Brand Names

Desyrel, Oleptro, Raldesy

Indication Specific Dosing

For the treatment of major depression

Oral dosage (immediate-release)

Adults

150 mg/day PO in divided doses, initially. May increase the dose by 50 mg/day every 3 to 4 days if inadequate response and depending on tolerability. Usual Max: 400 mg/day. Max: 600 mg/day, in divided doses.

Adolescents†

25 mg PO once daily at bedtime, or alternatively 1.5 to 2 mg/kg/day PO in divided doses, initially. May increase the dose every 3 to 4 days if inadequate response and based on tolerability. Max: 100 to 150 mg/day or 6 mg/kg/day in divided doses. Due to limited data, trazodone is not considered a first-line agent in this population.

Children† 6 to 12 years

1.5 to 2 mg/kg/day PO in divided doses, initially. May increase the dose every 3 to 4 days if inadequate response and based on tolerability. Max: 6 mg/kg/day in divided doses (not to exceed 150 mg/day). Due to limited data, trazodone is not considered a first-line agent in this population.

For the treatment of insomnia†

Oral dosage

Adults

25 to 50 mg PO once daily at bedtime, initially. Increase the dose as needed and

tolerated. Max: 150 mg/day. Guidelines recommend against trazodone for chronic insomnia based on a short-term trial which evaluated trazodone 50 mg/day and found no clinically significant improvement in sleep outcomes and significantly more side effects (e.g., headache, daytime somnolence) vs. placebo; other studies were considered inadequate for assessment. Antidepressants like trazodone may be considered for insomnia when there is a co-existing mood disorder and therapeutic antidepressant doses are used. Findings from one large systematic review suggest a small improvement in sleep quality during short-term use of low-dose trazodone; however, additional studies are needed to determine long-term safety and efficacy.

Children and Adolescents 8 to 17 years

12.5 to 25 mg PO once daily at bedtime, initially. Increase the dose as needed and tolerated. Max: 150 mg/day. Data to support the use of trazodone in pediatric patients is limited; most studies utilize adult data or include pediatric patients with concomitant neurodevelopmental disorders or depressive symptoms which may contribute to sleep disruptions. As sleep disturbances can be a presenting symptom of underlying physical or psychiatric concerns, treatment should occur after a careful evaluation of the patient.

For the treatment of generalized anxiety disorder (GAD)†

Oral dosage (immediate release)

Adults

150 mg/day PO in divided doses, initially. May increase by 50 mg/day every 3 to 4 days as needed/tolerated. In one study, the mean maximum daily effective dose was 255 mg/day. Usual outpatient max: 400 mg/day. Max: 600 mg/day.

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. Trazodone use should also be avoided in people with a hypersensitivity to other phenylpiperazine antidepressants (e.g., nefazodone).

adolescents, children, suicidal ideation

Safety and efficacy of trazodone for the treatment of depression have not been established in pediatric patients less than 18 years of age. A boxed warning in the product label describes the risk of suicidality and suicidal ideation in children, adolescents, and young adults receiving antidepressants. Monitor all patients receiving antidepressants closely for clinical worsening, suicidal ideation, and unusual changes in mood or behavior, especially during the first few months of therapy and after any dosage adjustment. Instruct caregivers and patients to immediately notify the prescriber of changes in behavior or suicidal ideation. Consider changing the therapeutic regimen or discontinuing the medication in patients with persistent or worrisome symptoms, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. In a pooled analysis of placebo-controlled trials of antidepressants (n = 4,500 pediatrics and 77,000 adults), there was an increased risk for suicidal thoughts and behaviors in people 24 years of age and younger receiving an antidepressant versus placebo, with considerable variation in the risk of suicidality among drugs. The difference in absolute risk of suicidal thoughts and behaviors across different indications was highest in those with major depression. The need for an antidepressant in children, adolescents, or young adults for any use must be weighed against the risk of suicidality; it is unknown if this risk extends to long-term use. Monitor for symptom worsening or suicidality, especially at treatment initiation or after dose changes.

bipolar disorder

Activation of mania, hypomania, or a mixed episode may occur with medications used to treat depression, especially in people predisposed to bipolar disorder. A major depressive episode may be the initial presentation of bipolar disorder. Prior to initiating treatment with trazodone, people with depressive symptoms should be screened for risk factors for bipolar disorder, including a detailed personal psychiatric history and family history of bipolar disorder, suicide, and/or depression. If an individual taking trazodone develops symptoms consistent with mania or hypomania, the medication should be discontinued, and appropriate therapy should be initiated.

bradycardia, cardiac disease, cardiomyopathy, congenital long QT syndrome, coronary artery disease, females, hypocalcemia, hypokalemia, hypomagnesemia, myocardial infarction, QT prolongation

Avoid use of trazodone 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. Trazodone should also be avoided in people with a history of cardiac arrhythmias and is not recommended for use in during the initial recovery phase of myocardial infarction. Clinical studies indicate that trazodone may be arrhythmogenic in people with pre-existing cardiac disease; caution and close monitoring is advised when giving trazodone to people with cardiac disease.

activities requiring coordination and concentration, driving or operating machinery

Trazodone has the potential to impair judgment, thinking, or motor skills. Patients should use caution when driving or operating machinery or participating in other activities requiring coordination and concentration until they are reasonably certain that trazodone does not affect them adversely. Trazodone may enhance the response to alcohol, barbiturates, and other CNS depressants.

hypovolemia

Antidepressants, including trazodone, are associated with significant hyponatremia resulting from the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Older adults, people taking diuretics, and those who have hypovolemia appear to be at greatest risk. Hyponatremia during antidepressant use has resulted in serum sodium levels less than 110 mmol/L in some cases. However, the adverse effect appears to be reversible upon discontinuation of the causative medication. Symptomatic hyponatremia may require discontinuation of trazodone, as well as implementation of the appropriate medical interventions.

electroconvulsive therapy (ECT)

There is limited data examining the use of trazodone during electroconvulsive therapy (ECT). While limited case reports indicate minimal effect on ECT-related seizure duration with trazodone, there have been reports of reduced seizure threshold and increased risk of serotonin syndrome when other serotonergic agents were given concomitantly with ECT.

closed-angle glaucoma, narrow iridocorneal angles

Caution is recommended when prescribing trazodone to people with closed-angle

glaucoma. The pupillary dilation that can occur with antidepressants may precipitate a closed-angle glaucoma attack in those with anatomically narrow iridocorneal angles who do not have a patent iridectomy.

leukemia, multiple myeloma, penile angulation, Peyronie disease, priapism, sickle cell disease

Use trazodone with caution in people who have conditions that might predispose them to priapism (e.g., sickle cell disease, multiple myeloma, or leukemia), or in people with anatomical deformation of the penis (e.g., penile angulation, cavernosal fibrosis, or Peyronie disease). Rare cases of priapism have been reported with trazodone use.

geriatric

Clinical experience with trazodone has not identified differences in response to the drug in geriatric compared to younger adults, but data are limited. Geriatric adults appear more susceptible than younger adults to trazodone adverse reactions such as sedation, orthostatic hypotension, or hyponatremia due to SIADH. The U.S. Omnibus Budget Reconciliation Act (OBRA) regulates antidepressant use in long-term care facilities. When used to manage behavior, stabilize mood, or treat a psychiatric disorder, tapering as outlined in the OBRA guidelines should be attempted unless clinically contraindicated. Dosages and durations of treatment used should align with prescribing labels, published literature recommendations, and expert guidelines.

