants [28225], trifluoperazine [28415], vandetanib [43901], vardenafil [28261], vemurafenib [45335], voriconazole [28158], and vorinostat [32789]

Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP).[31266] Among 42 patients receiving a 4 mg bolus dose of intravenous ondansetron for the treatment of postoperative nausea and vomiting, the mean maximal QTc interval prolongation was 20 +/- 13 msec at the third minute after antiemetic administration ($p < 0.0001$).[9564] Ondansetron should be used cautiously with anthracyclines such as daunorubicin, doxorubicin, epirubicin, and idarubicin due to the potential risks for anthracycline cardiac toxicity.[5037] Acute cardiotoxicity can occur during administration of daunorubicin or doxorubicin; cumulative, dose-dependent cardiomyopathy may also occur. Acute ECG changes during anthracycline therapy are usually transient and include ST-T wave changes, QT prolongation, and changes in QRS voltage. Sinus tachycardia is the most common arrhythmia, but other arrhythmias such as supraventricular tachycardia (SVT), ventricular tachycardia, heart block, and premature ventricular contractions (PVCs) have been reported during anthracycline therapy.[2022] If ondansetron must be coadministered with daunorubicin or doxorubicin, ECG monitoring is recommended.[31266]

Ondansetron may interact with cyclophosphamide. In one cohort study of breast cancer patients receiving high-dose cyclophosphamide along with other chemotherapy agents, the patients who received a continuous infusion of ondansetron were noted to have lower median cyclophosphamide AUC's (roughly 17% lower) versus a group of historically matched placebo controls.[2146] A similar interaction between ondansetron and cyclophosphamide, resulting in a 15% decrease in cyclophosphamide AUC, has been reported in another study.[3179] It is unknown if patients receiving ondansetron continuous infusions would experience lowered tumor responses to cyclophosphamide treatment.[2146]

Ondansetron may interact with cisplatin. In one cohort study, the median cisplatin AUC's were reported to be roughly 10% higher in those receiving ondansetron versus historically matched placebo controls.[2146] Another study noted the exact opposite effect, a 19% decrease in cisplatin AUC occurred when ondansetron was given concurrently with cisplatin.[3179] The mechanism and the clinical implications of such interactions have not been evaluated. In humans, cisplatin does not affect the pharmacokinetics of ondansetron.[7619]

In humans, carmustine, etoposide, and cisplatin do not affect the pharmacokinetics of ondansetron.[7619]

Ondansetron elimination may be affected by cytochrome P-450 inducers.[7619] In a pharmacokinetic study of 16 patients with epilepsy who were maintained

chronically on CYP3A4 inducers (e.g., barbiturates), carbamazepine, phenytoin (or fosphenytoin), a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance.[7620] However, on the basis of available data, no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.[7619]

Ondansetron elimination may be affected by cytochrome P-450 inducers.[7619] In a small study of healthy volunteers [2704], pretreatment with rifampin decreased the AUC and mean half-life of IV and oral ondansetron. Compared to placebo, concurrent rifampin administration decreased the AUC of oral ondansetron 65% and the half-life by 49% to about 2.8 hours. Similar effects were noted for IV ondansetron following rifampin administration. In addition, the oral bioavailability of ondansetron was reduced.[2704] However, on the basis of available data, no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.[7619]

Ondansetron elimination may be affected by cytochrome P-450 inducers, such as rifabutin.[7619] [4718] However, on the basis of available data, no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.[7619]

Ondansetron elimination may be affected by cytochrome P-450 inducers, such as rifapentine.[7619] [5213] However, on the basis of available data, no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.[7619]

Ondansetron elimination may be affected by cytochrome P-450 inducers, such as bosentan.[7619] [4718] However, on the basis of available data, no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.[7619]

Ondansetron elimination may be affected by cytochrome P-450 inducers, such as St. John's wort, Hypericum perforatum.[7619] [4718] However, on the basis of available data, no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.[7619]

Based on limited study, ondansetron does not appear to interact with nondepolarizing neuromuscular blockers.[7619] Ondansetron does not alter the respiratory depressant effects produced by alfentanil or the degree of neuromuscular blockade produced by atracurium. Interactions during general or local anesthesia have not been studied.[7619]

In a crossover study in 76 pediatric patients, intravenous ondansetron did not increase blood concentrations of high-dose methotrexate.[7619]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as tramadol. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266] Although no pharmacokinetic drug interaction between ondansetron and tramadol has been observed, data from a few small studies indicate that ondansetron may reduce the analgesic effects of tramadol.[7619] [7621] Because adverse effects may occur when tramadol is administered in excessive dosage as patients try to obtain pain relief, clinicians should be alert to increases in the patient reported frequency of tramadol administration during concurrent use.

Ondansetron is metabolized by both CYP1A2 and CYP3A4. *In vivo* data indicate that echinacea may inhibit CYP1A2, induce hepatic CYP3A4, and inhibit intestinal CYP3A4. The efficacy and safety of ondansetron if used in combination with echinacea are unknown. Close monitoring of patients for changes in efficacy or toxicity may be prudent if ondansetron is used in combination with echinacea until more data are available.[7566] [8894]

Anagrelide has been shown to inhibit CYP1A2. In theory, coadministration of anagrelide with substrates of CYP1A2, including ondansetron, could lead to increases in the serum concentrations of these drugs and, thus, adverse effects. Patients receiving anagrelide and ondansetron concomitantly should be monitored for increased toxicity of ondansetron.[6912]

Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). [31266] Among 42 patients receiving a 4 mg bolus dose of intravenous ondansetron for the treatment of postoperative nausea and vomiting, the mean maximal QTc interval prolongation was 20 +/- 13 msec at the third minute after antiemetic administration ($p < 0.0001$).[9564] Ondansetron should be administered with caution in patients taking drugs with potential to induce QT prolongation. Rare cases of TdP have been reported with ciprofloxacin during post-marketing surveillance.[28225] [5149] [43411] [5507] [6579] Although less likely than with most quinolones, coadministration of ciprofloxacin with drugs known to prolong the QT interval could increase the risk of developing TdP in predisposed patients. Additionally ciprofloxacin inhibits the CYP1A2 isoenzyme, while ondansetron is metabolized by hepatic CYP450 drug-metabolizing enzymes (i.e., CYP3A4, CYP2D6, CYP1A2).[5496] [5839] [7619] In theory, ciprofloxacin may change the clearance and, hence, the half-life of ondansetron.

