Brand Names

Zofran, Zofran in Dextrose, Zofran ODT, Zofran Solution, Zuplenz

Indication Specific Dosing

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. NOTE: Since 2012, a 32 mg IV single-dose regimen is no longer indicated because of the risk of QT prolongation.

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. 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. Alternatively, ondansetron has been administered every 8 hours and continued for 1 to 5 days after completion of therapy. 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.

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.

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/m2 or more. Multiday, single dose administration of ondansetron 24 mg has not been studied.

Adults receiving radiotherapy (general dosage)

8 mg PO 3 times daily.

Adults receiving total body irradiation

8 mg PO 1 to 2 hours prior to each fraction of radiotherapy each day.

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.

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. Further doses may be given every 12 hours for 1 to 2 days after completion of therapy. 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. Alternatively, a single 24 mg PO dose may be given prior to chemotherapy.

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. Further doses may be given every 8 hours for 1 to 2 days after completion of therapy. 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. Alternatively, a single 12 mg PO dose may be given prior to chemotherapy.

Infants† and Children less than 4 years† with a body surface area more than 1 meter-squared

4 mg PO 3 times daily. Give the first dose 30 minutes prior to chemotherapy or 1 to 2 hours prior to radiation. May be continued for 1 to 5 days after completion of therapy.

Infants† and Children less than 4 years† with a body surface area 0.6 to 1 meter-squared

3 mg PO 3 times daily. Give the first dose 30 minutes prior to chemotherapy or 1 to 2 hours prior to radiation. May be continued for 1 to 5 days after completion of therapy.

Infants† and Children less than 4 years† with a body surface area 0.3 to 0.6 meter-squared

2 mg PO 3 times daily. Give the first dose 30 minutes prior to chemotherapy or 1 to 2 hours prior to radiation. May be continued for 1 to 5 days after completion of therapy.

Infants† and Children less than 4 years† with a body surface area less than 0.3 meter-squared

1 mg PO 3 times daily. Give the first dose 30 minutes prior to chemotherapy or 1 to 2 hours prior to radiation. May be continued for 1 to 5 days after completion of therapy.

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

Intravenous dosage

Adults and Adolescents

4 mg IV once; a 5-HT3 antagonist is recommended if no prophylaxis was given, or for those who received a prophylactic antiemetic from another drug class. 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.

Children weighing more than 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.

Infants and Children weighing 40 kg or less

0.05 to 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. Among children who had at least 2 postoperative episodes 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.

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.

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.

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.

Oral dosage

Adults

16 mg PO as single dose given 1 hour before anesthesia induction. 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.

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. 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.

For the treatment of pregnancy-induced nausea/vomiting†

Oral dosage

Adults

4 mg PO every 8 hours as needed.

Intravenous dosage

Adults

8 mg IV every 12 hours as needed.

For the treatment of nausea/vomiting associated with acute gastroenteritis†

Intravenous dosage

Infants, Children, and Adolescents

0.15 mg/kg/dose (Max: 8 mg/dose) IV as a single dose has been used along with oral or IV rehydration. Although routine use of antiemetics is not recommended, some studies have shown that single IV doses of ondansetron are safe and

effective for reducing vomiting and increasing patients' ability to tolerate oral rehydration.

Oral dosage

Children and Adolescents weighing more than 30 kg

0.2 mg/kg/dose (Max: 8 mg/dose) PO as a single dose along with oral or IV rehydration. Alternatively, 0.2 mg/kg/dose PO every 8 hours for 3 doses has also been studied. Studies have shown that single and multiple oral doses of ondansetron are safe and effective for reducing vomiting and increasing individuals' ability to tolerate oral rehydration.

Children weighing 15 to 30 kg

0.2 mg/kg/dose (Max: 4 mg/dose) PO as a single dose along with oral or IV rehydration. Alternatively, 0.2 mg/kg/dose PO every 8 hours for 3 doses has also been studied. Studies have shown that single and multiple oral doses of ondansetron are safe and effective for reducing vomiting and increasing individuals' ability to tolerate oral rehydration.

Infants 3 to 11 months and Children weighing less than 15 kg

0.2 mg/kg/dose (Max: 2 mg/dose) PO as a single dose along with oral or IV rehydration. Alternatively, 0.2 mg/kg/dose PO every 8 hours for 3 doses has also been studied. Studies have shown that single and multiple oral doses of ondansetron are safe and effective for reducing vomiting and increasing individuals' ability to tolerate oral rehydration.

For the maintenance treatment of alcohol dependence† (alcohol use disorder† or AUD)

Oral dosage

Adults

4 mcg/kg PO twice daily, combined with weekly standardized group behavioral therapy, was effective in reducing alcohol consumption/days abstinent in people with an onset of AUD before 25 years of age. Other regimens have been used (e.g., 8 mg PO twice daily). Other studies suggest utility in selected patients with genetic predisposition to AUD; it is not a routine option and further studies are needed.

For the treatment of cyclic vomiting syndrome†

Intravenous dosage

Adults

8 mg IV every 4 to 6 hours as needed.

Children and Adolescents 2 to 17 years

0.3 to 0.4 mg/kg/dose (Max: 20 mg/dose) IV every 4 to 6 hours as needed.

Oral dosage (disintegrating tablet)

Adults

8 mg PO every 6 to 8 hours as needed for 24 to 48 hours if intravenous therapy is initially effective.

For the treatment of nausea/vomiting†

For the treatment of nausea/vomiting† in the emergency department or prehospital

Intravenous or Intramuscular dosage

Adults

4 mg IV or IM as a single dose.

Children and Adolescents 4 to 17 years

4 mg IV or IM as a single dose.

Oral dosage

Adults

4 mg PO as a single dose.

Children and Adolescents 4 to 17 years

4 mg PO as a single dose.

For the treatment of nausea/vomiting† associated with small bowel obstruction

Intravenous dosage

Adults

4 mg IV every 6 to 8 hours.

For the treatment of nausea/vomiting† associated with Ebola virus (species *Orthoebolavirus zairense*) infection

Intravenous dosage

Adults

4 mg IV every 8 hours as needed.

Children and Adolescents weighing 40 kg or more

0.15 mg/kg/dose (Max: 8 mg/dose) IV every 12 hours as needed. Alternatively, 4 mg IV as a single dose.

Children and Adolescents weighing less than 40 kg

0.15 mg/kg/dose IV every 12 hours as needed. Alternatively, 0.1 mg/kg/dose IV as a single dose.

Oral dosage

Adults

8 mg PO every 12 hours as needed.

Children and Adolescents

0.15 mg/kg/dose (Max: 8 mg/dose) PO every 12 hours as needed.

For the treatment of pruritus† secondary to cholestasis

Intravenous and Oral dosage

Adults

8 mg PO 2 or 3 times per day or, alternatively, 4 to 8 mg IV up to every 6 hours as

needed are typical dosage regimens. Reports of efficacy are mixed, depending on rating scores used in clinical trials. Some studies report an initial reduction in itching severity by 30% to 50%, while other studies do not find that ondansetron reduces scratching compared to placebo. Ondansetron is usually reserved when standard treatments are not effective.

Contraindications And Precaution

Drug Interactions

The coadministration of certain medications may lead to harm and require avoidance or therapy modification; review all drug interactions prior to concomitant use of other medications.

Hypersensitivity

This medication is contraindicated in patients with a history of hypersensitivity to it or any of its components. Use with caution in individuals with known granisetron hypersensitivity, palonosetron hypersensitivity, dolasetron hypersensitivity, or sensitivity to related drugs. 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. Antagonism at serotonin (5-HT) receptors, and the subsequent increased concentrations of serotonin, may increase the risk of developing bronchospasm and/or vasoconstriction.

General Information

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. Ondansetron is not a drug that stimulates gastric or intestinal peristalsis; it should not be used instead of nasogastric suction.