pregnancy

Although available studies cannot definitively establish the absence of risk, published prospective cohort studies, case series, and case reports over several decades have not identified an association with the use of trazodone during pregnancy and major birth defects, miscarriage, or other adverse outcomes. However, available studies have methodological limitations, including small sample sizes and inconsistent comparator groups. Consider the risk of untreated depression versus the potential for adverse fetal outcomes when discontinuing or changing treatment with trazodone during pregnancy and postpartum. In a prospective study of 201 pregnant individuals with a history of major depressive disorder who were euthymic and on antidepressants at pregnancy onset, those who discontinued antidepressants were more likely to experience a relapse than those who continued treatment. There is a pregnancy exposure registry that monitors outcomes in pregnant people exposed to trazodone; information about the registry can be obtained at womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/antidepressants or by calling 1-866-961-2388 or 1-844-405-6185.

breast-feeding

Use trazodone with caution during breast-feeding. Trazodone is excreted into human milk at low levels. Limited data from postmarketing reports have not identified trazodone-associated adverse effects in the breastfed child. There are no data regarding the effect of trazodone on milk production. Consider an alternative therapy for individuals wanting to breast-feed. A pooled analysis found that the use of sertraline, nortriptyline, and paroxetine during breast-feeding usually produced undetectable or low drug concentrations in infant serum and, therefore, may be the preferred antidepressants for breast-feeding individuals. However, the individual's prior antidepressant trials and the risk of symptom relapse during transition to a new medication may preclude the use of alternatives. Consider the benefits of breast-feeding, the patient's clinical need for treatment, and any potential adverse effects on the breast-fed child from the medication or from the patient's underlying medical condition.

Pregnancy And Lactation

Although available studies cannot definitively establish the absence of risk, published prospective cohort studies, case series, and case reports over several decades have not identified an association with the use of trazodone during pregnancy and major birth defects, miscarriage, or other adverse outcomes. However, available studies have methodological limitations, including small sample sizes and inconsistent comparator groups. Consider the risk of untreated depression versus the potential for adverse fetal outcomes when discontinuing or changing treatment with trazodone during pregnancy and postpartum. In a prospective study of 201 pregnant individuals with a history of major depressive disorder who were euthymic and on antidepressants at pregnancy onset, those who discontinued antidepressants were more likely to experience a relapse than those who continued treatment. There is a pregnancy exposure registry that monitors outcomes in pregnant people exposed to trazodone; information about the registry can be obtained at womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/antidepressants or by calling 1-866-961-2388 or 1-844-405-6185.

Interactions

Acebutolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with

trazodone.
Acetaminophen; Aspirin, ASA; Caffeine: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Acetaminophen; Aspirin: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Acetaminophen; Aspirin; diphenhydrAMINE: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant. (Moderate) Monitor for unusual drowsiness and sedation during coadministration of diphenhydramine and trazodone due to the risk for additive CNS depression.
Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) Using trazodone and dihydrocodeine together may increase the risk for drowsiness, sedation, and CNS depression. There may be an increased risk for serotonin syndrome. Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dihydrocodeine with trazadone. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Acetaminophen; Caffeine; Pyrilamine: (Moderate) Antihistamines that may cause sedation, such as pyrilamine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Acetaminophen; Chlorpheniramine: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Acetaminophen; Chlorpheniramine; Dextromethorphan: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients

receiving trazodone because of additive CNS-depressant effects.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Acetaminophen; Chlorpheniramine; Phenylephrine : (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Acetaminophen; Codeine: (Moderate) Because of the potential risk and severity of excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Acetaminophen; Dextromethorphan; Doxylamine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of doxylamine and trazodone due to the risk for additive CNS depression.
Acetaminophen; diphenhydrAMINE: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of diphenhydramine and trazodone due to the risk for additive CNS depression.
Acetaminophen; HYDROcodone: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering hydrocodone with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Acetaminophen; Ibuprofen: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding

complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Acetaminophen; oxyCODONE: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering oxycodone with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Acetaminophen; Pamabrom; Pyrilamine: (Moderate) Antihistamines that may cause sedation, such as pyrilamine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
acetaZOLAMIDE: (Moderate) Trazodone can lower the seizure threshold of anticonvulsants, although the overall risk is low at therapeutic doses. Patients may require increased concentrations of anticonvulsants to achieve equivalent effects if trazodone is added.
Adagrasib: (Major) Avoid concomitant use of adagrasib and trazodone due to the potential for increased trazodone exposure and additive risk for QT/QTc prolongation and torsade de pointes (TdP). If use is necessary, consider a reduced dose of trazodone based on tolerability. Additionally, consider taking steps to minimize the risk for QT prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring. Trazodone is a CYP3A substrate, adagrasib is a strong CYP3A inhibitor, and both medications have been associated with QT interval prolongation.
ALFentanil: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering alifentanil with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Alfuzosin: (Major) Concomitant use of trazodone 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.
Aliskiren; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Almotriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
ALPRAZolam: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Alteplase: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving thrombolytic agents. Patients should be closely monitored for signs and symptoms of bleeding when a thrombolytic agent is administered with trazodone.
aMILoride: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
aMILoride; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Aminosalicylate sodium, Aminosalicylic acid: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Amiodarone: (Major) Concomitant use of amiodarone and trazodone 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. 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 trazodone 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.
Amitriptyline: (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for additive CNS depression and serotonin syndrome.
amLODIPine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
amLODIPine; Atorvastatin: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
amLODIPine; Benazepril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
amLODIPine; Celecoxib: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive

agent may be required when given with trazodone.
amLODIPine; Olmesartan: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
amLODIPine; Valsartan: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
amLODIPine; Valsartan; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Amobarbital: (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and amobarbital. Concurrent use may result in additive CNS depression.
Amoxapine: (Moderate) Monitor for excessive sedation and somnolence during coadministration of amoxapine and trazodone. Concurrent use may result in additive CNS depression.
Amoxicillin; Clarithromycin; Omeprazole: (Major) Avoid coadministration of trazodone with clarithromycin due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; clarithromycin is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Amphetamine: (Moderate) Coadministration of trazodone and amphetamines may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. The MAOI activity of amphetamines may also be of concern with trazodone. Inform patients taking this combination of the possible increased risk and

monitor for the emergence of serotonin syndrome. Serotonergic agents should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.
Amphetamine; Dextroamphetamine: (Moderate) Coadministration of trazodone and amphetamines may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. The MAOI activity of amphetamines may also be of concern with trazodone. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Serotonergic agents should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.
Amphetamines: (Moderate) Coadministration of trazodone and amphetamines may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. The MAOI activity of amphetamines may also be of concern with trazodone. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Serotonergic agents should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.
Anagrelide: (Major) Torsades de pointes (TdP) and ventricular tachycardia have been reported during post-marketing use of anagrelide. A cardiovascular examination, including an ECG, should be obtained in all patients prior to initiating anagrelide therapy. Monitor patients during anagrelide therapy for cardiovascular effects and evaluate as necessary. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with anagrelide include trazodone.
In addition, platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving platelet inhibitors. Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with an antiplatelet medication and to promptly report any bleeding events to the practitioner.
Angiotensin II receptor antagonists: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Angiotensin-converting enzyme inhibitors: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Anticoagulants: (Moderate) Patients should be instructed to monitor for signs and

symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Antithrombin III: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Apalutamide: (Moderate) Consider increasing the trazodone dose based on therapeutic response when coadministered with apalutamide. Concurrent use may decrease trazodone exposure. Trazodone is a CYP3A4 substrate; apalutamide is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Apixaban: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Apomorphine: (Major) Apomorphine should be avoided in combination with trazodone due to the potential for additive QT prolongation and sedation. Dose-related QTc prolongation is associated with therapeutic apomorphine exposure. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are postmarketing reports of torsade de pointes (TdP). Apomorphine also causes considerable somnolence, and concomitant administration of apomorphine and CNS depressants like trazodone could result in additive CNS effects.
Aprepitant, Fosaprepitant: (Major) Use caution if trazodone and aprepitant, fosaprepitant are used concurrently and monitor for an increase in trazodone-related adverse effects for several days after administration of a multi-day aprepitant regimen. Trazodone 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 and may increase plasma concentrations of trazodone. For example, a 5-day oral aprepitant

regimen increased the AUC of another CYP3A4 substrate, midazolam (single dose), by 2.3-fold on day 1 and by 3.3-fold on day 5. After a 3-day oral aprepitant regimen, the AUC of midazolam (given on days 1, 4, 8, and 15) increased by 25% on day 4, and then decreased by 19% and 4% on days 8 and 15, respectively. As a single 125 mg or 40 mg oral dose, the inhibitory effect of aprepitant on CYP3A4 is weak, with the AUC of midazolam increased by 1.5-fold and 1.2-fold, respectively. After administration, fosaprepitant is rapidly converted to aprepitant and shares many of the same drug interactions. However, as a single 150 mg intravenous dose, fosaprepitant only weakly inhibits CYP3A4 for a duration of 2 days; there is no evidence of CYP3A4 induction. Fosaprepitant 150 mg IV as a single dose increased the AUC of midazolam (given on days 1 and 4) by approximately 1.8-fold on day 1; there was no effect on day 4. Less than a 2-fold increase in the midazolam AUC is not considered clinically important.
Argatroban: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
ARIPiprazole: (Major) QT prolongation has occurred during therapeutic use of aripiprazole and following overdose. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are postmarketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval.
Arsenic Trioxide: (Major) Concomitant use of trazodone 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.
Artemether; Lumefantrine: (Major) Concomitant use of trazodone 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.
Asenapine: (Major) Asenapine has been associated with QT prolongation. According to the manufacturer of asenapine, the drug should be avoided in combination with other agents also known to have this effect, such as trazodone. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of

torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval. In addition, coadministration may increase adverse effects such as drowsiness, sedation, and dizziness.
Aspirin, ASA: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Aspirin, ASA; Butalbital; Caffeine: (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and butalbital. Concurrent use may result in additive CNS depression. (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Aspirin, ASA; Caffeine: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Aspirin, ASA; Caffeine; Orphenadrine: (Moderate) CNS depressants, such as skeletal muscle relaxants, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension. A dose reduction of one or both drugs may be warranted. (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Aspirin, ASA; Carisoprodol; Codeine: (Moderate) Because of the potential risk and

severity of excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. (Moderate) CNS depressants, such as carisoprodol, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension. A dose reduction of one or both drugs may be warranted. (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Aspirin, ASA; Citric Acid; Sodium Bicarbonate: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Aspirin, ASA; Dipyridamole: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant. (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving platelet inhibitors (e.g., cilostazol, clopidogrel, dipyridamole,

ticlopidine, platelet glycoprotein IIb/IIIa inhibitors). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with an antiplatelet medication and to promptly report any bleeding events to the practitioner.
Aspirin, ASA; Omeprazole: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Aspirin, ASA; oxyCODONE: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering oxycodone with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Atazanavir: (Major) Avoid coadministration of trazodone with atazanavir due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; atazanavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Atazanavir; Cobicistat: (Major) Avoid coadministration of trazodone with atazanavir due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; atazanavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased

the exposure of trazodone compared to the use of trazodone alone. (Major) Avoid coadministration of trazodone with cobicistat due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; cobicistat is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Atenolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Atenolol; Chlorthalidone: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Atomoxetine: (Major) Concomitant use of atomoxetine and trazodone 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.
Atropine; Difenoxin: (Moderate) Concurrent administration of diphenoxylate/difenoxin with trazodone can potentiate the CNS-depressant effects of diphenoxylate/difenoxin. Use caution during coadministration.
Azelastine: (Moderate) Monitor for excessive sedation and somnolence during coadministration of azelastine and trazodone. Concurrent use may result in additive CNS depression.
Azelastine; Fluticasone: (Moderate) Monitor for excessive sedation and somnolence during coadministration of azelastine and trazodone. Concurrent use may result in additive CNS depression.
Azilsartan: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Azilsartan; Chlorthalidone: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Azithromycin: (Major) Concomitant use of azithromycin and trazodone 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.
Baclofen: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of baclofen and trazodone due to the risk for additive CNS depression.
Bedaquiline: (Major) Avoid coadministration of bedaquiline and trazodone. Bedaquiline has been reported to prolong the QT interval. Prior to initiating bedaquiline, obtain serum electrolyte concentrations and a baseline ECG. An ECG should also be performed at least 2, 12, and 24 weeks after starting bedaquiline therapy. Coadministration with other QT prolonging drugs may result in additive or synergistic prolongation of the QT interval. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval.
Belladonna; Opium: (Moderate) Concomitant use of opioid agonists with trazodone may cause excessive sedation, somnolence, and increased risk of serotonin syndrome. Limit the use of opioid medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Educate patients about the risks and symptoms of excessive CNS depression and serotonin syndrome.
Benazepril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Benazepril; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Benzhydrocodone; Acetaminophen: (Moderate) Concomitant use of benzhydrocodone with trazodone may cause excessive sedation, somnolence, and increased risk of serotonin syndrome. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Educate patients about the risks and symptoms of excessive CNS depression and serotonin syndrome.
Benzodiazepines: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Contraindicated) According to the manufacturer of trazodone, treatment initiation with trazodone is contraindicated in patients currently receiving intravenous methylene blue

due to an increased risk of serotonin syndrome. If urgent psychiatric treatment is required, interventions other than trazodone (e.g., alternative medication, hospitalization) should be considered. Conversely, in patients receiving trazodone and requiring urgent treatment with intravenous methylene blue, trazodone should be discontinued immediately and methylene blue therapy initiated only if acceptable alternatives are not available and the potential benefits of methylene blue outweigh the risks. The patient should be monitored for serotonin syndrome for 2 weeks or until 24 hours after the last dose of methylene blue, whichever comes first. Trazodone may be re-initiated 24 hours after the last dose of methylene blue. Methylene blue is a thiazine dye that is also a potent, reversible inhibitor of the enzyme responsible for the catabolism of serotonin in the brain (MAO-A) and trazodone increases central serotonin effects. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving serotonergic agents such as selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving intravenous methylene blue with other serotonergic psychiatric agents are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. Serotonin syndrome is characterized by rapid development of various symptoms such as hyperthermia, hypertension, myoclonus, rigidity, hyperhidrosis, incoordination, diarrhea, mental status changes (e.g., confusion, delirium, or coma), and in rare cases, death. (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant. Benzphetamine: (Moderate) Coadministration of trazodone and amphetamines may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. The MAOI activity of amphetamines may also be of concern with trazodone. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Serotonergic agents should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.