Coadministration of nilotinib and a drug that prolongs the QT interval is not advised; nilotinib prolongs the QT interval. Ondansetron is associated with a possible risk for QT prolongation and torsade de pointes (TdP).[31266] Also, nilotinib is an inhibitor of the efflux transporter P-glycoprotein (P-gp, ABCB1) and of cytochrome P450 (CYP) isoenzymes 2D6 and 3A4,[10409] and ondansetron is a P-glycoprotein, CYP3A4, and CYP2D6 substrate.[4718] Increased concentrations of ondansetron are likely if it is coadministered with nilotinib; exercise caution.[10409] If concurrent administration of nilotinib and ondansetron is unavoidable, the manufacturer of nilotinib recommends interruption of nilotinib treatment. If nilotinib must be continued, closely monitor the patient for QT interval prolongation.[10409]

Etravirine is a CYP3A4 inducer/substrate and a P-glycoprotein (PGP) inhibitor and ondansetron is a CYP3A4 and PGP substrate.[7619] [11512] [33718] Caution is warranted if these drugs are coadministered.

The concurrent use of saquinavir boosted with ritonavir and ondansetron should be avoided if possible due to the risk of life threatening arrhythmias such as torsades de pointes (TdP).[28995] Saquinavir boosted with ritonavir is a potent inhibitor of CYP3A4, an isoenzyme responsible for the metabolism of ondansetron.[7619] [11512] [11416] [11417] [28995] Further, both saquinavir and ondansetron are substrates of P-glycoprotein, which when administered together may increase the absorption or decrease the clearance of the other drug. This complex interaction may ultimately result in altered plasma concentrations of both ondansetron and saquinavir.[7619] [11512] [11416] [11417] [28995] Additionally, saquinavir boosted with ritonavir causes dose-dependent QT and PR prolongation; if possible, avoid use with other drugs that may prolong the QT or PR interval, such as ondansetron.[31266] [39156] If no alternative therapy is acceptable, perform a baseline ECG prior to initiation of concomitant therapy and follow recommended ECG monitoring.[28995]

The coadministration of ondansetron with diuretics associated with hypokalemia could increase the risk of QT prolongation.[5037] Patients taking certain diuretics may develop an electrolyte abnormality that may lead to cardiac dysrhythmias and/or QT prolongation. Hypokalemia or hypomagnesemia may occur with administration of potassium-depleting drugs such as loop diuretics and thiazide diuretics, increasing the potential for cardiac arrhythmias. Potassium levels should be within the normal range prior to and during therapy with ondansetron.

Because of the potential risk and severity of serotonin syndrome or QT prolongation, use caution and monitor closely when administering ondansetron with other drugs that have serotonergic properties or may prolong the QT interval, such as citalopram.[28269] [31266] If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. In addition, ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). Risk for QT prolongation increases with increased dosage. If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended.[31266]

Because of the potential risk and severity of serotonin syndrome or QT prolongation, use caution and monitor closely when administering ondansetron with other drugs that have serotonergic properties or may prolong the QT interval, such as escitalopram.[28270] [31266] If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. In addition, ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). Risk for QT prolongation increases with increased dosage. If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended.[31266]

Because of the potential risk and severity of serotonin syndrome or QT prolongation, use caution and monitor closely when administering ondansetron with other drugs that have serotonergic properties or may prolong the QT interval, such as venlafaxine.[31266] [33715] If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. In addition, ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). Risk for QT prolongation increases with increased dosage. If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as desvenlafaxine. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as duloxetine. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as fentanyl. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because QT prolongation and torsade de pointes (TdP) have been reported in patients treated with fluoxetine, the manufacturer of fluoxetine recommends caution during use with other drugs that prolong the QT interval. Ondansetron is associated with a possible risk of QT prolongation and TdP. In addition, because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as fluoxetine. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266] [32127]

Because QT prolongation and torsade de pointes (TdP) have been reported in patients treated with fluoxetine and olanzapine, the manufacturer of fluoxetine; olanzapine recommends caution during use with other drugs that prolong the QT interval. Ondansetron is associated with a possible risk of QT prolongation and TdP. In addition, because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as fluoxetine; olanzapine. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266] [43077]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as fluvoxamine. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as isocarboxazid. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as milnacipran. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as levomilnacipran. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such

as linezolid. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[28599] [31266]

Ondansetron and lithium are associated with QT prolongation.[31266] [59809] [59810] [59811] Coadministration may increase the risk of QT prolongation; therefore, ondansetron and lithium should be coadministered with caution and close monitoring. Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as lithium. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as methylene blue. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as mirtazapine. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as paroxetine. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as phenelzine. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as rasagiline. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as selegiline. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as selegiline, transdermal. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as sertraline. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as acetaminophen; tramadol. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as tranylcypromine. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Granisetron has been associated with QT prolongation. According to the manufacturer, use of granisetron in patients concurrently treated with drugs known to prolong the QT interval and/or are arrhythmogenic, may result in clinical consequences.[31723] Drugs with a possible risk for QT prolongation and torsade de pointes (TdP) that should be used cautiously and with close monitoring with granisetron include ondansetron [31266]. The two drugs are from the same therapeutic class, and would not be expected to be prescribed together. Serotonergic actions of the two drugs might also increase the risk for additive serotonergic side effects.