Child-Pugh class C, hepatic failure

Ondansetron is extensively metabolized in the liver and should be used with caution in individuals with hepatic failure or elevated hepatic enzymes because of possible increased plasma levels, reduced clearance, and subsequent toxicity. A dosage adjustment is required for individuals with severe hepatic impairment (Child-Pugh class C).

phenylketonuria

Individuals 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 less than 0.03 mg phenylalanine.

bradycardia, cardiomyopathy, congenital long QT syndrome, coronary artery disease, females, geriatric, heart failure, hypocalcemia, hypokalemia, hypomagnesemia, QT prolongation

Avoid use of ondansetron in people with baseline QT prolongation or who have conditions that may increase the risk of QT prolongation or torsade de pointes, including bradycardia, congenital long QT syndrome, hypocalcemia, hypokalemia, hypomagnesemia, geriatric adults, females, structural abnormalities that interfere with electrical conduction (e.g., cardiomyopathy, coronary artery disease, ischemic heart disease), or in those who have other additional risk factors for QT prolongation or torsade de pointes. The use of other medications that have been associated with QT prolongation or torsade de pointes may further increase risk. Electrocardiogram (ECG) monitoring and cautious use is recommended in individuals with hypokalemia, hypomagnesemia, heart failure, significant bradycardia, or in individuals receiving other medications known to prolong the QT interval.

pregnancy

Data on the use of ondansetron during pregnancy from published clinical and epidemiological studies are inconsistent and have important methodological limitations, including the uncertainty of whether people who filled a prescription actually took the medicine, the concomitant use of other medications or treatments, recall bias, and other un-adjusted confounders, that do not reliably inform a drug associated risk of adverse fetal outcomes. In aggregate analysis, ondansetron exposure in utero has not been associated with major congenital malformations. Some studies have not shown a statistically significant increase in the risk of birth defects with the use of ondansetron; however, others have shown a possible increased risk of cleft palate and cardiovascular malformations. Ondansetron has been shown to cross the placenta in early pregnancy with a median fetal to maternal ratio of 0.41. Evidence is limited on the safety or efficacy of the serotonin 5HT-3 inhibitors for nausea and vomiting of pregnancy. There are more data for ondansetron use during pregnancy than with other 5HT-3 antagonists. The American College of Obstetricians and Gynecologists (ACOG) includes oral ondansetron as a third-line pharmacologic treatment option for nausea and vomiting of pregnancy in patients who are not dehydrated and have failed other therapies and IV ondansetron for patients who are dehydrated, require IV fluid replacement, and have failed other therapies. Although some studies have shown an increased risk of birth defects with early ondansetron use, other studies have not and the absolute risk to any fetus is considered, per ACOG, to be low. Some studies have suffered from small sample sizes

and potential methodological bias. However, women should be counseled regarding the available data, and the use of ondansetron before 10 weeks of gestation should be individualized weighing the risks and benefits.

breast-feeding

Ondansetron is considered compatible with breast-feeding. Small amounts are present in human milk with a relative infant dose of 1.6% to 3.7% and an estimated daily infant dose of 0.002 mg/kg/day. Ondansetron is labeled for use in infants as young as 1 month of age; infant exposure from human milk is significantly below doses for therapeutic use. No infant adverse effects have been reported with postpartum use. There is no data on the effects of ondansetron on milk production.

Pregnancy And Lactation

Data on the use of ondansetron during pregnancy from published clinical and epidemiological studies are inconsistent and have important methodological limitations, including the uncertainty of whether people who filled a prescription actually took the medicine, the concomitant use of other medications or treatments, recall bias, and other un-adjusted confounders, that do not reliably inform a drug associated risk of adverse fetal outcomes. In aggregate analysis, ondansetron exposure in utero has not been associated with major congenital malformations. Some studies have not shown a statistically significant increase in the risk of birth defects with the use of ondansetron; however, others have shown a possible increased risk of cleft palate and cardiovascular malformations. Ondansetron has been shown to cross the placenta in early pregnancy with a median fetal to maternal ratio of 0.41. Evidence is limited on the safety or efficacy of the serotonin 5HT-3 inhibitors for nausea and vomiting of pregnancy. There are more data for ondansetron use during pregnancy than with other 5HT-3 antagonists. The American College of Obstetricians and Gynecologists (ACOG) includes oral ondansetron as a third-line pharmacologic treatment option for nausea and vomiting of pregnancy in patients who are not dehydrated and have failed other therapies and IV ondansetron for patients who are dehydrated, require IV fluid replacement, and have failed other therapies. Although some studies have shown an increased risk of birth defects with early ondansetron use, other studies have not and the absolute risk to any fetus is considered, per ACOG, to be low. Some studies have suffered from small sample sizes and potential methodological bias. However, women should be counseled regarding the available data, and the use of ondansetron before 10 weeks of gestation should be individualized weighing the risks and benefits.

Interactions

Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dihydrocodeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Acetaminophen; Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Acetaminophen; HYDROcodone: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering hydrocodone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Acetaminophen; oxyCODONE: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering oxycodone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Adagrasib: (Major) Concomitant use of adagrasib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation

associated with ondansetron significantly increases above this dose.
ALFentanil: (Moderate) If concomitant use of alfentanil and ondansetron is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Alfuzosin: (Major) Concomitant use of ondansetron and alfuzosin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Amiodarone: (Major) Concomitant use of amiodarone and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. Due to the extremely long half-life of amiodarone, a drug interaction is possible for days to weeks after drug discontinuation.
Amisulpride: (Major) Concomitant use of ondansetron and amisulpride increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Amobarbital: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Amoxicillin; Clarithromycin; Omeprazole: (Major) Concomitant use of ondansetron and clarithromycin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and

TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Anagrelide: (Major) Concomitant use of ondansetron and anagrelide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Apomorphine: (Contraindicated) The concurrent use of apomorphine and serotonin-receptor antagonists is contraindicated due to the possibility of an excessive lowering of blood pressure and unconsciousness. Additionally, additive QT prolongation is possible during coadministration of apomorphine with dolasetron, granisetron, and ondansetron.
Aprepitant, Fosaprepitant: (Minor) Aprepitant, fosaprepitant is indicated for the prophylaxis of chemotherapy-induced nausea/vomiting in combination with a 5HT3 antagonist, one of which is ondansetron. Ondansetron is a CYP3A4 substrate. Aprepitant, when administered as a 3-day oral regimen (125 mg/80 mg/80 mg), is a moderate CYP3A4 inhibitor and inducer; substitution of fosaprepitant 115 mg IV on day 1 of the 3-day regimen may lessen the inhibitory effects of CYP3A4. The AUC of another CYP3A4 substrate, midazolam, was increased for several days after aprepitant dosing when the two drugs were coadministered; however, in clinical drug interaction studies, aprepitant did not have clinically important effects on the pharmacokinetics of ondansetron.
ARIPiprazole: (Major) If ondansetron and aripiprazole must be coadministered, ECG monitoring is recommended. Ondansetron has been associated with a dose-related increase in the QT interval and postmarketing reports of torsade de pointes (TdP). QT prolongation has occurred during therapeutic use of aripiprazole and following overdose.
Arsenic Trioxide: (Major) Concomitant use of ondansetron and arsenic trioxide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Artemether; Lumefantrine: (Major) Concomitant use of ondansetron and lumefantrine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP.

Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Asenapine: (Major) Concomitant use of ondansetron and asenapine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Aspirin, ASA; Butalbital; Caffeine: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Aspirin, ASA; Carisoprodol; Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Aspirin, ASA; oxyCODONE: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering oxycodone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Atazanavir: (Moderate) 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.
Atazanavir; Cobicistat: (Moderate) 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. (Moderate) 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 strong inhibitor of CYP3A4 and an inhibitor of CYP2D6 and P-glycoprotein (P-gp) inhibitor. Ondansetron is a CYP3A4, CYP2D6, and P-gp substrate.
Atomoxetine: (Major) Concomitant use of ondansetron and atomoxetine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Azithromycin: (Major) Concomitant use of azithromycin and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Barbiturates: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Bedaquiline: (Major) Concomitant use of ondansetron and bedaquiline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Benzhydrocodone; Acetaminophen: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering benzhydrocodone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all

serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Major) 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.
Bismuth Subcitrate Potassium; metroNIDAZOLE; Tetracycline: (Major) Concomitant use of metronidazole and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Bismuth Subsalicylate; metroNIDAZOLE; Tetracycline: (Major) Concomitant use of metronidazole and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Buprenorphine: (Major) Due to the potential for QT prolongation, cautious use and close monitoring are advisable if concurrent use of ondansetron and buprenorphine is necessary. Ondansetron may cause QT interval prolongation and a risk for torsade de pointes (TdP); buprenorphine caused QT prolongation in some patients during clinical trials. ECG monitoring is recommended if these drugs are used concurrently. In addition, concurrent use of opioids with other drugs that modulate serotonergic function, such as ondansetron, has resulted in serotonin syndrome in some cases. Patients should be carefully observed, particularly during treatment initiation and during dose adjustments. Discontinue the serotonergic medications if serotonin syndrome is suspected.
Buprenorphine; Naloxone: (Major) Due to the potential for QT prolongation, cautious use and close monitoring are advisable if concurrent use of ondansetron and buprenorphine is necessary. Ondansetron may cause QT interval prolongation and a risk for torsade de pointes (TdP); buprenorphine caused QT prolongation in some patients during clinical trials. ECG monitoring is recommended if these drugs are used concurrently. In addition, concurrent use of opioids with other drugs that modulate serotonergic function, such as ondansetron, has resulted in serotonin syndrome in some cases. Patients should be carefully observed, particularly during treatment initiation and during dose adjustments. Discontinue the serotonergic medications if serotonin syndrome is suspected.