Beta-adrenergic blockers: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Betaxolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Bismuth Subcitrate Potassium; metroNIDAZOLE; Tetracycline: (Major) Concomitant use of metronidazole and trazodone 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: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Bismuth Subsalicylate; metroNIDAZOLE; Tetracycline: (Major) Concomitant use of metronidazole and trazodone 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) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Bisoprolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Bisoprolol; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have

excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Bivalirudin: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Brexpiprazole: (Moderate) Due to the CNS effects of brexpiprazole, caution is advisable when brexpiprazole is given in combination with other centrally-acting medications including trazodone. Sedation may occur.
Brimonidine; Timolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Brivaracetam: (Moderate) Trazodone can lower the seizure threshold of anticonvulsants, although the overall risk is low at therapeutic doses. Patients may require increased concentrations of anticonvulsants to achieve equivalent effects if trazodone is added. Finally, drowsiness may be additive between trazodone and other anticonvulsants.
Brompheniramine: (Moderate) Antihistamines that may cause sedation, such as brompheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Brompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Antihistamines that may cause sedation, such as brompheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Brompheniramine; Phenylephrine: (Moderate) Antihistamines that may cause sedation, such as brompheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Brompheniramine; Pseudoephedrine: (Moderate) Antihistamines that may cause sedation, such as brompheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Brompheniramine; Pseudoephedrine; Dextromethorphan: (Moderate) Antihistamines that may cause sedation, such as brompheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Bumetanide: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
BUPivacaine; Meloxicam: (Moderate) Platelet aggregation may be impaired by trazodone

due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Buprenorphine: (Major) Due to the potential for QT prolongation, additive CNS depressant effects, and a potential for serotonin syndrome, cautious use and close monitoring are advisable if concurrent use of trazodone and buprenorphine is necessary. Buprenorphine has been associated with QT prolongation and has a possible risk of torsade de pointes (TdP). Trazodone has a possible risk for QT prolongation. FDA-approved labeling for some buprenorphine products recommend avoiding use with any drug that has the potential to prolong the QT interval. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Buprenorphine; Naloxone: (Major) Due to the potential for QT prolongation, additive CNS depressant effects, and a potential for serotonin syndrome, cautious use and close monitoring are advisable if concurrent use of trazodone and buprenorphine is necessary. Buprenorphine has been associated with QT prolongation and has a possible risk of torsade de pointes (TdP). Trazodone has a possible risk for QT prolongation. FDA-approved labeling for some buprenorphine products recommend avoiding use with any drug that has the potential to prolong the QT interval. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
busPIRone: (Moderate) Coadministration of trazodone and buspirone may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for

the emergence of serotonin syndrome. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Butalbital; Acetaminophen: (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and butalbital. Concurrent use may result in additive CNS depression.
Butalbital; Acetaminophen; Caffeine: (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and butalbital. Concurrent use may result in additive CNS depression.
Butalbital; Acetaminophen; Caffeine; Codeine: (Moderate) Because of the potential risk and severity of excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and butalbital. Concurrent use may result in additive CNS depression.
Butalbital; Aspirin; Caffeine; Codeine: (Moderate) Because of the potential risk and severity of excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and butalbital. Concurrent use may result in additive CNS depression. (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper

gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Butorphanol: (Moderate) Because of the potential risk and severity of CNS depression, respiratory depression, and serotonin syndrome, caution should be observed when administering butorphanol with trazodone. 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.
Cabotegravir; Rilpivirine: (Major) Concomitant use of trazodone and rilpivirine 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. 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.
Calcium-channel blockers: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Candesartan: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Candesartan; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Cannabidiol: (Moderate) Monitor for excessive sedation and somnolence during coadministration of cannabidiol and trazodone. CNS depressants can potentiate the effects of cannabidiol.
Capsaicin; Metaxalone: (Moderate) Coadministration of trazodone with metaxalone may result in additive CNS-depressant effects, such as sedation, and may increase the risk for serotonin syndrome. Use with caution and monitor for the emergence of excessive sedation or serotonin syndrome. If serotonin syndrome is suspected, serotonergic agents should be discontinued and appropriate medical treatment instituted.
Captopril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with

trazodone.
Captopril; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
carBAMazepine: (Moderate) Consider increasing the trazodone dose based on therapeutic response when coadministered with carbamazepine. Concurrent use may decrease trazodone exposure. Trazodone is a CYP3A4 substrate; carbamazepine is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Carbidopa; Levodopa; Entacapone: (Major) COMT inhibitors should be given cautiously with other agents that cause CNS depression, such as trazodone, due to the possibility of additive sedation. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.
Carbinoxamine: (Moderate) Antihistamines that may cause sedation, such as carbinoxamine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Cariprazine: (Moderate) Due to the CNS effects of cariprazine, caution is advisable when cariprazine is given in combination with other centrally-acting medications including trazodone.
Carisoprodol: (Moderate) CNS depressants, such as carisoprodol, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension. A dose reduction of one or both drugs may be warranted.
Carteolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Carvedilol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Celecoxib: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be

instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Celecoxib; Tramadol: (Major) Reserve concomitant prescribing of tramadol and trazodone for use in patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death. If concomitant use is necessary, also monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue therapy immediately if serotonin syndrome is suspected. Also, the concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system, such as trazodone, has resulted in serotonin syndrome. (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Cenobamate: (Moderate) Monitor for excessive sedation and somnolence during coadministration of cenobamate and trazodone. Concurrent use may result in additive CNS depression.
Ceritinib: (Major) Avoid coadministration of ceritinib with trazodone due to an increased risk for QT prolongation and torsade de pointes (TdP). Systemic exposure of trazodone may also be increased resulting in increase in treatment-related adverse reactions. Ceritinib is a strong CYP3A4 inhibitor that has been shown to prolong the QT interval in a concentration-dependent manner. Trazodone is a CYP3A4 substrate that can also prolong the QT/QTc interval at therapeutic doses; in addition, there are postmarketing reports of TdP. Concomitant use may increase the risk for QT prolongation.
Cetirizine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and trazodone due to the risk for additive CNS depression.
Cetirizine; Pseudoephedrine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of cetirizine and trazodone due to the risk for additive CNS depression.
Chlophedianol; Dexchlorpheniramine; Pseudoephedrine: (Moderate) Antihistamines that may cause sedation, such as dexchlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Chloramphenicol: (Major) Avoid coadministration of trazodone with chloramphenicol

due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; chloramphenicol is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Chlorcyclizine: (Moderate) Antihistamines that may cause sedation, such as chlorcyclizine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
chlordiazePOXIDE: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
chlordiazePOXIDE; Amitriptyline: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression. (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for additive CNS depression and serotonin syndrome.
chlordiazePOXIDE; Clidinium: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Chloroquine: (Major) Concomitant use of trazodone 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.
Chlorothiazide: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Chlorpheniramine: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Chlorpheniramine; Codeine: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects. (Moderate) Because of the potential risk and severity of excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest

effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Chlorpheniramine; Dextromethorphan: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Chlorpheniramine; HYDROcodone: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects. (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering hydrocodone with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Chlorpheniramine; Ibuprofen; Pseudoephedrine: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects. (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Chlorpheniramine; Phenylephrine: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone

because of additive CNS-depressant effects.
Chlorpheniramine; Pseudoephedrine: (Moderate) Antihistamines that may cause sedation, such as chlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
chlorproMAZINE: (Major) Chlorpromazine, a phenothiazine, is associated with an established risk of QT prolongation and torsade de pointes (TdP) and should be avoided in combination with trazodone. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of TdP. Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval. In addition, CNS depressants, such as phenothiazines, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension.
Chlorthalidone: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Chlorzoxazone: (Moderate) CNS depressants, such as skeletal muscle relaxants, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension. A dose reduction of one or both drugs may be warranted.
Choline Salicylate; Magnesium Salicylate: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Cilostazol: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving platelet inhibitors (e.g., cilostazol, clopidogrel, dipyridamole, ticlopidine, platelet glycoprotein IIb/IIIa inhibitors). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with an antiplatelet medication and to promptly report any bleeding events to the practitioner.
Ciprofloxacin: (Major) Concomitant use of ciprofloxacin and trazodone 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.
Cisapride: (Contraindicated) Avoid concomitant use of trazodone and cisapride due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation.
Citalopram: (Major) Avoid coadministration of trazodone and citalopram due to the potential for QT prolongation. If concurrent therapy is considered essential, ECG monitoring is recommended. Concurrent use also increases the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue citalopram and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Clarithromycin: (Major) Avoid coadministration of trazodone with clarithromycin due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; clarithromycin is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Clemastine: (Moderate) Antihistamines that may cause sedation, such as clemastine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Clevidipine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Clofazimine: (Major) Concomitant use of clofazimine and trazodone 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.
clomiPRAMINE: (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for additive CNS depression and serotonin syndrome.
clonazePAM: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
cloNIDine: (Moderate) Monitor for unusual drowsiness or excess sedation during coadministration of clonidine and trazodone due to risk for additive CNS depression.
Clopidogrel: (Moderate) Monitor for signs and symptoms of bleeding while using

trazodone concurrently with an antiplatelet medication. Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication in patients receiving platelet inhibitors, such as clopidogrel.
Clorazepate: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
cloZAPine: (Major) Concomitant use of trazodone 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.
Cobicistat: (Major) Avoid coadministration of trazodone with cobicistat due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; cobicistat is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Codeine: (Moderate) Because of the potential risk and severity of excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and 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 excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and 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 excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and 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 excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and 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 promethazine and trazodone 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. Because promethazine causes pronounced sedation, an enhanced CNS depressant effect or additive drowsiness may also occur when it is combined with other CNS depressants including trazodone. (Moderate) Because of the potential risk and severity of excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and 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 promethazine and trazodone 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. Because promethazine causes pronounced sedation, an enhanced CNS depressant effect or additive drowsiness may also occur when it is combined with other CNS depressants including trazodone. (Moderate) Because of the potential risk and severity of excessive hypotension, sedation, respiratory depression, and serotonin syndrome, caution should be observed when administering codeine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking trazodone, use a lower initial dose of the opiate and titrate to clinical response. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
COMT inhibitors: (Major) COMT inhibitors should be given cautiously with other agents that cause CNS depression, such as trazodone, due to the possibility of additive sedation. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.
Crizotinib: (Major) Concomitant use of trazodone 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.
Cyclobenzaprine: (Moderate) Increased CNS depressant effects, including sedation, may be seen if cyclcobenzaprine and trazodone are administered concurrently.
Cyproheptadine: (Moderate) CNS depressants should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension.
Dabigatran: (Moderate) Patients should be instructed to monitor for signs and

symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Dalteparin: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Dantrolene: (Moderate) CNS depressants, such as skeletal muscle relaxants, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension. A dose reduction of one or both drugs may be warranted.
Darunavir: (Major) Avoid coadministration of trazodone with darunavir due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; darunavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Darunavir; Cobicistat: (Major) Avoid coadministration of trazodone with cobicistat due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; cobicistat is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone. (Major) Avoid coadministration of trazodone with darunavir due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; darunavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Major) Avoid coadministration of trazodone with cobicistat due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on

tolerability. Trazodone is a CYP3A4 substrate; cobicistat is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone. (Major) Avoid coadministration of trazodone with darunavir due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; darunavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Dasatinib: (Major) Concomitant use of trazodone 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.
Degarelix: (Major) Concomitant use of trazodone 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.
Desflurane: (Major) Concomitant use of trazodone 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.
Desipramine: (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for additive CNS depression and serotonin syndrome.
Desvenlafaxine: (Moderate) Coadministration of trazodone and desvenlafaxine may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue desvenlafaxine and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Deutetrabenazine: (Major) Avoid coadministration of trazodone with deutetrabenazine due to the potential for additive QT prolongation. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are 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. Concurrent use of deutetrabenazine and drugs that cause CNS depression, such as trazodone, may have additive effects and worsen drowsiness or sedation.
Dexchlorpheniramine: (Moderate) Antihistamines that may cause sedation, such as dexchlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Dexchlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Antihistamines that may cause sedation, such as dexchlorpheniramine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
dexmedeTOMIDine: (Major) Concomitant use of dexmedetomidine and trazodone 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.
Dextroamphetamine: (Moderate) Coadministration of trazodone and amphetamines may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. The MAOI activity of amphetamines may also be of concern with trazodone. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Serotonergic agents should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.
Dextromethorphan; diphenhydrAMINE; Phenylephrine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of diphenhydramine and trazodone due to the risk for additive CNS depression.
Dextromethorphan; quiNIDine: (Major) Concomitant use of trazodone and quinidine 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.
diazePAM: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Diclofenac: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be

instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Diclofenac; miSOPROStol: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Difelikefalin: (Moderate) Monitor for dizziness, somnolence, mental status changes, and gait disturbances if concomitant use of difelikefalin with CNS depressants is necessary. Concomitant use may increase the risk for these adverse reactions.
Diflunisal: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Digoxin: (Moderate) Monitor digoxin concentrations before initiating concomitant trazodone and continually during therapy; decrease digoxin dose as clinically necessary. Trazodone may increase digoxin concentrations.
dilTIAZem: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
dimenhyDRINATE: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of dimenhydrinate and trazodone due to the risk for additive CNS depression.
diphenhydrAMINE: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of diphenhydramine and trazodone due to the risk for additive CNS depression.
diphenhydrAMINE; Ibuprofen: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of diphenhydramine and trazodone due to the risk for additive CNS depression. (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone

concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
diphenhydrAMINE; Naproxen: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of diphenhydramine and trazodone due to the risk for additive CNS depression. (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
diphenhydrAMINE; Phenylephrine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of diphenhydramine and trazodone due to the risk for additive CNS depression.
Diphenoxylate; Atropine: (Moderate) Concurrent administration of diphenoxylate/difenoxin with trazodone can potentiate the CNS-depressant effects of diphenoxylate/difenoxin. Use caution during coadministration.
Dipyridamole: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving platelet inhibitors (e.g., cilostazol, clopidogrel, dipyridamole, ticlopidine, platelet glycoprotein IIb/IIIa inhibitors). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with an antiplatelet medication and to promptly report any bleeding events to the practitioner.
Disopyramide: (Major) Concomitant use of trazodone 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.
Dofetilide: (Major) Concomitant use of trazodone 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.
Dolasetron: (Major) Concomitant use of trazodone and dolasetron 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.