Because of the potential risk and severity of serotonin syndrome, use caution when administering ondansetron with other drugs that have serotonergic properties such as vilazodone. If serotonin syndrome is suspected, discontinue ondansetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.[31266]

Drugs with a possible risk for QT prolongation and torsades de pointes (TdP) such as ondansetron should be used cautiously and with close monitoring with lenvatinib. QT prolongation was reported in patients with radioactive iodine-refractory differentiated thyroid cancer (RAI-refractory DTC) in a double-blind, randomized, placebo-

controlled clinical trial after receiving lenvatinib daily at the recommended dose; the QT/QTc interval was not prolonged, however, after a single 32 mg dose (1.3 times the recommended daily dose) in healthy subjects.[31266] [58782]

The plasma concentrations of ondansetron may be elevated when administered concurrently with cobicistat. Clinical monitoring for adverse effects, such as GI or CNS effects, is recommended during coadministration. Cobicistat is a CYP3A4, CYP2D6, and p-glycoprotein (P-gp) inhibitor, while ondansetron is a CYP3A4, CYP2D6, and P-gp substrate.[40241] [34653] [58000]

The plasma concentrations of ondansetron may be elevated when administered concurrently with darunavir. Clinical monitoring for adverse effects, such as GI or CNS effects, is recommended during coadministration. Darunavir is an inhibitor of CYP3A4 and CYP2D6. Ondansetron is a CYP3A4 and CYP2D6, and substrate.[40241] [34653] [32432]

The plasma concentrations of ondansetron may be elevated when administered concurrently with darunavir; cobicistat. Clinical monitoring for adverse effects, such as GI or CNS effects, is recommended during coadministration. Darunavir and cobicistat are inhibitors of CYP3A4 and CYP2D6; cobicistat is also a P-glycoprotein (P-gp) inhibitor. Ondansetron is a CYP3A4, CYP2D6, and P-gp substrate.[40241] [34653] [58000] [58763]

The plasma concentrations of ondansetron may be elevated when administered concurrently with atazanavir. Clinical monitoring for adverse effects, such as GI or CNS effects, is recommended during coadministration. Atazanavir is an inhibitor of CYP3A4. Ondansetron is a CYP3A4 substrate.[40241] [34653] [28142]

The plasma concentrations of ondansetron may be elevated when administered concurrently with atazanavir; cobicistat. Clinical monitoring for adverse effects, such as GI or CNS effects, is recommended during coadministration. Atazanavir and cobicistat are inhibitors of CYP3A4, and cobicistat is also an inhibitor of CYP2D6 and P-glycoprotein (P-gp) inhibitor. Ondansetron is a CYP3A4, CYP2D6, and P-gp substrate.[40241] [34653] [58000] [58761]

The plasma concentrations of ondansetron may be elevated when administered concurrently with cobicistat; elvitegravir; emtricitabine; tenofovir disoproxil fumarate. Clinical monitoring for adverse effects, such as GI or CNS effects, is recommended during coadministration. Cobicistat is a CYP3A4, CYP2D6, and P-glycoprotein (P-gp) inhibitor, while ondansetron is a CYP3A4, CYP2D6, and P-gp substrate.[40241] [34653] [51664]

The plasma concentrations of ondansetron may be elevated when administered concurrently with cobicistat; elvitegravir; emtricitabine; tenofovir alafenamide. Clinical monitoring for adverse effects, such as GI or CNS effects, is recommended during coadministration. Ondansetron is a CYP3A4, CYP2D6, and P-glycoprotein (P-gp) substrate. Cobicistat is a CYP3A4, CYP2D6, and P-gp inhibitor, while tenofovir alafenamide is a weak in vitro CYP3A inhibitor.[40241] [34653] [60269]

The co-administration of panobinostat with antiemetic agents such as ondansetron may increase the risk of QT prolongation. If concomitant use cannot be avoided, obtain electrocardiograms frequently and closely monitor patients for signs and symptoms of ondansetron toxicity, including QT prolongation and cardiac arrhythmias. Panobinostat is a CYP2D6 inhibitor and ondansetron is a CYP2D6 substrate. When a single-dose of a CYP2D6-sensitive substrate was administered after 3 doses of panobinostat (20 mg given on days 3, 5, and 8), the CYP2D6 substrate Cmax increased by 20% to 200% and the AUC value increased by 20% to 130% in 14 patients with advanced cancer; exposure was highly variable (coefficient of variance > 150%).[31266] [58821]

Mirabegron is a moderate CYP2D6 inhibitor. Exposure of drugs partially metabolized by CYP2D6, such as ondansetron may be increased when coadministered with mirabegron. Therefore, appropriate monitoring and dose adjustment may be necessary.[31266] [34653] [51111]

Use caution when administering ivacaftor and ondansetron concurrently. Ivacaftor is an inhibitor of CYP3A and P-glycoprotein (Pgp). Coadministration of ivacaftor with CYP3A and Pgp substrates, such as ondansetron, can increase ondansetron exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.[48524] [31266] [34653]

Avoid coadministration of conivaptan, a CYP3A4/P-glycoprotein (P-gp) inhibitor and ondansetron, a CYP3A4/P-gp substrate. Concurrent use may result in elevated ondansetron serum concentrations. According to the manufacturer of conivaptan, concomitant use of conivaptan, a strong CYP3A4 inhibitor, and CYP3A substrates, such as ondansetron, should be avoided. Coadministration of conivaptan with other CYP3A substrates (midazolam, simvastatin, amlodipine) has resulted in increased mean AUC values (2—3 times). Theoretically, similar pharmacokinetic effects could be seen with ondansetron. Treatment with ondansetron may be initiated no sooner than 1 week after completion of conivaptan therapy.[31266] [31764] [34653] [56579]

Systemic exposure of ondansetron, a P-glycoprotein (P-gp) substrate, may be increased when administered concurrently with daclatasvir, a P-gp inhibitor. Taking these drugs together could increase or prolong the therapeutic effects of ondansetron; monitor patients for potential adverse effects.[31266] [34653] [60001]