Butalbital; Acetaminophen: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Butalbital; Acetaminophen; Caffeine: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Butalbital; Acetaminophen; Caffeine; Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Butalbital; Aspirin; Caffeine; Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life

was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Cabotegravir; Rilpivirine: (Major) Concomitant use of rilpivirine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. The degree of QT prolongation associated with rilpivirine is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose.
Capsaicin; Metaxalone: (Moderate) Concomitant use of metaxalone and serotonin-receptor antagonists (5HT-3 receptor antagonists) may increase the risk for serotonin syndrome. Monitor patients for serotonin syndrome if concomitant use is necessary.
Celecoxib; Tramadol: (Moderate) Monitor for opioid withdrawal and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant ondansetron and tramadol use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome. Also, data from 2 small trials indicate that concomitant use of ondansetron may result in reduced analgesic activity of tramadol; patients receiving ondansetron used tramadol more frequently leading to an increased cumulative dose in patient-controlled administration of tramadol.
Ceritinib: (Major) Concomitant use of ondansetron and ceritinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Chloroquine: (Major) Concomitant use of ondansetron and chloroquine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Chlorpheniramine; Codeine: (Moderate) Because of the potential risk and severity of

serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Chlorpheniramine; HYDROcodone: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering hydrocodone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
chlorproMAZINE: (Major) Concomitant use of ondansetron and chlorpromazine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Ciprofloxacin: (Major) If ondansetron and ciprofloxacin must be coadministered, ECG monitoring is recommended. Ondansetron has been associated with a dose-related increase in the QT interval and postmarketing reports of torsade de pointes (TdP). Additionally, rare cases of QT prolongation and torsade de pointes (TdP) have been reported with ciprofloxacin during postmarketing surveillance. Additionally ciprofloxacin inhibits the CYP1A2 isoenzyme, while ondansetron is metabolized by several isoenzymes, including CYP1A2.
Cisapride: (Contraindicated) Avoid concomitant use of ondansetron and cisapride due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Citalopram: (Major) Concomitant use of ondansetron and citalopram increases the risk of QT/QTc prolongation, torsade de pointes (TdP), and serotonin syndrome. Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. If concomitant use is necessary, consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, and monitor for serotonin syndrome.
Clarithromycin: (Major) Concomitant use of ondansetron and clarithromycin increases

the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Clofazimine: (Major) Concomitant use of clofazimine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
cloZAPine: (Major) Concomitant use of ondansetron and clozapine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Cobicistat: (Moderate) 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 strong inhibitor of CYP3A4 and an inhibitor of CYP2D6 and P-glycoprotein (P-gp) inhibitor. Ondansetron is a CYP3A4, CYP2D6, and P-gp substrate.
Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Codeine; Dexbrompheniramine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and

initiate symptomatic treatment if serotonin syndrome occurs.
Codeine; guaiFENesin: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Codeine; guaiFENesin; Pseudoephedrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Codeine; Phenylephrine; Promethazine: (Major) Concomitant use of ondansetron and promethazine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Codeine; Promethazine: (Major) Concomitant use of ondansetron and promethazine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and

monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Crizotinib: (Major) Concomitant use of ondansetron and crizotinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Darunavir: (Moderate) 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.
Darunavir; Cobicistat: (Moderate) 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 strong inhibitor of CYP3A4 and an inhibitor of CYP2D6 and P-glycoprotein (P-gp) inhibitor. Ondansetron is a CYP3A4, CYP2D6, and P-gp substrate. (Moderate) 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.
Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Moderate) 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 strong inhibitor of CYP3A4 and an inhibitor of CYP2D6 and P-glycoprotein (P-gp) inhibitor. Ondansetron is a CYP3A4, CYP2D6, and P-gp substrate. (Moderate) 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.
Dasatinib: (Major) Concomitant use of ondansetron and dasatinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.

Degarelix: (Major) Concomitant use of ondansetron and degarelix increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Desflurane: (Major) Concomitant use of ondansetron and halogenated anesthetics increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Desvenlafaxine: (Major) 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.
Deutetrabenazine: (Major) If ondansetron and deutetrabenazine must be coadministered, ECG monitoring is recommended. Ondansetron has been associated with a dose-related increase in the QT interval and postmarketing reports of torsade de pointes (TdP). Deutetrabenazine may prolong the QT interval, but the degree of QT prolongation is not clinically significant when deutetrabenazine is administered within the recommended dosage range.
dexmedeTOMIDine: (Major) Concomitant use of dexmedetomidine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Dextromethorphan; quiNIDine: (Contraindicated) Quinidine administration is associated with QT prolongation and torsades de pointes (TdP). Quinidine inhibits CYP2D6 and has QT-prolonging actions; quinidine is contraindicated with other drugs that prolong the QT interval and are metabolized by CYP2D6 as the effects on the QT interval may be increased during concurrent use of these agents. Drugs that prolong the QT and are substrates for CYP2D6 that are contraindicated with quinidine include ondansetron.

Disopyramide: (Major) Concomitant use of ondansetron and disopyramide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Dofetilide: (Major) Concomitant use of ondansetron and dofetilide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Dolasetron: (Major) These drugs would not be expected to be given together due to therapeutic class duplication; side effects, such as serotonergic actions, may be additive. Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended. Dolasetron is associated with a lower, but possible risk for QT prolongation and TdP.
Dolutegravir; Rilpivirine: (Major) Concomitant use of rilpivirine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. The degree of QT prolongation associated with rilpivirine is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose.
Donepezil: (Major) Concomitant use of ondansetron and donepezil increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Donepezil; Memantine: (Major) Concomitant use of ondansetron and donepezil increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP.

Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Dordaviprone: (Major) Concomitant use of dordaviprone and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Dronedarone: (Contraindicated) 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). Dronedarone administration is associated with a dose-related increase in the QTc interval. The increase in QTc is approximately 10 milliseconds at doses of 400 mg twice daily (the FDA-approved dose) and up to 25 milliseconds at doses of 1600 mg twice daily. 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.
droPERidol: (Major) Concomitant use of ondansetron and droperidol increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
DULoxetine: (Moderate) 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.
Efavirenz: (Major) Coadministration of efavirenz and ondansetron may increase the risk for QT prolongation and torsade de pointes (TdP). QT prolongation has been observed with use of efavirenz. Although data are limited, the manufacturer of efavirenz recommends an alternative antiretroviral be considered for patients receiving

medications with a known risk for TdP. Ondansetron has been associated with QT prolongation and post-marketing reports of TdP. 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. If these drugs must be coadministered, ECG monitoring is recommended. In addition, efavirenz induces CYP3A4 and may decrease serum concentrations of drugs metabolized by this enzyme, such as ondansetron.
Efavirenz; Emtricitabine; Tenofovir Disoproxil Fumarate: (Major) Coadministration of efavirenz and ondansetron may increase the risk for QT prolongation and torsade de pointes (TdP). QT prolongation has been observed with use of efavirenz. Although data are limited, the manufacturer of efavirenz recommends an alternative antiretroviral be considered for patients receiving medications with a known risk for TdP. Ondansetron has been associated with QT prolongation and post-marketing reports of TdP. 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. If these drugs must be coadministered, ECG monitoring is recommended. In addition, efavirenz induces CYP3A4 and may decrease serum concentrations of drugs metabolized by this enzyme, such as ondansetron.
Efavirenz; lamiVUDine; Tenofovir Disoproxil Fumarate: (Major) Coadministration of efavirenz and ondansetron may increase the risk for QT prolongation and torsade de pointes (TdP). QT prolongation has been observed with use of efavirenz. Although data are limited, the manufacturer of efavirenz recommends an alternative antiretroviral be considered for patients receiving medications with a known risk for TdP. Ondansetron has been associated with QT prolongation and post-marketing reports of TdP. 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. If these drugs must be coadministered, ECG monitoring is recommended. In addition, efavirenz induces CYP3A4 and may decrease serum concentrations of drugs metabolized by this enzyme, such as ondansetron.
Elbasvir; Grazoprevir: (Moderate) Administering ondansetron with elbasvir; grazoprevir may result in elevated ondansetron plasma concentrations. Ondansetron is a substrate of CYP3A; grazoprevir is a weak CYP3A inhibitor. If these drugs are used together, closely monitor for signs of adverse events.
Eliglustat: (Major) Coadminister ondansetron and eliglustat cautiously with close monitoring; there may be an increased risk of QT prolongation and/or ondansetron-associated adverse effects. Ondansetron dosage reduction may be considered, depending on the clinical situation. Eliglustat is a CYP2D6 and P-glycoprotein (P-gp) inhibitor that is predicted to cause PR, QRS, and/or QT prolongation at significantly elevated plasma concentrations. Although ondansetron is primarily metabolized by other CYP450 isoenzymes (i.e., CYP3A4 and CYP1A2), it is metabolized to a lesser extent by CYP2D6 and is considered a P-gp substrate. In addition, ondansetron has been

associated with QT prolongation and post-marketing reports of torsade de pointes (TdP).
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Alafenamide: (Moderate) 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 strong inhibitor of CYP3A4 and an inhibitor of CYP2D6 and P-glycoprotein (P-gp) inhibitor. Ondansetron is a CYP3A4, CYP2D6, and P-gp substrate.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) 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 strong inhibitor of CYP3A4 and an inhibitor of CYP2D6 and P-glycoprotein (P-gp) inhibitor. Ondansetron is a CYP3A4, CYP2D6, and P-gp substrate.
Emtricitabine; Rilpivirine; Tenofovir alafenamide: (Major) Concomitant use of rilpivirine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. The degree of QT prolongation associated with rilpivirine is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose.
Emtricitabine; Rilpivirine; Tenofovir Disoproxil Fumarate: (Major) Concomitant use of rilpivirine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. The degree of QT prolongation associated with rilpivirine is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose.
Encorafenib: (Major) Concomitant use of ondansetron and encorafenib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.