Dolutegravir; Rilpivirine: (Major) Concomitant use of trazodone and rilpivirine 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. 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 trazodone 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.
Donepezil; Memantine: (Major) Concomitant use of trazodone 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.
Dordaviprone: (Major) Concomitant use of dordaviprone and trazodone 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.
Dorzolamide; Timolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Doxazosin: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Doxepin: (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for additive CNS depression and serotonin syndrome.
Doxylamine: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of doxylamine and trazodone due to the risk for additive CNS depression.
Doxylamine; Pyridoxine: (Moderate) Monitor for unusual drowsiness and sedation

during coadministration of doxylamine and trazodone due to the risk for additive CNS depression.
droNABinol: (Moderate) CNS depressants, such as dronabinol, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension. A dose reduction of one or both drugs may be warranted.
Dronedarone: (Contraindicated) Avoid concomitant use of trazodone and dronedarone due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation.
droPERidol: (Major) Coadministration of droperidol and trazodone should be avoided. Droperidol administration is associated with an established risk for QT prolongation and torsades de pointes (TdP). In December 2001, the FDA issued a black box warning regarding the use of droperidol and its association with QT prolongation and potential for cardiac arrhythmias based on post-marketing surveillance data. According to the revised 2001 labeling for droperidol, any drug known to have potential to prolong the QT interval should not be coadministered with droperidol. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval. In addition, CNS depressants, inlcluding droperidol, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension.
DULoxetine: (Moderate) Coadministration of trazodone and duloxetine may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Edoxaban: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Efavirenz: (Major) Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval, such as efavirenz. In addition, efavirenz may induce the CYP3A4 metabolism of trazodone; potentially reducing the efficacy of trazodone by decreasing its systemic exposure.

Efavirenz; Emtricitabine; Tenofovir Disoproxil Fumarate: (Major) Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval, such as efavirenz. In addition, efavirenz may induce the CYP3A4 metabolism of trazodone; potentially reducing the efficacy of trazodone by decreasing its systemic exposure.
Efavirenz; lamiVUDine; Tenofovir Disoproxil Fumarate: (Major) Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval, such as efavirenz. In addition, efavirenz may induce the CYP3A4 metabolism of trazodone; potentially reducing the efficacy of trazodone by decreasing its systemic exposure.
Elbasvir; Grazoprevir: (Moderate) Administering trazodone with elbasvir; grazoprevir may result in elevated trazodone plasma concentrations. Trazodone is a substrate of CYP3A; grazoprevir is a weak CYP3A inhibitor. If these drugs are used together, closely monitor for signs of adverse events.
Eletriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Eliglustat: (Major) Concomitant use of trazodone and eliglustat 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.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Alafenamide: (Major) Avoid coadministration of trazodone with cobicistat due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; cobicistat is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Disoproxil Fumarate: (Major) Avoid coadministration of trazodone with cobicistat due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; cobicistat is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Emtricitabine; Rilpivirine; Tenofovir alafenamide: (Major) Concomitant use of trazodone

and rilpivirine 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. 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 trazodone and rilpivirine 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. 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.
Enalapril, Enalaprilat: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Enalapril; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Encorafenib: (Major) Concomitant use of encorafenib and trazodone increases the risk of QT/QTc prolongation and torsade de pointes (TdP) and may decrease trazodone exposure and efficacy. Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. If concomitant use is necessary, monitor for altered response to trazodone and increase the trazodone dose as needed based on therapeutic response. Additionally, consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring. Trazodone is a CYP3A substrate, encorafenib is a strong CYP3A inducer, and both medications have been associated with QT/QTc prolongation. Coadministration with other strong CYP3A inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Enoxaparin: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be

prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Entacapone: (Major) COMT inhibitors should be given cautiously with other agents that cause CNS depression, such as trazodone, due to the possibility of additive sedation. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.
Entrectinib: (Major) Concomitant use of trazodone 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.
Enzalutamide: (Moderate) Consider increasing the trazodone dose based on therapeutic response when coadministered with enzalutamide. Concurrent use may decrease trazodone exposure. Trazodone is a CYP3A4 substrate; enzalutamide is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Eplerenone: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Epoprostenol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Eptifibatide: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving platelet inhibitors (e.g., cilostazol, clopidogrel, dipyridamole, ticlopidine, platelet glycoprotein IIb/IIIa inhibitors). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with an antiplatelet medication and to promptly report any bleeding events to the practitioner.
eriBULin: (Major) Concomitant use of trazodone 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.
Erythromycin: (Major) Concomitant use of trazodone and erythromycin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Concomitant use may also increase trazadone concentrations. 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. Trazadone is a CYP3A4 substrate and erythromycin is a moderate CYP3A4 inhibitor.
Escitalopram: (Major) Due to the risk of QT prolongation and torsade de pointes (TdP), the manufacturer of trazodone recommends avoiding use with other drugs that increase the QT interval. Escitalopram has been associated with a risk of QT prolongation and TdP. In addition, coadministration of trazodone and escitalopram may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue escitalopram and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Esketamine: (Major) Closely monitor patients receiving esketamine and trazodone for sedation and other CNS depressant effects. Instruct patients who receive a dose of esketamine not to drive or engage in other activities requiring alertness until the next day after a restful sleep.
Esmolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Estazolam: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Eszopiclone: (Moderate) Eszopiclone should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension. If used together, a reduction in the dose of one or both drugs may be needed.
Ethacrynic Acid: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Ethanol: (Major) Advise patients to avoid alcohol consumption while taking CNS depressants. Alcohol consumption may result in additive CNS depression.
Etodolac: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g.,

gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Etrasimod: (Major) Concomitant use of etrasimod and trazodone 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. 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.
Felodipine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Fenfluramine: (Moderate) Use fenfluramine and trazodone with caution due to an increased risk of serotonin syndrome and additive CNS depression. Monitor for excessive sedation, somnolence, and serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Fenoldopam: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Fenoprofen: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
fentaNYL: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering fentanyl with trazodone. Limit the use of opiod pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment.

Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Fexinidazole: (Major) Concomitant use of fexinidazole and trazodone 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.
Fingolimod: (Major) Concomitant use of trazodone 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.
Flecainide: (Major) Concomitant use of flecainide and trazodone 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.
Flibanserin: (Moderate) The concomitant use of flibanserin with CNS depressants, such as trazodone, may increase the risk of CNS depression (e.g., dizziness, somnolence) compared to the use of flibanserin alone. Patients should avoid activities requiring full alertness (e.g., operating machinery or driving) until at least 6 hours after each dose and until they know how flibanserin affects them.
Fluconazole: (Contraindicated) The concurrent use of fluconazole with drugs that are associated with QT prolongation and are CYP3A4 substrates, such as trazodone, is contraindicated. Fluconazole has been associated with QT prolongation; QT prolongation and torsade de pointes (TdP) have been observed during trazodone treatment. Additionally, fluconazole has been associated with prolongation of the QT interval as well as rare cases of TdP; avoid use with other drugs that may prolong the QT interval and are metabolized through CYP3A4, such as trazodone.
FLUoxetine: (Major) Trazodone and fluoxetine may both cause QT prolongation. Concurrent use may also increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate appropriate treatment if serotonin syndrome occurs.
fluPHENAZine: (Minor) Fluphenazine, a phenothiazine, is associated with a possible risk for QT prolongation. Theoretically, the risk of QT prolongation may be increased if coadministered with drugs with a possible risk for QT prolongation, such as trazodone. In addition, phenothiazines can potentiate the CNS-depressant action of other drugs