Concurrent administration of ondansetron with ombitasvir; paritaprevir; ritonavir may result in an increased risk for QT prolongation and increased ondansetron plasma concentrations. While ombitasvir; paritaprevir; ritonavir did not prolong the QTc interval to a clinically relevant extent in healthy subjects, ritonavir has been associated with QT prolongation in other trials. Ondansetron has been associated with dose-dependent QT prolongation and Torsade de Pointes. The manufacturer of ondansetron recommends ECG monitoring if it is coadministered with other drugs that are known to prolong the QT interval. Ondansetron is metabolized by the hepatic isoenzymes CYP3A4, CYP2D6, and CYP1A2; ritonavir inhibits 2 of these enzymes (CYP3A4 and CYP2D6). In addition, ondansetron is a substrate of the drug transporter P-glycoprotein (P-gp), which ritonavir and paritaprevir also inhibit. Caution and close monitoring are advised if these drugs are administered together.[60002] [11512]

Concurrent administration of ondansetron with dasabuvir; ombitasvir; paritaprevir; ritonavir may result in an increased risk for QT prolongation and increased ondansetron plasma concentrations. While dasabuvir; ombitasvir; paritaprevir; ritonavir did not prolong the QTc interval to a clinically relevant extent in healthy subjects, ritonavir has been associated with QT prolongation in other trials. Ondansetron has been associated with dose-dependent QT prolongation and Torsade de Pointes. The manufacturer of ondansetron recommends ECG monitoring if it is coadministered with other drugs that are known to prolong the QT interval. Ondansetron is metabolized by the hepatic isoenzymes CYP3A4, CYP2D6, and CYP1A2; ritonavir inhibits 2 of these enzymes (CYP3A4 and CYP2D6). In addition, ondansetron is a substrate of the drug transporter P-glycoprotein (P-gp), which ritonavir and paritaprevir also inhibit. Caution and close monitoring are advised if these drugs are administered together.[58664] [11512]

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Adverse Reactions

- agitation
- anaphylactoid reactions
- angina
- angioedema
- anxiety
- atrial fibrillation
- AV block
- blurred vision
- bradycardia
- bronchospasm
- cardiac arrest
- chest pain (unspecified)
- chills
- constipation
- diarrhea
- dizziness
- drowsiness
- dyspnea
- dystonic reaction
- elevated hepatic enzymes
- fatigue
- fever
- flushing
- headache
- hepatic failure
- hypokalemia
- hypotension
- injection site reaction
- laryngeal edema
- laryngospasm
- malaise
- palpitations
- paresthesias
- premature ventricular contractions (PVCs)
- pruritus
- QT prolongation
- rash (unspecified)
- respiratory arrest
- seizures
- serotonin syndrome
- sinus tachycardia
- ST-T wave changes
- Stevens-Johnson syndrome
- supraventricular tachycardia (SVT)
- syncope
- torsade de pointes
- toxic epidermal necrolysis
- urinary retention
- urticaria
- ventricular tachycardia
- visual impairment

Diarrhea (2—16%) and constipation (6—11%) were among the most frequently reported adverse events in patients receiving ondansetron during clinical trials for chemotherapy-induced nausea and vomiting (CINV) with moderate-high emetogenic agents.[31266] [49444]

Urinary retention (5%) and gynecological disorder (7%) have been reported in patients receiving oral ondansetron for postoperative nausea and vomiting (PONV) during clinical trials.[49444]

Headache (9—27%) was the most frequently reported adverse event during clinical trials of ondansetron and appeared to be more common in patients receiving the drug for chemotherapy-induced nausea and vomiting (CINV). Preliminary observations in a small number of subjects suggest a higher incidence of headache when ondansetron orally disintegrating tablets are taken with water, when compared to without water. Other neurologic side effects reported include drowsiness (8—20%), malaise and fatigue (9—13%), anxiety or agitation (<= 6%), paresthesias (2%), and dizziness (4—7%). Transient dizziness associated with intravenous infusion has been reported post-marketing. Rarely, extrapyramidal reactions, including oculogyric crisis appearing alone or with other types of dystonic reaction, have been reported with ondansetron use.[31266] [49444] In one case, extrapyramidal reactions were confirmed by rechallenge.[31899] In addition, there have been rare reports of grand mal seizures in patients receiving ondansetron, although a casual relationship has not been established.[31266]

Elevated hepatic enzymes were reported in patients receiving either cisplatin- or cyclophosphamide-based chemotherapy during clinical trials. The elevation did not appear to be related to ondansetron dose or duration of therapy. The enzyme levels exceeded twice the upper limit of normal (ULN) in approximately 5% of chemotherapy patients receiving injection dosing, and 1—2% of patients receiving oral therapy, but the increases were transient in nature and did not cause symptomatic hepatic disease. Repeat exposure showed similar elevations in some instances. In addition, hepatic failure and death have been reported in patients with cancer receiving concomitant medications including potentially hepatotoxic cytotoxic chemotherapy and antibiotics; the etiology of the hepatic failure is unclear.[31266] [49444]

Rare cases of hypokalemia have been reported following treatment with ondansetron in oncology patients; the relationship to ondansetron is unclear.[31266] [49444] It may be prudent to monitor serum electrolytes in select patients, as hypokalemia is a risk factor for electrocardiogram (ECG) changes.[31266] [49444]

Ondansetron has been associated with QT prolongation and torsade de pointes. Patients at risk for developing torsade de pointes include those with underlying heart conditions, such as congenital long QT syndrome (avoid use), those who are predisposed to hypokalemia and hypomagnesemia, and those taking other medications that lead to QT prolongation.[45648] Other cardiovascular adverse events reported during clinical trials with ondansetron include angina, chest pain (unspecified), ECG alterations (including second-degree AV block, QT prolongation, and ST-T wave changes), hypotension (5%), and sinus tachycardia. Bradycardia (6% vs. 6% placebo) was reported in patients receiving oral ondansetron for postoperative nausea and vomiting (PONV). Syncope, palpitations, and arrhythmias, including ventricular tachycardia and supraventricular tachycardia (SVT), bradycardia, premature ventricular contractions (PVCs), and atrial fibrillation have been reported during post-marketing use of intravenous formulations of ondansetron.[31266] [49444] In June 2012, the FDA announced preliminary results from a study suggesting that intravenous (IV) ondansetron given as a single 32 mg dose causes QT prolongation in a dose-dependent manner.[51100] Hence, single IV doses should not exceed 16 mg; the 32 mg IV single dose regimen is no longer indicated for chemotherapy-induced nausea and vomiting (CINV). Oral dosing recommendations have not changed.[51100] ECG monitoring is recommended in patients with electrolyte imbalance (e.g., hypokalemia or hypomagnesemia), congestive heart failure, significant bradycardia, or in patients taking other medications that can lead to QT prolongation.[31266] [49444] Both patients and health care providers should report ondansetron related adverse events to FDA's MedWatch Safety Information and Adverse Event Reporting Program.[45648]