Entrectinib: (Major) Concomitant use of ondansetron and entrectinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
eriBULin: (Major) Concomitant use of ondansetron and eribulin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Erythromycin: (Major) Concomitant use of ondansetron and erythromycin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Escitalopram: (Major) Concomitant use of ondansetron and escitalopram increases the risk of QT/QTc prolongation, torsade de pointes (TdP), and serotonin syndrome. Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. If concomitant use is necessary, consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, and monitor for serotonin syndrome.
Etrasimod: (Major) Concomitant use of etrasimod and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. Etrasimod has a limited effect on the QT/QTc interval at therapeutic doses but may cause bradycardia and atrioventricular conduction delays which may increase the risk for TdP in patients with a prolonged QT/QTc interval.
Etravirine: (Moderate) Etravirine is a CYP3A4 inducer/substrate and a P-glycoprotein (PGP) inhibitor and ondansetron is a CYP3A4 and PGP substrate. Caution is warranted if these drugs are coadministered.
Fenfluramine: (Moderate) Monitor for decreased efficacy of fenfluramine if coadministered with serotonin receptor antagonists. Concurrent use may decrease the

activity of fenfluramine. Also monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
fentaNYL: (Moderate) If concomitant use of fentanyl and ondansetron is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Fexinidazole: (Major) Concomitant use of ondansetron and fexinidazole increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Fingolimod: (Major) Concomitant use of ondansetron and fingolimod increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Flecainide: (Major) Concomitant use of ondansetron and flecainide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Fluconazole: (Contraindicated) 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. 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. Fluconazole is a CYP3A4 inhibitor. 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; however, since the publication of this data, ondansetron has been found to produce concentration-dependent QT prolongation. 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).
FLUoxetine: (Major) Due to the potential for QT prolongation, cautious use and close monitoring are advisable if concurrent use of fluoxetine and ondansetron is necessary. Both medications may cause QT interval prolongation and a risk for torsade de pointes (TdP). ECG monitoring has been recommended for at-risk patients. In addition, concurrent use of ondansetron with other drugs that modulate serotonergic function, such as fluoxetine, has resulted in serotonin syndrome in some cases. Patients should be carefully observed, particularly during treatment initiation and during dose adjustments. Discontinue the serotonergic medications if serotonin syndrome is suspected.
fluPHENAZine: (Minor) If ondansetron and fluphenazine must be coadministered, ECG monitoring is recommended. Ondansetron has been associated with a dose-related increase in the QT interval and postmarketing reports of torsade de pointes (TdP). Fluphenazine is associated with a possible risk for QT prolongation. Theoretically, fluphenazine may increase the risk of QT prolongation if coadministered with other drugs that have a risk of QT prolongation.
fluvoxaMINE: (Major) Concomitant use of fluvoxamine and ondansetron may increase the risk of serotonin syndrome, QT prolongation, and torsade de pointes (TdP). Cases of QT prolongation and TdP have been reported during postmarketing use of fluvoxamine. Ondansetron has been associated with a dose-related increase in the QT interval and postmarketing reports of TdP. If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended. In addition, both fluvoxamine and ondansetron have central serotonin enhancing effects; therefore, serotonin syndrome is possible. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical treatment should be implemented.
Fosamprenavir: (Moderate) Concomitant use of ondansetron and fosamprenavir may result in altered ondansetron plasma concentrations. Ondansetron is a substrate of the hepatic isoenzyme CYP3A4 and drug transporter P-glycoprotein (P-gp). Amprenavir, the active metabolite of fosamprenavir, is an inducer of P-gp and a potent inhibitor and moderate inducer of CYP3A4.
Foscarnet: (Major) Concomitant use of ondansetron and foscarnet increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation

associated with ondansetron significantly increases above this dose.
Fosphenytoin: (Minor) Fosphenytoin may reduce the efficacy of ondansetron by decreasing its systemic exposure; however, based on available data, no ondansetron dosage adjustment is recommended. If used together, monitor patients for antiemetic efficacy. Fosphenytoin is a strong CYP3A inducer. Ondansetron is a substrate for CY1A2, CYP2D6, and CYP3A4, with CYP3A4 playing a predominant role in ondansetron turnover. During pharmacokinetic studies, patients treated with strong CYP3A inducers (i.e., phenytoin, carbamazepine, rifampin) and ondansetron had significantly increased ondansetron clearance, resulting in significant reductions in AUC, Cmax, and half-life. However, these changes in ondansetron exposure are not thought to be clinically relevant.
Fostemsavir: (Major) Concomitant use of ondansetron and fostemsavir increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. The degree of QT prolongation associated with fostemsavir is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Gemifloxacin: (Major) Concomitant use of ondansetron and gemifloxacin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Gemtuzumab Ozogamicin: (Major) Concomitant use of ondansetron and gemtuzumab ozogamicin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Gepirone: (Major) Concomitant use of gepirone and ondansetron increases the risk of QT/QTc prolongation, torsade de pointes (TdP), and serotonin syndrome. Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, and monitor for

serotonin syndrome if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. QT prolongation with gepirone has been observed at 2 times the maximum recommended dose.
Gepotidacin: (Major) Concomitant use of gepotidacin and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Gilteritinib: (Major) Concomitant use of ondansetron and gilteritinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Givinostat: (Major) Concomitant use of givinostat and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. The degree of QT prolongation associated with givinostat is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 5 times the maximum recommended dose.
Glasdegib: (Major) Concomitant use of ondansetron and glasdegib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Glecaprevir; Pibrentasvir: (Moderate) Caution is advised with the coadministration of glecaprevir and ondansetron as coadministration may increase serum concentrations of ondansetron and increase the risk of adverse effects. Ondansetron is a substrate of P-glycoprotein (P-gp); glecaprevir is a P-gp inhibitor. (Moderate) Caution is advised with the coadministration of pibrentasvir and ondansetron as coadministration may increase

serum concentrations of ondansetron and increase the risk of adverse effects. Ondansetron is a substrate of P-glycoprotein (P-gp); pibrentasvir is a P-gp inhibitor.
Goserelin: (Major) Concomitant use of ondansetron and goserelin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Granisetron: (Major) 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. 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. 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.
Halogenated Anesthetics: (Major) Concomitant use of ondansetron and halogenated anesthetics increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Haloperidol: (Major) Concomitant use of ondansetron and haloperidol increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. The intravenous route may carry a higher risk for haloperidol-induced QT/QTc prolongation than other routes of administration.
Histrelin: (Major) Concomitant use of ondansetron and histrelin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.

Homatropine; HYDROcodone: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering hydrocodone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
HYDROcodone: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering hydrocodone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
HYDROcodone; Ibuprofen: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering hydrocodone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
HYDROmorphone: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering hydromorphone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Hydroxychloroquine: (Major) Concomitant use of hydroxychloroquine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
hydrOXYzine: (Major) Concomitant use of ondansetron and hydroxyzine increases the

risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate; Sodium Biphosphate: (Major) 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.
Ibutilide: (Major) Concomitant use of ondansetron and ibutilide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Idelalisib: (Major) Avoid concomitant use of idelalisib, a strong CYP3A inhibitor, with ondansetron, a CYP3A substrate, as ondansetron toxicities may be significantly increased. The AUC of a sensitive CYP3A substrate was increased 5.4-fold when coadministered with idelalisib.
Iloperidone: (Major) Concomitant use of ondansetron and iloperidone increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Inotuzumab Ozogamicin: (Major) Concomitant use of ondansetron and inotuzumab increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Isavuconazonium: (Moderate) Concomitant use of isavuconazonium with ondansetron may result in increased serum concentrations of ondansetron. Ondansetron is a substrate of the hepatic isoenzyme CYP3A4 and drug transporter P-glycoprotein (P-gp);

isavuconazole, the active moiety of isavuconazonium is an inhibitor of CYP3A4 and P-gp. Caution and close monitoring are advised if these drugs are used together.
Isocarboxazid: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant monoamine oxidase inhibitor (MAOI) and ondansetron use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Isoflurane: (Major) Concomitant use of ondansetron and halogenated anesthetics increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Itraconazole: (Major) Caution is advised when administering itraconazole with drugs that are known to prolong that QT interval and are metabolized by CYP3A4, such as ondansetron. Both ondansetron and itraconazole are associated with QT prolongation; coadministration may increase this risk. If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended. In addition, coadministration of itraconazole (a potent CYP3A4 inhibitor) with ondansetron (a CYP3A4 substrate) may result in elevated ondansetron plasma concentrations and an increased risk for adverse events, including QT prolongation. If itraconazole therapy is stopped, it may be prudent to continue close monitoring for up to 2 weeks after discontinuing itraconazole. Once discontinued, the plasma concentration of itraconazole decreases to almost undetectable concentrations within 7 to 14 days. The decline in plasma concentrations may be even more gradual in patients with hepatic cirrhosis or who are receiving concurrent CYP3A4 inhibitors.
Ivosidenib: (Major) Concomitant use of ondansetron and ivosidenib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Ketoconazole: (Contraindicated) Avoid concomitant use of ketoconazole and ondansetron due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. Ketoconazole is associated with an established risk for QT prolongation and TdP. Electrocardiogram (ECG) monitoring is recommended in patients at risk if use together cannot be avoided and is medically necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.