such as trazodone. Clinicians should note that additive CNS effects (e.g., oversedation, respiratory depression, and hypotension) may occur if fluphenazine is administered concomitantly with trazodone.
Flurazepam: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Flurbiprofen: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
fluvoxaMINE: (Major) Due to the risk of QT prolongation and torsade de pointes (TdP), the manufacturer of trazodone recommends avoiding use with other drugs that increase the QT interval. Cases of QT prolongation and TdP have been reported during postmarketing use of fluvoxamine. In addition, coadministration of trazodone and fluvoxamine may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue fluvoxamine and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Fondaparinux: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Food: (Major) Advise patients to avoid cannabis use while taking CNS depressants due to the risk for additive CNS depression and potential for other cognitive adverse reactions.
Fosamprenavir: (Major) Avoid coadministration of trazodone with fosamprenavir due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; fosamprenavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Foscarnet: (Major) Concomitant use of trazodone 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.
Fosinopril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Fosinopril; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Fosphenytoin: (Moderate) Monitor phenytoin concentrations and consider increasing the trazodone dose based on therapeutic response when coadministered with fosphenytoin; a fosphenytoin dose adjustment may also be necessary. Concurrent use may increase serum phenytoin concentrations and decrease trazodone exposure. Trazodone is a CYP3A substrate; fosphenytoin is a strong CYP3A inducer. Coadministration with other strong CYP3A inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Fostemsavir: (Major) Concomitant use of trazodone 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. 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.
Frovatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Furosemide: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Gabapentin: (Major) Initiate gabapentin at the lowest recommended dose and monitor patients for symptoms of sedation and somnolence during coadministration of gabapentin and trazodone. Concomitant use of gabapentin with trazodone may cause additive CNS depression. Educate patients about the risks and symptoms of excessive CNS depression.

Gemifloxacin: (Major) Concomitant use of trazodone 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.
Gemtuzumab Ozogamicin: (Major) Concomitant use of trazodone 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.
Gepirone: (Major) Concomitant use of gepirone 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. 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. QT prolongation with gepirone has been observed at 2 times the maximum recommended dose.
Gepotidacin: (Major) Concomitant use of gepotidacin and trazodone 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.
Gilteritinib: (Major) Concomitant use of trazodone 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.
Ginkgo, Ginkgo biloba: (Moderate) Use trazodone with caution in any patient taking ginkgo biloba. A case report of a potential interaction between trazodone and ginkgo biloba has been described in a patient with dementia. The interaction purportedly led to oversedation requiring medical intervention. The mechanism is uncertain. Clinically, the flavonoids of ginkgo do not usually produce significant sedative effects. However, the addition of trazodone may have enhanced activity of the ginkgo flavonoids on GABA in the CNS.
Givinostat: (Major) Concomitant use of givinostat and trazodone 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. 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 trazodone 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.
Goserelin: (Major) Concomitant use of trazodone 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.
Granisetron: (Major) Because trazodone can prolong the QT/QTc interval at therapeutic doses and there are postmarketing reports of torsade de pointes (TdP), the manufacturer of trazodone recommends avoiding use in patients receiving other drugs that increase the QT interval, such as granisetron. In addition, coadministration of trazodone and granisetron may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue granisetron and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Grapefruit juice: (Major) Advise patients to avoid coadministration of trazodone with grapefruit juice due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. Trazodone is a CYP3A4 substrate; grapefruit juice is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
guanFACINE: (Moderate) Guanfacine may potentiate the CNS-depressive effects of other sedating drugs, such as trazodone. Monitor blood pressure to ensure blood pressure remains controlled.
Halogenated Anesthetics: (Major) Concomitant use of trazodone 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.
Haloperidol: (Major) Concomitant use of trazodone 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. The intravenous route may carry a higher risk for haloperidol-induced QT/QTc prolongation than other routes of administration.
Heparin: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Histrelin: (Major) Concomitant use of trazodone 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.
Homatropine; HYDROcodone: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering hydrocodone with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
hydrALAZINE: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
hydrALAZINE; Isosorbide Dinitrate, ISDN: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
hydroCHLOROthiazide, HCTZ; Moexipril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have

excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
HYDROcodone: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering hydrocodone with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and 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 excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering hydrocodone with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
HYDROmorphone: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering hydromorphone with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and 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 trazodone 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.
hydrOXYzine: (Major) Concomitant use of hydroxyzine and trazodone increases the risk of QT/QTc prolongation and torsade de pointes (TdP). In addition, because hydroxyzine is a sedating antihistamine and may cause pronounced sedation, an enhanced CNS depressant effect may occur when it is combined with other CNS depressants including trazodone. 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: (Contraindicated) According to the manufacturer of trazodone, treatment initiation with trazodone is contraindicated in patients currently receiving intravenous methylene blue due to an increased risk of serotonin syndrome. If urgent psychiatric treatment is required, interventions other than trazodone (e.g., alternative medication, hospitalization) should be considered. Conversely, in patients receiving trazodone and requiring urgent treatment with intravenous methylene blue, trazodone should be discontinued immediately and methylene blue therapy initiated only if acceptable alternatives are not available and the potential benefits of methylene blue outweigh the risks. The patient should be monitored for serotonin syndrome for 2 weeks or until 24 hours after the last dose of methylene blue, whichever comes first. Trazodone may be re-initiated 24 hours after the last dose of methylene blue. Methylene blue is a thiazine dye that is also a potent, reversible inhibitor of the enzyme responsible for the catabolism of serotonin in the brain (MAO-A) and trazodone increases central serotonin effects. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving serotonergic agents such as selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving intravenous methylene blue with other serotonergic psychiatric agents are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. Serotonin syndrome is characterized by rapid development of various symptoms such as hyperthermia, hypertension, myoclonus, rigidity, hyperhidrosis, incoordination, diarrhea, mental status changes (e.g., confusion, delirium, or coma), and

in rare cases, death. (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Ibuprofen: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Ibuprofen; Famotidine: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Ibuprofen; Pseudoephedrine: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Ibutilide: (Major) Concomitant use of trazodone 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.
Idelalisib: (Major) Avoid coadministration of trazodone with idelalisib due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; idelalisib is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Iloperidone: (Major) Concomitant use of trazodone 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.
Iloprost: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Imipramine: (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for additive CNS depression and serotonin syndrome.
Indomethacin: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Inotuzumab Ozogamicin: (Major) Concomitant use of trazodone 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.
Irbesartan: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Irbesartan; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Isavuconazonium: (Moderate) Concomitant use of isavuconazonium with trazodone may result in increased serum concentrations of trazodone. Trazodone is a substrate of the hepatic isoenzyme CYP3A4; isavuconazole, the active moiety of isavuconazonium, is a moderate inhibitor of this enzyme. Caution and close monitoring are advised if these drugs are used together.
Isocarboxazid: (Contraindicated) Due to the risk of serotonin syndrome, monoamine oxidase inhibitors (MAOIs) intended to treat psychiatric disorders are contraindicated for