Several reports of anaphylactoid reactions have been associated with serotonin (5-HT_3) receptor antagonists, such as ondansetron.[23534] [52212] Manifestations of anaphylactoid reactions have included angioedema, bronchospasm, dyspnea, hypotension, laryngeal edema, stridor, and/or urticaria. Laryngospasm, shock, cardiac arrest, and respiratory arrest have been reported during allergic reactions in patients receiving injectable ondansetron. Rash (unspecified) (1%), pruritus (2—5%), and flushing have been reported in clinical trials with both oral and injectable formulations.[31266] [49444] Stevens-Johnson syndrome and toxic epidermal necrolysis (TENS) have been reported with post-marketing use of ondansetron.[31266] [49444]

An injection site reaction (4%) was reported in patients receiving ondansetron injection intravenously over 2 to 5 minutes during clinical trials for post-operative nausea/vomiting (PONV); symptoms included pain, erythema, and burning at the site.[31266]

Visual impairment has occurred with ondansetron use. Cases of transient blindness, predominantly during intravenous (IV) administration, have been reported; resolution occurred within minutes up to 48 hours. Sudden blindness (amaurosis) of 2—3 minute duration occurred in one patient who was administered ondansetron 72 mg IV as a single dose.[49444] [31266] In another case, transient blindness was reported in a patient who received ondansetron 4mg as a post-operative rapid IV bolus dose.[31837] The mechanism by which ondansetron may cause visual impairment is not well understood. Clinicians in the latter case suggest that it may be related to the rate of administration. Transient blurred vision, in some cases associated with accommodation disorder, has also been reported during post-marketing experience.[31266]

Fever (2—8%) and shivers or chills (2—5%) were reported in patients receiving ondansetron during clinical trials. Wound problems (28% vs. 31% placebo) were reported in patients receiving oral ondansetron for postoperative nausea and vomiting (PONV).[31266] [49444]

Serotonin syndrome has been reported with 5-HT_3 receptor antagonists, such as ondansetron, during concurrent use of other medications known to increase CNS or peripheral serotonin levels or during overdose. Some of the reported cases were fatal; most occurred in a post-anesthesia care unit or infusion center. If serotonin syndrome becomes evident during treatment, discontinue ondansetron and any other serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is a range of signs and symptoms that can include mental status changes (e.g., agitation, hallucinations, delirium, coma), gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), and/or seizures. Cases consistent with serotonin syndrome have been reported in pediatric patients after inadvertent overdose of oral ondansetron (estimated ingestion > 5 mg/kg). Symptoms reported in these cases included somnolence, agitation, tachycardia, tachypnea, hypertension, flushing, mydriasis, diaphoresis, myoclonic movements, horizontal nystagmus, hyperreflexia, and seizures. Patients required supportive care, including intubation in some cases, with complete recovery in 1—2 days.[31266] [49444]

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How Supplied

Dextrose, Ondansetron Hydrochloride Solution for injection

Ondansetron Hydrochloride 32mg/50ml in Dextrose 5% Solution for Injection (55390-0234) (Bedford Laboratories, A Hikma Company) (off market)	
Ondansetron Hydrochloride 32mg/50ml in Dextrose 5% Solution for Injection (00409-4760) (Hospira Worldwide Inc.)	
Ondansetron Hydrochloride 32mg/50ml in Dextrose 5% Solution for Injection (00069-0700) (Pfizer Injectables) (off market)	
Ondansetron Hydrochloride 32mg/50ml in Dextrose 5% Solution for Injection (00703-7239) (Sicor Pharmaceuticals Inc A subsidiary of Teva Pharmaceuticals USA) (off market)	
Zofran 32mg/50ml in Dextrose 5% Solution for Injection (00173-0461) (GlaxoSmithKline Group of Companies) (off market)	

Ondansetron Hydrochloride Oral solution

Ondansetron Hydrochloride 4mg/5ml Solution (65162-0691) (Amneal Pharmaceuticals LLC)	
Ondansetron Hydrochloride 4mg/5ml Solution (60505-0381) (Apotex Corp) (off market)	
Ondansetron Hydrochloride 4mg/5ml Solution (16714-0671) (Northstar Rx LLC)	
Ondansetron Hydrochloride 4mg/5ml Solution (50111-0819) (Pliva Inc a Division of Teva USA) (off market)	
Ondansetron Hydrochloride 4mg/5ml Solution (68094-0325) (Precision Dose, Inc.)	
Ondansetron Hydrochloride 4mg/5ml Solution (68094-0763) (Precision Dose, Inc.)	
Ondansetron Hydrochloride 4mg/5ml Solution (00054-0064) (Roxane Laboratories Inc)	
Ondansetron Hydrochloride 4mg/5ml Solution (54838-0555) (Silarx Pharmaceuticals Inc)	
Ondansetron Hydrochloride 4mg/5ml Solution (51672-4091) (Taro Pharmaceuticals USA Inc)	
Zofran 4mg/5ml Solution (00173-0489) (GlaxoSmithKline Group of Companies) (off market)	
Zofran 4mg/5ml Solution (00173-0489) (Novartis Vaccines and Diagnostics, Inc.)	