Lansoprazole; Amoxicillin; Clarithromycin: (Major) Concomitant use of ondansetron and clarithromycin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Lapatinib: (Major) Concomitant use of ondansetron and lapatinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Lasmiditan: (Moderate) Serotonin syndrome may occur during coadministration of lasmiditan and serotonin-receptor antagonists. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly after a dose increase or the addition of other serotonergic medications to an existing regimen. Discontinue all serotonergic agents if serotonin syndrome occurs and implement appropriate medical management.
Ledipasvir; Sofosbuvir: (Moderate) Caution and close monitoring of ondansetron-associated adverse reactions is advised with concomitant administration of ledipasvir. Ondansetron is a substrate of the drug transporter P-glycoprotein (P-gp); ledipasvir is a P-gp inhibitor. Taking these drugs together may increase ondansetron plasma concentrations.
Lefamulin: (Major) Concomitant use of ondansetron and lefamulin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Lenvatinib: (Major) Concomitant use of ondansetron and lenvatinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Leuprolide: (Major) Concomitant use of ondansetron and leuprolide increases the risk of

QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Leuprolide; Norethindrone: (Major) Concomitant use of ondansetron and leuprolide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
levoFLOXacin: (Major) Concomitant use of ondansetron and levofloxacin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Levoketoconazole: (Contraindicated) Avoid concomitant use of ketoconazole and ondansetron due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. Ketoconazole is associated with an established risk for QT prolongation and TdP. Electrocardiogram (ECG) monitoring is recommended in patients at risk if use together cannot be avoided and is medically necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Levomilnacipran: (Major) 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.
Levorphanol: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering levorphanol with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.

Linezolid: (Major) 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.
Lithium: (Major) Due to the potential for QT prolongation, cautious use and close monitoring are advisable if concurrent use of lithium and ondansetron is necessary. Both medications may cause QT interval prolongation and a risk for torsade de pointes (TdP). ECG monitoring has been recommended for at-risk patients. In addition, concurrent use of ondansetron with other drugs that modulate serotonergic function, such as lithium, has resulted in serotonin syndrome in some cases. Patients should be carefully observed, particularly during treatment initiation and during dose adjustments. Discontinue the serotonergic medications if serotonin syndrome is suspected.
(Moderate) Moderate to significant dietary sodium changes, or changes in sodium and fluid intake, may affect lithium excretion. Systemic sodium chloride administration may result in increased lithium excretion and therefore, decreased serum lithium concentrations. In addition, high fluid intake may increase lithium excretion. For patients receiving sodium-containing intravenous fluids, symptom control and lithium concentrations should be carefully monitored. It is recommended that patients taking lithium maintain consistent dietary sodium consumption and adequate fluid intake during the initial stabilization period and throughout lithium treatment. Supplemental oral sodium and fluid should be only be administered under careful medical supervision.
Lofexidine: (Major) Concomitant use of ondansetron and lofexidine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Loperamide: (Major) Concomitant use of ondansetron and loperamide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Loperamide; Simethicone: (Major) Concomitant use of ondansetron and loperamide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP.

Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Lopinavir; Ritonavir: (Major) Concomitant use of ondansetron and lopinavir increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. (Moderate) Caution and close monitoring are advised if these drugs are administered together. Ondansetron exposure may be altered resulting in increased adverse effects or decreased efficacy. Ondansetron is metabolized by the hepatic isoenzymes CYP3A4, CYP2D6, and CYP1A2; ritonavir inhibits CYP3A4 and CYP2D6 and induces CYP1A2.
Lumacaftor; Ivacaftor: (Minor) Lumacaftor; ivacaftor may reduce the efficacy of ondansetron by decreasing its systemic exposure; however, based on available data, no ondansetron dosage adjustment is recommended. If used together, monitor patients for antiemetic efficacy. Lumacaftor is a strong CYP3A inducer. Ondansetron is a substrate for CY1A2, CYP2D6, and CYP3A4, with CYP3A4 playing a predominant role in ondansetron turnover. During pharmacokinetic studies, patients treated with strong CYP3A inducers (i.e., phenytoin, carbamazepine, rifampin) and ondansetron had significantly increased ondansetron clearance, resulting in significant reductions in AUC, Cmax, and half-life. However, these changes in ondansetron exposure are not thought to be clinically relevant.
Lumacaftor; Ivacaftor: (Minor) Lumacaftor; ivacaftor may reduce the efficacy of ondansetron by decreasing its systemic exposure; however, based on available data, no ondansetron dosage adjustment is recommended. If used together, monitor patients for antiemetic efficacy. Lumacaftor is a strong CYP3A inducer. Ondansetron is a substrate for CY1A2, CYP2D6, and CYP3A4, with CYP3A4 playing a predominant role in ondansetron turnover. During pharmacokinetic studies, patients treated with strong CYP3A inducers (i.e., phenytoin, carbamazepine, rifampin) and ondansetron had significantly increased ondansetron clearance, resulting in significant reductions in AUC, Cmax, and half-life. However, these changes in ondansetron exposure are not thought to be clinically relevant.
Macimorelin: (Major) Concomitant use of ondansetron and macimorelin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation

associated with ondansetron significantly increases above this dose.
Maprotiline: (Major) Concomitant use of ondansetron and maprotiline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Mavorixafor: (Major) Concomitant use of mavorixafor and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. The degree of QT prolongation associated with mavorixafor is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Mefloquine: (Major) Concomitant use of ondansetron and mefloquine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Meperidine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering meperidine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Metaxalone: (Moderate) Concomitant use of metaxalone and serotonin-receptor antagonists (5HT-3 receptor antagonists) may increase the risk for serotonin syndrome. Monitor patients for serotonin syndrome if concomitant use is necessary.
Methadone: (Major) Concomitant use of ondansetron and methadone increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte

monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine: (Major) 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.
Methohexital: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Methylene Blue: (Major) 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.
metroNIDAZOLE: (Major) Concomitant use of metronidazole and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Midostaurin: (Major) Concomitant use of ondansetron and midostaurin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
miFEPRIStone: (Major) Concomitant use of ondansetron and mifepristone increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps

to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Mirabegron: (Moderate) Mirabegron is a moderate CYP2D6 inhibitor. Exposure of drugs partially metabolized by CYP2D6, such as ondansetron may be increased when co-administered with mirabegron. Therefore, appropriate monitoring and dose adjustment may be necessary.
Mirtazapine: (Major) Due to the potential for QT prolongation, cautious use and close monitoring are advisable if concurrent use of mirtazapine and ondansetron is necessary. Both medications may cause QT interval prolongation and a risk for torsade de pointes (TdP). ECG monitoring has been recommended for at-risk patients. In addition, concurrent use of ondansetron with other drugs that modulate serotonergic function, such as mirtazapine, has resulted in serotonin syndrome in some cases. Patients should be carefully observed, particularly during treatment initiation and during dose adjustments. Discontinue the serotonergic medications if serotonin syndrome is suspected.
Mitotane: (Minor) Use caution if mitotane and ondansetron are used concomitantly, and monitor for decreased efficacy of ondansetron and a possible change in dosage requirements. Mitotane is a strong CYP3A4 inducer and ondansetron is a CYP3A4 substrate; coadministration may result in decreased plasma concentrations of ondansetron. During pharmacokinetic studies, patients treated with strong CYP3A inducers (i.e., phenytoin, carbamazepine, rifampin) and ondansetron had significantly increased ondansetron clearance, resulting in significant reductions in AUC, Cmax, and half-life. However, these changes in ondansetron exposure are not thought to be clinically relevant.
Mobocertinib: (Major) Concomitant use of ondansetron and mobocertinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Monoamine oxidase inhibitors: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant monoamine oxidase inhibitor (MAOI) and ondansetron use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Morphine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering morphine with serotonin-receptor antagonist. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic

medications. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Moxifloxacin: (Major) Concomitant use of ondansetron and moxifloxacin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Nalbuphine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering nalbuphine with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Nilotinib: (Major) Avoid coadministration of nilotinib with ondansetron due to an increased risk for QT prolongation and torsade de pointes (TdP). Systemic exposure of ondansetron may also be increased resulting in an increase in ondansetron-related adverse reactions. Nilotinib is a moderate CYP3A4 inhibitor; sudden death and QT interval prolongation have occurred in patients who received nilotinib therapy. Ondansetron is a CYP3A4 substrate that has also been associated with a dose-related increase in the QT interval and postmarketing reports of TdP.
Nirmatrelvir; Ritonavir: (Moderate) Caution and close monitoring are advised if these drugs are administered together. Ondansetron exposure may be altered resulting in increased adverse effects or decreased efficacy. Ondansetron is metabolized by the hepatic isoenzymes CYP3A4, CYP2D6, and CYP1A2; ritonavir inhibits CYP3A4 and CYP2D6 and induces CYP1A2.
Ofloxacin: (Major) Concomitant use of ondansetron and ofloxacin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
OLANZapine: (Major) Concomitant use of ondansetron and olanzapine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte

monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
OLANZapine; FLUoxetine: (Major) Concomitant use of ondansetron and olanzapine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
(Major) Due to the potential for QT prolongation, cautious use and close monitoring are advisable if concurrent use of fluoxetine and ondansetron is necessary. Both medications may cause QT interval prolongation and a risk for torsade de pointes (TdP). ECG monitoring has been recommended for at-risk patients. In addition, concurrent use of ondansetron with other drugs that modulate serotonergic function, such as fluoxetine, has resulted in serotonin syndrome in some cases. Patients should be carefully observed, particularly during treatment initiation and during dose adjustments. Discontinue the serotonergic medications if serotonin syndrome is suspected.
OLANZapine; Samidorphan: (Major) Concomitant use of ondansetron and olanzapine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Oliceridine: (Moderate) If concomitant use of oliceridine and serotonin-receptor antagonists is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Omeprazole; Amoxicillin; Rifabutin: (Minor) Monitor for altered response to ondansetron during coadministration of rifabutin. Rifabutin may increase the clearance and decrease blood concentrations of ondansetron. However, no dosage adjustment for ondansetron is recommended during coadministration.
Oritavancin: (Minor) Ondansetron is metabolized by CYP3A4 and CYP2D6; oritavancin is a weak CYP3A4 and CYP2D6 inducer. Plasma concentrations and efficacy of ondansetron may be reduced if these drugs are administered concurrently.
Osilodrostat: (Major) Concomitant use of osilodrostat and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps

to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Osimertinib: (Major) Concomitant use of osimertinib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Oxaliplatin: (Major) Concomitant use of oxaliplatin and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
oxyCODONE: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering oxycodone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
oxyMORphone: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering oxymorphone with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Ozanimod: (Major) Concomitant use of ozanimod and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation

associated with ondansetron significantly increases above this dose. Ozanimod has a limited effect on the QT/QTc interval at therapeutic doses but may cause bradycardia and atrioventricular conduction delays which may increase the risk for TdP in patients with a prolonged QT/QTc interval.
Pacritinib: (Major) Concomitant use of pacritinib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Paliperidone: (Major) Concomitant use of paliperidone and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Panobinostat: (Major) 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%).
PARoxetine: (Major) Concomitant use of ondansetron and paroxetine increases the risk for serotonin syndrome. Avoid concomitant use if possible and monitor for serotonin syndrome if use is necessary.
Pasireotide: (Major) Concomitant use of pasireotide and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
PAZOPanib: (Major) Concomitant use of pazopanib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to

minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Pentamidine: (Major) Concomitant use of pentamidine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
PENTobarbital: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Perphenazine: (Minor) Due to a possible risk for QT prolongation and torsade de pointes (TdP), ondansetron and perphenazine should be used together cautiously. Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). 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 ($p < 0.0001$). If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended. Perphenazine, a phenothiazine, is associated with a possible risk for QT prolongation.
Perphenazine; Amitriptyline: (Minor) Due to a possible risk for QT prolongation and torsade de pointes (TdP), ondansetron and perphenazine should be used together cautiously. Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). 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 ($p < 0.0001$). If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended. Perphenazine, a phenothiazine, is associated with a possible risk for QT prolongation.
Phenelzine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant monoamine oxidase inhibitor (MAOI) and ondansetron use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.

PHENobarbital: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
PHENobarbital; Hyoscyamine; Atropine; Scopolamine: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Phenytoin: (Minor) Phenytoin may reduce the efficacy of ondansetron by decreasing its systemic exposure; however, based on available data, no ondansetron dosage adjustment is recommended. If used together, monitor patients for antiemetic efficacy. Phenytoin is a strong CYP3A inducer. Ondansetron is a substrate for CY1A2, CYP2D6, and CYP3A4, with CYP3A4 playing a predominant role in ondansetron turnover. During pharmacokinetic studies, patients treated with strong CYP3A inducers (i.e., phenytoin, carbamazepine, rifampin) and ondansetron had significantly increased ondansetron clearance, resulting in significant reductions in AUC, Cmax, and half-life. However, these changes in ondansetron exposure are not thought to be clinically relevant.
Pimavanserin: (Major) Concomitant use of pimavanserin and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Pimozide: (Contraindicated) Avoid concomitant use of pimozide and ondansetron due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Pitolisant: (Major) Concomitant use of pitolisant and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation

associated with ondansetron significantly increases above this dose.
Ponesimod: (Major) In general, do not initiate ponesimod in patients taking ondansetron due to the risk of additive bradycardia, QT prolongation, and torsade de pointes (TdP). If treatment initiation is considered, seek advice from a cardiologist. Ponesimod initiation may result in a transient decrease in heart rate and atrioventricular conduction delays. Ponesimod has not been studied in patients taking concurrent QT prolonging drugs; however, QT prolonging drugs have been associated with TdP in patients with bradycardia. Ondansetron has been associated with a dose-related increase in the QT interval and postmarketing reports of TdP.
Posaconazole: (Contraindicated) Concomitant administration of posaconazole and drugs that both prolong the QT interval and are CYP3A substrates is contraindicated according to the FDA-approved product labeling. 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. Posaconazole is a strong CYP3A inhibitor. 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; however, since the publication of this data, ondansetron has been found to produce concentration-dependent QT prolongation. It is not clear what degree of enzyme inhibition or increased concentration is required to increase the risk of QT prolongation.
Primaquine: (Major) Concomitant use of primaquine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Primidone: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Procainamide: (Major) Concomitant use of procainamide and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps

to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Prochlorperazine: (Minor) Due to a possible risk for QT prolongation and torsade de pointes (TdP), ondansetron and prochlorperazine should be used together cautiously. Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). 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 ($p < 0.0001$). If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended.
Phenothiazines have been reported to prolong the QT interval. If coadministration is considered necessary, and the patient has known risk factors for cardiac disease or arrhythmia, then close monitoring is essential.
Promethazine: (Major) Concomitant use of ondansetron and promethazine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Promethazine; Dextromethorphan: (Major) Concomitant use of ondansetron and promethazine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Promethazine; Phenylephrine: (Major) Concomitant use of ondansetron and promethazine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Propafenone: (Major) Concomitant use of ondansetron and propafenone increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
QUEtiapine: (Major) Avoid coadministration of ondansetron and quetiapine due to the risk of QT prolongation. Monitor ECG for evidence of QT prolongation if concurrent use cannot be avoided. Limited data, including some case reports, suggest that quetiapine

may be associated with a significant prolongation of the QTc interval in rare instances. Ondansetron has been associated with a dose-related increase in the QT interval and postmarketing reports of torsade de pointes (TdP).
quiNIDine: (Contraindicated) Quinidine administration is associated with QT prolongation and torsades de pointes (TdP). Quinidine inhibits CYP2D6 and has QT-prolonging actions; quinidine is contraindicated with other drugs that prolong the QT interval and are metabolized by CYP2D6 as the effects on the QT interval may be increased during concurrent use of these agents. Drugs that prolong the QT and are substrates for CYP2D6 that are contraindicated with quinidine include ondansetron.
quiNINE: (Major) Concurrent use of quinine and ondansetron should be avoided due to an increased risk for QT prolongation and torsade de pointes (TdP). Both drugs have been associated with prolongation of the QT interval and rare cases of TdP. In addition, concentrations of ondansetron may be increased with concomitant use of quinine. Ondansetron is a CYP3A4 and CYP2D6 substrate and quinine is an inhibitor of both enzymes.
Quizartinib: (Major) Concomitant use of quizartinib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Ranolazine: (Major) Due to a possible risk for QT prolongation and torsade de pointes (TdP), ondansetron and ranolazine should be used together cautiously. Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). 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 ($p < 0.0001$). If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended. Ranolazine is associated with dose- and plasma concentration-related increases in the QTc interval. The mean increase in QTc is about 6 milliseconds, measured at the tmax of the maximum dosage (1000 mg PO twice daily). However, in 5% of the population studied, increases in the QTc of at least 15 milliseconds have been reported. Although there are no studies examining the effects of ranolazine in patients receiving other QT prolonging drugs, coadministration of such drugs may result in additive QT prolongation. In addition, ondansetron is a substrate for CYP3A4 and CYP2D6 and P-glycoprotein (P-gp). Ranolazine is an inhibitor of CYP3A4 and CYP2D6 and P-gp. Concurrent administration of ranolazine and ondansetron may result in increased ondansetron concentrations.
Relugolix: (Major) Concomitant use of relugolix and ondansetron increases the risk of

QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Relugolix; Estradiol; Norethindrone acetate: (Major) Concomitant use of relugolix and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Remifentanil: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering remifentanil with serotonin-receptor antagonists. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Revumenib: (Major) Concomitant use of revumenib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Ribociclib: (Major) Avoid coadministration of ribociclib with ondansetron due to an increased risk for QT prolongation and torsade de pointes (TdP). Systemic exposure of ondansetron may also be increased resulting in an increase in ondansetron-related adverse reactions. Ribociclib is a strong CYP3A4 inhibitor that has been shown to prolong the QT interval in a concentration-dependent manner. Ondansetron is a CYP3A4 substrate that has also been associated with a dose-related increase in the QT interval and postmarketing reports of TdP. Concomitant use may increase the risk for QT prolongation.
Ribociclib; Letrozole: (Major) Avoid coadministration of ribociclib with ondansetron due to an increased risk for QT prolongation and torsade de pointes (TdP). Systemic exposure of ondansetron may also be increased resulting in an increase in ondansetron-related adverse reactions. Ribociclib is a strong CYP3A4 inhibitor that has been shown to prolong the QT interval in a concentration-dependent manner. Ondansetron is a CYP3A4 substrate that has also been associated with a dose-related increase in the QT interval

and postmarketing reports of TdP. Concomitant use may increase the risk for QT prolongation.
Rifabutin: (Minor) Monitor for altered response to ondansetron during coadministration of rifabutin. Rifabutin may increase the clearance and decrease blood concentrations of ondansetron. However, no dosage adjustment for ondansetron is recommended during coadministration.
rifAMPin: (Minor) Rifampin may reduce the efficacy of ondansetron by decreasing its systemic exposure; however, based on available data, no ondansetron dosage adjustment is recommended. If used together, monitor patients for antiemetic efficacy. In a pharmacokinetic study of 10 healthy subjects receiving a single-dose intravenous dose of ondansetron 8 mg after 600 mg rifampin once daily for 5 days, the AUC and the half-life of ondansetron were reduced by 48% and 46%, respectively. The proposed mechanism is rifampin-related induction of ondansetron metabolism through cytochrome P450 3A4. These changes in ondansetron exposure with CYP3A4 inducers are not thought to be clinically relevant.
Rilpivirine: (Major) Concomitant use of rilpivirine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. The degree of QT prolongation associated with rilpivirine is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose.
risperiDONE: (Major) Concomitant use of risperidone and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Ritonavir: (Moderate) Caution and close monitoring are advised if these drugs are administered together. Ondansetron exposure may be altered resulting in increased adverse effects or decreased efficacy. Ondansetron is metabolized by the hepatic isoenzymes CYP3A4, CYP2D6, and CYP1A2; ritonavir inhibits CYP3A4 and CYP2D6 and induces CYP1A2.
Rolapitant: (Major) Use caution if ondansetron and rolapitant are used concurrently, and monitor for ondansetron-related adverse effects. Ondansetron is a substrate of CYP2D6 and P-glycoprotein (P-gp) and rolapitant is an inhibitor of CYP2D6 and P-gp. The

inhibitory effect of rolapitant is expected to persist beyond 28 days for an unknown duration. Exposure to another CYP2D6 substrate, following a single dose of rolapitant increased about 3-fold on Days 8 and Day 22. The inhibition of CYP2D6 persisted on Day 28 with a 2.3-fold increase in the CYP2D6 substrate concentrations, the last time point measured. When oral rolapitant was administered with another P-gp substrate, the day 1 Cmax and AUC were increased by 70% and 30%, respectively; the Cmax and AUC on day 8 were not studied. When the P-gp substrate was administered with a single dose of intravenous rolapitant, no effect on AUC and a 21% increase in the Cmax of P-gp substrate was observed.
romiDEPsin: (Major) Concomitant use of romidepsin and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Saquinavir: (Major) Concurrent use of saquinavir boosted with ritonavir and ondansetron should be avoided if possible due to the risk of life threatening arrhythmias such as torsade de pointes (TdP). Saquinavir boosted with ritonavir is a potent inhibitor of CYP3A4, an isoenzyme responsible for the metabolism of ondansetron. 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. 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. If no alternative therapy is acceptable, perform a baseline ECG prior to initiation of concomitant therapy and follow recommended ECG monitoring.
Secobarbital: (Minor) Ondansetron elimination may be affected by cytochrome P-450 inducers. In a pharmacokinetic study of 16 patients with epilepsy who were maintained chronically on CYP3A4 inducers (e.g., barbiturates) a reduction in ondansetron AUC, Cmax, and half-life was observed, resulting in a significant increase in ondansetron clearance. However, these changes in ondansetron exposure are not thought to be clinically relevant; no dosage adjustment for ondansetron is recommended when CYP450 inducers are used concurrently.
Selegiline: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant selegiline and serotonin-receptor antagonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Selpercatinib: (Major) Concomitant use of selpercatinib and ondansetron increases the

risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Sertraline: (Major) Due to the potential for QT prolongation, cautious use and close monitoring are advisable if concurrent use of sertraline and ondansetron is necessary. Both medications may cause QT interval prolongation. The risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease. ECG monitoring has been recommended for at-risk patients. In addition, concurrent use of ondansetron with other drugs that modulate serotonergic function, such as SSRIs, has resulted in serotonin syndrome in some cases. Patients should be carefully observed, particularly during treatment initiation and during dose adjustments. Discontinue the serotonergic medications if serotonin syndrome is suspected.
Sevoflurane: (Major) Concomitant use of ondansetron and halogenated anesthetics increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Siponimod: (Major) Concomitant use of siponimod and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Sofosbuvir; Velpatasvir; Voxilaprevir: (Moderate) Plasma concentrations of ondansetron, a P-glycoprotein (P-gp) substrate, may be increased when administered concurrently with voxilaprevir, a P-gp inhibitor. Monitor patients for increased side effects if these drugs are administered concurrently.
Solifenacin: (Major) Concomitant use of solifenacin and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not

exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
SORAfenib: (Major) Concomitant use of sorafenib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Sotalol: (Major) Concomitant use of ondansetron and sotalol increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
St. John's Wort, Hypericum perforatum: (Minor) St. John's Wort may reduce the efficacy of ondansetron by decreasing its systemic exposure; however, based on available data, no ondansetron dosage adjustment is recommended. If used together, monitor patients for antiemetic efficacy. St. John's Wort is a strong CYP3A inducer. Ondansetron is a substrate for CY1A2, CYP2D6, and CYP3A4, with CYP3A4 playing a predominant role in ondansetron turnover. During pharmacokinetic studies, patients treated with strong CYP3A inducers (i.e., phenytoin, carbamazepine, rifampin) and ondansetron had significantly increased ondansetron clearance, resulting in significant reductions in AUC, Cmax, and half-life. However, these changes in ondansetron exposure are not thought to be clinically relevant.
SUFentanil: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering sufentanil with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
SUNItinib: (Major) Concomitant use of sunitinib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Tacrolimus: (Major) Concomitant use of tacrolimus and ondansetron increases the risk

of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Taletrectinib: (Major) Concomitant use of taletrectinib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Tamoxifen: (Major) Concomitant use of ondansetron and tamoxifen increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Tapentadol: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering tapentadol with serotonin-receptor antagonists. The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists, mostly when used in combination with other serotonergic medications. Inform patients taking this combination of the possible increased risks and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Telavancin: (Major) Concomitant use of telavancin and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Tetrabenazine: (Major) Concomitant use of tetrabenazine and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.

Thioridazine: (Contraindicated) Avoid concomitant use of thioridazine and ondansetron due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Tolterodine: (Major) Due to the potential for QT prolongation and torsade de pointes (TdP), caution is advised when administering tolterodine with ondansetron. If these drugs must be coadministered, ECG monitoring is recommended. Tolterodine has been associated with dose-dependent prolongation of the QT interval, especially in poor CYP2D6 metabolizers. Ondansetron has been associated with QT prolongation and post-marketing reports of TdP. 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 ($p < 0.0001$). 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.
Tolvaptan: (Moderate) Coadministration of tolvaptan and hypertonic saline (e.g., 3% NaCl injection solution) is not recommended. The use of hypertonic sodium chloride in combination with tolvaptan may result in a too rapid correction of hyponatremia and increase the risk of osmotic demyelination (i.e., central pontine myelinolysis).
Toremifene: (Major) Concomitant use of toremifene and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
traMADol: (Moderate) Monitor for opioid withdrawal and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant ondansetron and tramadol use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome. Also, data from 2 small trials indicate that concomitant use of ondansetron may result in reduced analgesic activity of tramadol; patients receiving ondansetron used tramadol more frequently leading to an increased cumulative dose in patient-controlled administration of tramadol.
Tramadol; Acetaminophen: (Moderate) Monitor for opioid withdrawal and for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant ondansetron and tramadol use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome. Also, data from 2 small trials indicate that concomitant use of ondansetron may result in reduced analgesic activity of tramadol; patients receiving ondansetron used tramadol