Ondansetron Hydrochloride Oral tablet

Ondansetron Hydrochloride 24mg Tablet (55111-0156) (Dr. Reddy's Laboratories, Inc.)	
Ondansetron Hydrochloride 24mg Tablet (00143-2424) (West-Ward Pharmaceutical)	
Ondansetron Hydrochloride 4mg Tablet (45963-0538) (Actavis Inc.)	
Ondansetron Hydrochloride 4mg Tablet (52152-0538) (Actavis Inc. Towata LLC) (off market)	
Ondansetron Hydrochloride 4mg Tablet (68084-0220) (American Health Packaging)	
Ondansetron Hydrochloride 4mg Tablet (60505-1311) (Apotex Corp)	
Ondansetron Hydrochloride 4mg Tablet (67877-0169) (Ascend Laboratories, LLC a Subsidiary of Alkem Laboratories Ltd)	
Ondansetron Hydrochloride 4mg Tablet (65862-0187) (Aurobindo Pharma USA Inc.)	

Ondansetron Hydrochloride 4mg Tablet	(55111-0153)	(Dr. Reddy's Laboratories, Inc.)	
Ondansetron Hydrochloride 4mg Tablet	(68462-0105)	(Glenmark Pharmaceuticals)	
Ondansetron Hydrochloride 4mg Tablet	(59762-2990)	(Greenstone Ltd) (off market)	
Ondansetron Hydrochloride 4mg Tablet	(00904-6208)	(Major Pharmaceuticals Inc) (off market)	
Ondansetron Hydrochloride 4mg Tablet	(51079-0524)	(Mylan Institutional LLC formerly UDL Laboratories Inc)	
Ondansetron Hydrochloride 4mg Tablet	(00378-0315)	(Mylan Pharmaceuticals Inc)	
Ondansetron Hydrochloride 4mg Tablet	(45802-0127)	(Perrigo Pharmaceuticals Company)	
Ondansetron Hydrochloride 4mg Tablet	(63304-0458)	(Ranbaxy Pharmaceuticals Inc. a Sun Pharma Company)	
Ondansetron Hydrochloride 4mg Tablet	(00781-5257)	(Sandoz Inc)	
Ondansetron Hydrochloride 4mg Tablet	(00781-1679)	(Sandoz Inc)	
Ondansetron Hydrochloride 4mg Tablet	(62756-0130)	(Sun Pharmaceutical Industries, Inc.)	
Ondansetron Hydrochloride 4mg Tablet	(00093-0233)	(Teva Pharmaceuticals USA Inc)	
Ondansetron Hydrochloride 4mg Tablet	(00143-2422)	(West-Ward Pharmaceutical) (off market)	
Ondansetron Hydrochloride 8mg Tablet	(45963-0539)	(Actavis Inc.)	
Ondansetron Hydrochloride 8mg Tablet	(52152-0539)	(Actavis Inc. Towata LLC) (off market)	
Ondansetron Hydrochloride 8mg Tablet	(68084-0221)	(American Health Packaging)	
Ondansetron Hydrochloride 8mg Tablet	(60505-1312)	(Apotex Corp)	
Ondansetron Hydrochloride 8mg Tablet	(67877-0170)	(Ascend Laboratories, LLC a Subsidiary of Alkem Laboratories Ltd)	
Ondansetron Hydrochloride 8mg Tablet	(65862-0188)	(Aurobindo Pharma USA Inc.)	
Ondansetron Hydrochloride 8mg Tablet	(55111-0154)	(Dr. Reddy's Laboratories, Inc.)	
Ondansetron Hydrochloride 8mg Tablet	(68462-0106)	(Glenmark Pharmaceuticals)	
Ondansetron Hydrochloride 8mg Tablet	(59762-2993)	(Greenstone Ltd) (off market)	
Ondansetron Hydrochloride 8mg Tablet	(00904-6209)	(Major Pharmaceuticals Inc) (off market)	
Ondansetron Hydrochloride 8mg Tablet	(51079-0525)	(Mylan Institutional LLC formerly UDL Laboratories Inc)	
Ondansetron Hydrochloride 8mg Tablet	(00378-0344)	(Mylan Pharmaceuticals Inc)	
Ondansetron Hydrochloride 8mg Tablet	(45802-0205)	(Perrigo Pharmaceuticals Company)	
Ondansetron Hydrochloride 8mg Tablet	(63304-0459)	(Ranbaxy Pharmaceuticals Inc. a Sun Pharma Company)	
Ondansetron Hydrochloride 8mg Tablet	(00781-5258)	(Sandoz Inc)	
Ondansetron Hydrochloride 8mg Tablet	(00781-1681)	(Sandoz Inc)	
Ondansetron Hydrochloride 8mg Tablet	(62756-0131)	(Sun Pharmaceutical Industries, Inc.)	
Ondansetron Hydrochloride 8mg Tablet	(00093-7236)	(Teva Pharmaceuticals USA Inc)	
Ondansetron Hydrochloride 8mg Tablet	(00143-2423)	(West-Ward Pharmaceutical) (off market)	
Zofran 24mg Tablet	(00173-0680)	(GlaxoSmithKline Group of Companies) (off market)	
Zofran 4mg Tablet	(00173-0446)	(GlaxoSmithKline Group of Companies) (off market)	
Zofran 4mg Tablet	(00173-0446)	(Novartis Vaccines and Diagnostics, Inc.)	
Zofran 8mg Tablet	(00173-0447)	(GlaxoSmithKline Group of Companies) (off market)	
Zofran 8mg Tablet	(00173-0447)	(Novartis Vaccines and Diagnostics, Inc.)	

Ondansetron Hydrochloride Solution for injection

BD Simplist Ondansetron Hydrochloride 4mg/2ml Prefilled Syringe Solution for Injection	(76045-0103)	(BD Rx Inc., a subsidiary of Becton, Dickinson & Company)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(23360-0016)	(Akorn-Strides LLC) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(23360-0016)	(Akorn-Strides LLC) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(60505-0744)	(Apotex Corp) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(60505-0744)	(Apotex Corp) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(10019-0905)	(Baxter Anesthesia/Critical Care) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(10019-0906)	(Baxter Anesthesia/Critical Care Oncology) (off market)	

Ondansetron Hydrochloride 2mg/ml Solution for Injection	(55390-0121)	(Bedford Laboratories, A Hikma Company) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(55390-0121)	(Bedford Laboratories, A Hikma Company)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(63323-0374)	(Fresenius Kabi USA, LLC formerly APP Pharmaceuticals)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(63323-0373)	(Fresenius Kabi USA, LLC formerly APP Pharmaceuticals)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(00409-4759)	(Hospira Worldwide Inc.)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(00409-1120)	(Hospira Worldwide Inc.)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(61703-0245)	(Mayne Pharma (USA) Inc a Division of Hospira Worldwide)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(61703-0244)	(Mayne Pharma (USA) Inc a Division of Hospira Worldwide)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(00781-3057)	(Sandoz Inc)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(00781-3057)	(Sandoz Inc)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(00781-3010)	(Sandoz Inc)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(00703-7221)	(Sicor Pharmaceuticals Inc A subsidiary of Teva Pharmaceuticals USA) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(00703-7221)	(Sicor Pharmaceuticals Inc A subsidiary of Teva Pharmaceuticals USA)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(62756-0182)	(Sun Pharmaceutical Industries, Inc.)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(62756-0181)	(Sun Pharmaceutical Industries, Inc.)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(00143-9891)	(West-Ward Pharmaceutical) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(00143-9890)	(West-Ward Pharmaceutical)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(00641-6078)	(West-Ward Pharmaceutical Corp)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(64679-0726)	(Wockhardt USA, LLC) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection	(64679-0727)	(Wockhardt USA, LLC) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection (Amerinet)	(00409-4755)	(Hospira Worldwide Inc.)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection (NOVAPLUS)	(10019-0906)	(Baxter Anesthesia/Critical Care Oncology) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection (NovaPlus)	(55390-0307)	(Bedford Laboratories, A Hikma Company) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection (NovaPlus)	(55390-0307)	(Bedford Laboratories, A Hikma Company) (off market)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection (NOVAPLUS)	(00641-6080)	(West-Ward Pharmaceutical Corp)	
Ondansetron Hydrochloride 2mg/ml Solution for Injection (NOVAPLUS)	(10019-0906)	(West-Ward Pharmaceutical Corp) (off market)	
Ondansetron Hydrochloride 40mg/20mL Solution for Injection	(55150-0126)	(AuroMedics Pharma LLC)	
Ondansetron Hydrochloride 40mg/20mL Solution for Injection	(36000-0013)	(Claris Lifescience Ltd)	
Ondansetron Hydrochloride 40mg/20mL Solution for Injection	(23155-0168)	(Heritage Pharmaceuticals Inc.)	
Ondansetron Hydrochloride 40mg/20mL Solution for Injection	(23155-0549)	(Heritage Pharmaceuticals Inc.)	
Ondansetron Hydrochloride 40mg/20ml Solution for Injection	(67457-0441)	(Mylan Institutional LLC formerly BionichePharma Inc.)	
Ondansetron Hydrochloride 40mg/20ml Solution for Injection	(00069-1340)	(Mylan Institutional LLC formerly UDL Laboratories Inc)	
Ondansetron Hydrochloride 40mg/20ml Solution for Injection	(00069-1340)	(Pfizer Injectables) (off market)	
Ondansetron Hydrochloride 40mg/20mL Solution for Injection	(25021-0782)	(Sagent Pharmaceuticals)	
Ondansetron Hydrochloride 40mg/20ml Solution for Injection	(00703-7226)	(Sicor Pharmaceuticals Inc A subsidiary of Teva Pharmaceuticals USA) (off market)	
Ondansetron Hydrochloride 40mg/20ml Solution for Injection	(00703-7226)	(Teva Pharmaceuticals)	
Ondansetron Hydrochloride 40mg/20ml Solution for Injection	(00641-6079)	(West-Ward Injectables)	
Ondansetron Hydrochloride 40mg/20ml Solution for Injection	(10019-0906)	(West-Ward Pharmaceutical Corp) (off market)	
Ondansetron Hydrochloride 40mg/20mL Solution for Injection (PREMIER ProRx)	(23155-0377)	(Heritage Pharmaceuticals Inc.)	
Ondansetron Hydrochloride 40mg/20mL Solution for Injection (PREMIER ProRx)	(23155-0550)	(Heritage Pharmaceuticals Inc.)	
Ondansetron Hydrochloride 4mg/2ml Solution for Injection	(55150-0125)	(AuroMedics Pharma LLC)	
Ondansetron Hydrochloride 4mg/2ml Solution for Injection	(36000-0012)	(Claris Lifescience Ltd)	
Ondansetron Hydrochloride 4mg/2ml Solution for Injection	(23155-0196)	(Heritage Pharmaceuticals Inc.)	

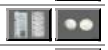
Ondansetron Hydrochloride 4mg/2mL Solution for Injection	(23155-0547)	(Heritage Pharmaceuticals Inc.)		
Ondansetron Hydrochloride 4mg/2ml Solution for Injection	(00409-4755)	(Hospira Worldwide Inc.)		
Ondansetron Hydrochloride 4mg/2ml Solution for Injection	(00409-1120)	(Hospira Worldwide Inc.)		
Ondansetron Hydrochloride 4mg/2ml Solution for Injection	(67457-0440)	(Mylan Institutional LLC formerly BionichePharma Inc.)		
Ondansetron Hydrochloride 4mg/2ml Solution for Injection	(00069-1340)	(Mylan Institutional LLC formerly UDL Laboratories Inc)		
Ondansetron Hydrochloride 4mg/2ml Solution for Injection	(00069-1340)	(Pfizer Injectables) (off market)		
Ondansetron Hydrochloride 4mg/2mL Solution for Injection	(25021-0777)	(Sagent Pharmaceuticals)		
Ondansetron Hydrochloride 4mg/2ml Solution for Injection	(00143-9891)	(West-Ward Pharmaceutical Corp)		
Ondansetron Hydrochloride 4mg/2ml Solution for Injection	(10019-0905)	(West-Ward Pharmaceutical Corp)		
Ondansetron Hydrochloride 4mg/2ml Solution for Injection (PREMIER ProRx)	(23155-0378)	(Heritage Pharmaceuticals Inc.)		
Ondansetron Hydrochloride 4mg/2mL Solution for Injection (PREMIER ProRx)	(23155-0548)	(Heritage Pharmaceuticals Inc.)		
Zofran 2mg/ml Solution for Injection	(00173-0442)	(GlaxoSmithKline Group of Companies) (off market)		
Zofran 2mg/ml Solution for Injection	(00173-0442)	(GlaxoSmithKline Group of Companies) (off market)		
Zofran 2mg/ml Solution for Injection	(00173-0442)	(Novartis Vaccines and Diagnostics, Inc.)		