more frequently leading to an increased cumulative dose in patient-controlled administration of tramadol.
Tranylcypromine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant monoamine oxidase inhibitor (MAOI) and ondansetron use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
traZODone: (Major) Concomitant use of ondansetron and trazodone increases the risk of QT/QTc prolongation, torsade de pointes (TdP), and serotonin syndrome. Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. If concomitant use is necessary, consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, and monitor for serotonin syndrome.
Triclabendazole: (Major) Concomitant use of triclabendazole and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Trifluoperazine: (Minor) Due to a possible risk for QT prolongation and torsade de pointes (TdP), ondansetron and trifluoperazine should be used together cautiously. Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). 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 ($p < 0.0001$). If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended. Trifluoperazine, a phenothiazine, is associated with a possible risk for QT prolongation.
Triptorelin: (Major) Concomitant use of triptorelin and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Vandetanib: (Major) Concomitant use of vandetanib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not

exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Vardenafil: (Major) Concomitant use of ondansetron and vardenafil increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Vemurafenib: (Major) Concomitant use of vemurafenib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Venlafaxine: (Major) Concomitant use of ondansetron and venlafaxine increases the risk of QT/QTc prolongation, torsade de pointes (TdP), and serotonin syndrome. Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. If concomitant use is necessary, consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, and monitor for serotonin syndrome.
Vilazodone: (Major) 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.
Voclosporin: (Major) Concomitant use of voclosporin and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose. The degree of QT prolongation associated with voclosporin is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose.
Vonoprazan; Amoxicillin; Clarithromycin: (Major) Concomitant use of ondansetron and clarithromycin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for

TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Voriconazole: (Major) Caution is advised when administering voriconazole with drugs that are known to prolong that QT interval and are metabolized by CYP3A4, such as ondansetron. Ondansetron has been associated with QT prolongation and postmarketing reports of torsade de pointes (TdP). Voriconazole has been associated with QT prolongation and rare cases of TdP, cardiac arrest, and sudden death. Use of these drugs together increases the risk for QT prolongation. If ondansetron and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended. In addition, coadministration of voriconazole (a strong CYP3A4 inhibitor) with ondansetron (a CYP3A4 substrate) may result in elevated ondansetron plasma concentrations and could increase the risk for adverse events, including QT prolongation. If these drugs are given together, closely monitor for prolongation of the QT interval. Rigorous attempts to correct any electrolyte abnormalities (i.e., potassium, magnesium, calcium) should be made before initiating concurrent therapy.
Vorinostat: (Major) Concomitant use of vorinostat and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Ziftomenib: (Major) Concomitant use of ziftomenib and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Ziprasidone: (Major) Concomitant use of ziprasidone and ondansetron increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. Do not exceed 16 mg of IV ondansetron in a single dose; the degree of QT prolongation associated with ondansetron significantly increases above this dose.
Zonisamide: (Minor) Zonisamide is a weak inhibitor of P-glycoprotein (P-gp), and ondansetron is a substrate of P-gp. There is theoretical potential for zonisamide to affect

the pharmacokinetics of drugs that are P-gp substrates. Use caution when starting or stopping zonisamide or changing the zonisamide dosage in patients also receiving drugs which are P-gp substrates.

Adverse Reaction

constipation, diarrhea, hiccups

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. Hiccups have been reported during post-marketing experience with ondansetron.

urinary retention

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

agitation, anxiety, dizziness, drowsiness, dystonic reaction, fatigue, headache, malaise, paresthesias, seizures

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. In one case, extrapyramidal reactions were confirmed by rechallenge. In addition, there have been rare reports of grand mal seizures in patients receiving ondansetron, although a casual relationship has not been established.

elevated hepatic enzymes, hepatic failure

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.

hypokalemia

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

acute myocardial ischemia, angina, atrial fibrillation, AV block, bradycardia, chest pain (unspecified), coronary vasospasm, hypotension, palpitations, premature ventricular contractions (PVCs), QT prolongation, sinus tachycardia, ST-T wave changes, supraventricular tachycardia (SVT), syncope, torsade de pointes, ventricular tachycardia

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. 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), atrial fibrillation, and acute myocardial ischemia have been reported during postmarketing use of ondansetron. In some cases, predominantly during intravenous administration, the symptoms of myocardial ischemia appeared immediately after administration but resolved with prompt treatment. Coronary vasospasm (coronary artery spasm) appears to be the most common cause of the ischemia. To minimize the risk of these adverse events in patients receiving intravenous treatment, do not exceed the recommended ondansetron infusion rate and monitor patients for signs and symptoms of myocardial ischemia during and after administration. In patients receiving

oral therapy, monitor or advise patients of these symptoms. Intravenous (IV) ondansetron given as a single 32 mg dose causes QT prolongation in a dose-dependent manner; therefore, single IV doses should not exceed 16 mg/dose IV; the 32 mg IV single-dose regimen is no longer indicated for chemotherapy-induced nausea and vomiting (CINV). Oral dosing recommendations have not changed. 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.

anaphylactoid reactions, angioedema, bronchospasm, cardiac arrest, dyspnea, flushing, laryngeal edema, laryngospasm, pruritus, rash (unspecified), respiratory arrest, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria

Several reports of anaphylactoid reactions have been associated with serotonin (5-HT3) receptor antagonists, such as ondansetron. 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. Stevens-Johnson syndrome and toxic epidermal necrolysis (TENS) have been reported with post-marketing use of ondansetron.

injection site reaction

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.

blurred vision, visual impairment

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.
In another case, transient blindness was reported in a patient who received ondansetron 4mg as a post-operative rapid IV bolus dose. 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.

chills, fever

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).

serotonin syndrome

Serotonin syndrome has been reported with 5-HT3 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.

Description

Ondansetron is an oral and parenteral serotonin (5-HT3) receptor antagonist. Ondansetron is used as an antiemetic agent for the prevention and treatment of nausea and vomiting during chemotherapy, radiation therapy, and surgery. 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. 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. When administered at optimal doses, ondansetron and other 5HT3 receptor antagonists (e.g., granisetron) are equally effective. The American Society of Clinical Oncology (ASCO) guidelines recommend that adult patients who are treated with moderate to high-emetic-risk chemotherapy agents should be offered a 3-drug combination of a 5-HT3 receptor antagonist, a neurokinin 1 (NK1) receptor antagonist, and dexamethasone; olanzapine is also added to the 3-drug combination during use of high-emetic-risk agents. Children receiving moderate to high-emetic-risk agents should be offered a 2-drug combination of a 5-HT3 receptor antagonist and dexamethasone; aprepitant is also added to the 2-drug combination during use of high-emetic-risk agents. The Society for Ambulatory Anesthesia (SAMBA) guidelines recommend the use of a 5-HT3 receptor antagonist as the first choice for prophylaxis of postoperative nausea and vomiting in children.

Mechanism Of Action

Ondansetron is a 5-HT3 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. Peripherally, ondansetron preferentially blocks the serotonin 5-hydroxytryptamine, type 3 (5-HT3) 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-HT1B, 5-HT1C, alpha-adrenergic, and opioid mu receptors; the clinical implications of these actions is uncertain. It has no activity at dopamine receptors.

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-HT3 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.

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.

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. 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. 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. 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.

- **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.

- **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.

- **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. 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. 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.

- **Geriatric**

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

- **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.

Administration

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

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.

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.

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 to 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.

Injectable Administration

Visually inspect parenteral products for particulate matter and discoloration prior to

administration whenever solution and container permit.

Intravenous Administration

IV Push
Doses up to 4 mg may be administered undiluted (2 mg/mL) over at least 30 seconds and preferably over a period of 2 to 5 minutes.

Intermittent IV Infusion
For doses more than 4 mg and for chemotherapy-induced nausea and vomiting (CINV), dilute ondansetron in 50 mL of 5% Dextrose Injection or 0.9% Sodium Chloride Injection.
For patients 6 months to 1 year of age and/or 10 kg or less: Doses may be diluted in 10 to 50 mL of 5% Dextrose Injection or 0.9% Sodium Chloride Injection, depending on the fluid needs of the individual patient.
Infuse IV over 15 minutes.
Storage: Dilution is stable for 48 hours at room temperature.

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.

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.

Dosage Forms

- Ondansetron 16mg Oral disintegrating tablet
- Ondansetron 4mg Oral disintegrating tablet
- Ondansetron 8mg Oral disintegrating tablet
- Ondansetron Hydrochloride 24mg Oral tablet
- Ondansetron Hydrochloride 2mg/1mL Solution for injection
- Ondansetron Hydrochloride 4mg Oral tablet
- Ondansetron Hydrochloride 4mg/5mL Oral solution
- Ondansetron Hydrochloride 8mg Oral tablet
- Ondansetron Hydrochloride Bulk powder
- Sumansetron Kit
- Zuplenz 4mg Oral Soluble Film
- Zuplenz 8mg Oral Soluble Film

Dosage Adjustment Guidelines

Hepatic Impairment

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. No specific pediatric recommendations are available.

Renal Impairment

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.