Ondansetron Hydrochloride, Sodium Chloride Solution for injection

Ondansetron Hydrochloride 32mg/50ml in Sodium Chloride 0.9% Solution for Injection	(00338-1762)	(Baxter Medication Delivery)		

Ondansetron Oral disintegrating tablet

Ondansetron 4mg Orally Disintegrating Tablet	(65862-0390)	(Aurobindo Pharma USA Inc.)		
Ondansetron 4mg Orally Disintegrating Tablet	(68001-0246)	(BluePoint Laboratories)		
Ondansetron 4mg Orally Disintegrating Tablet	(57237-0077)	(Citron Pharma LLC)		
Ondansetron 4mg Orally Disintegrating Tablet	(58177-0363)	(Ethex Corporation) (off market)		
Ondansetron 4mg Orally Disintegrating Tablet	(68462-0157)	(Glenmark Pharmaceuticals)		
Ondansetron 4mg Orally Disintegrating Tablet	(00378-7732)	(Mylan Pharmaceuticals Inc)		
Ondansetron 4mg Orally Disintegrating Tablet	(55289-0559)	(PD-RX Pharmaceuticals)		
Ondansetron 4mg Orally Disintegrating Tablet	(55289-0559)	(PD-RX Pharmaceuticals)		
Ondansetron 4mg Orally Disintegrating Tablet	(43063-0052)	(PD-Rx Pharmaceuticals Incorporated)		
Ondansetron 4mg Orally Disintegrating Tablet	(43063-0560)	(PD-Rx Pharmaceuticals Incorporated)		
Ondansetron 4mg Orally Disintegrating Tablet	(50111-0945)	(Pliva Inc a Division of Teva USA)		
Ondansetron 4mg Orally Disintegrating Tablet	(33358-0498)	(RxChange Co.)		
Ondansetron 4mg Orally Disintegrating Tablet	(00781-5265)	(Sandoz Inc)		
Ondansetron 4mg Orally Disintegrating Tablet	(00781-5238)	(Sandoz Inc)		
Ondansetron 4mg Orally Disintegrating Tablet	(62756-0240)	(Sun Pharmaceutical Industries, Inc.)		
Ondansetron 4mg Orally Disintegrating Tablet	(00093-7301)	(Teva Pharmaceuticals USA Inc) (off market)		
Ondansetron 8mg Orally Disintegrating Tablet	(65862-0391)	(Aurobindo Pharma USA Inc.)		
Ondansetron 8mg Orally Disintegrating Tablet	(68001-0247)	(BluePoint Laboratories)		
Ondansetron 8mg Orally Disintegrating Tablet	(57237-0078)	(Citron Pharma LLC)		
Ondansetron 8mg Orally Disintegrating Tablet	(58177-0364)	(Ethex Corporation) (off market)		
Ondansetron 8mg Orally Disintegrating Tablet	(68462-0158)	(Glenmark Pharmaceuticals)		
Ondansetron 8mg Orally Disintegrating Tablet	(00378-7734)	(Mylan Pharmaceuticals Inc)		
Ondansetron 8mg Orally Disintegrating Tablet	(43063-0273)	(PD-Rx Pharmaceuticals Incorporated)		
Ondansetron 8mg Orally Disintegrating Tablet	(43063-0592)	(PD-Rx Pharmaceuticals Incorporated)		
Ondansetron 8mg Orally Disintegrating Tablet	(50111-0946)	(Pliva Inc a Division of Teva USA)		
Ondansetron 8mg Orally Disintegrating Tablet	(33358-0512)	(RxChange Co.)		
Ondansetron 8mg Orally Disintegrating Tablet	(00781-5266)	(Sandoz Inc)		

Ondansetron 8mg Orally Disintegrating Tablet	(00781-5239)	(Sandoz Inc)	
Ondansetron 8mg Orally Disintegrating Tablet	(62756-0356)	(Sun Pharmaceutical Industries, Inc.)	
Ondansetron 8mg Orally Disintegrating Tablet	(00093-7302)	(Teva Pharmaceuticals USA Inc) (off market)	
Zofran ODT 4mg Orally Disintegrating Tablet	(00173-0569)	(GlaxoSmithKline Group of Companies) (off market)	
Zofran ODT 4mg Orally Disintegrating Tablet	(00173-0569)	(Novartis Vaccines and Diagnostics, Inc.)	
Zofran ODT 8mg Orally Disintegrating Tablet	(00173-0570)	(GlaxoSmithKline Group of Companies) (off market)	
Zofran ODT 8mg Orally Disintegrating Tablet	(00173-0570)	(Novartis Vaccines and Diagnostics, Inc.)	

Ondansetron Oral Dissolving film

Zuplenz 4mg Oral Soluble Film	(57881-0444)	(Galena Biopharma)
Zuplenz 4mg Oral Soluble Film	(49884-0324)	(Par Pharmaceuticals) (off market)
Zuplenz 4mg Oral Soluble Film	(43288-0104)	(Praelia Pharmaceuticals) (off market)
Zuplenz 8mg Oral Soluble Film	(57881-0448)	(Galena Biopharma)
Zuplenz 8mg Oral Soluble Film	(49884-0325)	(Par Pharmaceuticals) (off market)
Zuplenz 8mg Oral Soluble Film	(43288-0108)	(Praelia Pharmaceuticals) (off market)

Monitoring Parameters

- ECG
- LFTs
- serum electrolytes

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