use with trazodone or within 14 days of discontinuing treatment with trazodone. Conversely, trazodone should not be initiated within 14 days of stopping an MAOI.
Isoflurane: (Major) Concomitant use of trazodone 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.
Isradipine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Itraconazole: (Major) Avoid coadministration of itraconazole with trazodone due to the potential for additive effects on the QT interval; increased exposure to trazodone may also occur. Both trazodone and itraconazole are associated with QT prolongation; there are also postmarketing reports of torsade de pointes (TdP) with trazodone. In addition, coadministration of itraconazole (a potent CYP3A4 inhibitor) with trazodone (a CYP3A4 substrate) may result in elevated trazodone plasma concentrations and an increased risk for adverse events, including QT prolongation. Consider decreasing the dose of trazodone during coadministration with itraconazole. 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 trazodone 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.
Ketoconazole: (Contraindicated) Avoid concomitant use of ketoconazole and trazodone due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. Concomitant use may also increase the exposure of trazodone, further increasing the risk for adverse effects. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A substrate and ketoconazole is a strong CYP3A inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Ketoprofen: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in

patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Ketorolac: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Labetalol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Landiolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Lansoprazole; Amoxicillin; Clarithromycin: (Major) Avoid coadministration of trazodone with clarithromycin due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; clarithromycin is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Lapatinib: (Major) Concomitant use of trazodone 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.
Lasmiditan: (Moderate) Monitor for excessive sedation, somnolence, and serotonin syndrome during coadministration of lasmiditan and trazodone. Inform patients taking this combination of the risks and symptoms of excessive CNS depression and serotonin syndrome, particularly after a dose increase or the addition of other serotonergic medications to an existing regimen. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Lefamulin: (Major) Concomitant use of trazodone 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.
Lemborexant: (Moderate) Monitor for excessive sedation and somnolence during coadministration of lemborexant and trazodone. Dosage adjustments of lemborexant and trazodone may be necessary when administered together because of potentially additive CNS effects. The risk of next-day impairment, including impaired driving, is increased if lemborexant is taken with other CNS depressants. In general, the use of trazodone for sleep along with a hypnotic like lemborexant, should be avoided.
Lenvatinib: (Major) Concomitant use of trazodone 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.
Letermovir: (Moderate) An increase in the plasma concentration of trazodone may occur if given with letermovir. In patients who are also receiving treatment with cyclosporine, consider reducing the trazodone dose based on tolerability and monitor for cardiac arrhythmias or other trazodone toxicities because the magnitude of this interaction may be amplified. Trazodone is a CYP3A4 substrate. Letermovir is a moderate CYP3A4 inhibitor; however, when given with cyclosporine, the combined effect on CYP3A4 substrates may be similar to a strong CYP3A4 inhibitor.
Leuprolide: (Major) Concomitant use of trazodone 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.
Leuprolide; Norethindrone: (Major) Concomitant use of trazodone 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.
Levamlodipine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Levobunolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Levocetirizine: (Moderate) Monitor for unusual drowsiness and sedation during

coadministration of cetirizine and trazodone due to the risk for additive CNS depression.
levoFLOXacin: (Major) Concomitant use of levofloxacin and trazodone 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 trazodone due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. Concomitant use may also increase the exposure of trazodone, further increasing the risk for adverse effects. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A substrate and ketoconazole is a strong CYP3A inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Levomilnacipran: (Moderate) Coadministration of trazodone and levomilnacipran may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue levomilnacipran and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Levorphanol: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering levorphanol with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Reduce the initial dose of levorphanol by approximately 50% or more. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Linezolid: (Contraindicated) Concurrent use of linezolid and trazodone is contraindicated due to an increased risk of serotonin syndrome. Trazodone is a serotonergic antidepressant and linezolid is a nonselective inhibitor of monoamine oxidase which increases central serotonin levels. If urgent psychiatric treatment is required, interventions other than trazodone (e.g., alternative medication, hospitalization) should be considered. Conversely, in patients receiving trazodone and requiring urgent treatment with linezolid, trazodone should be discontinued immediately and linezolid therapy initiated only if acceptable alternatives are not available and the potential benefits of linezolid outweigh the risks. The patient should be monitored for serotonin

syndrome for 2 weeks or until 24 hours after the last dose of linezolid, whichever comes first. Trazodone may be resumed 24 hours after the last dose of linezolid.
Lisdexamfetamine: (Moderate) Coadministration of trazodone and amphetamines may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. The MAOI activity of amphetamines may also be of concern with trazodone. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Serotonergic agents should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.
Lisinopril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Lisinopril; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Lithium: (Major) Due to the risk of QT prolongation and torsade de pointes (TdP), the manufacturer of trazodone recommends avoiding use with other drugs that increase the QT interval. Lithium has been associated with a risk of QT prolongation. In addition, coadministration of trazodone and lithium may increase the risk of serotonin syndrome. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue lithium and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Lofexidine: (Major) Avoid coadministration of lofexidine with trazodone due to the potential for additive QT prolongation and torsade de pointes (TdP). Monitor ECG if coadministration cannot be avoided. Additionally, monitor for excessive hypotension and sedation during coadministration as lofexidine can potentiate the effects of CNS depressants. Lofexidine prolongs the QT interval. In addition, there are postmarketing reports of TdP. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are postmarketing reports of TdP.
Lonafarnib: (Major) Avoid coadministration of trazodone with lonafarnib due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; lonafarnib is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Loop diuretics: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension.

Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Loperamide: (Major) Concomitant use of trazodone 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 trazodone 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) Avoid coadministration of trazodone with ritonavir due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; ritonavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone. (Major) Concomitant use of trazodone 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.
LORazepam: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Losartan: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Losartan; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Lumacaftor; Ivacaftor: (Moderate) Consider increasing the trazodone dose based on therapeutic response when coadministered with lumacaftor; ivacaftor. Concurrent use may decrease trazodone exposure. Trazodone is a CYP3A4 substrate; lumacaftor; ivacaftor is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone.

Lumacaftor; Ivacaftor: (Moderate) Consider increasing the trazodone dose based on therapeutic response when coadministered with lumacaftor; ivacaftor. Concurrent use may decrease trazodone exposure. Trazodone is a CYP3A4 substrate; lumacaftor; ivacaftor is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Lumateperone: (Moderate) Monitor for excessive sedation and somnolence during coadministration of lumateperone and trazodone. Concurrent use may result in additive CNS depression.
Macimorelin: (Major) Concomitant use of trazodone 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.
Magnesium Salicylate: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Maprotiline: (Major) Concomitant use of trazodone 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.
Mavorixafor: (Major) Concomitant use of mavorixafor and trazodone 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. 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.
Mecamylamine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Meclizine: (Moderate) Antihistamines that may cause sedation, such as meclizine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.

Meclofenamate Sodium: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Mefenamic Acid: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Mefloquine: (Major) Concomitant use of trazodone 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.
Meloxicam: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Meloxicam; Rizatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome. (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Meperidine: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering meperidine with trazodone. Limit the use of meperidine with trazodone to only patients

for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Meprobamate: (Moderate) Meprobamate should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension. If used together, a reduction in the dose of one or both drugs may be needed.
Metaxalone: (Moderate) Coadministration of trazodone with metaxalone may result in additive CNS-depressant effects, such as sedation, and may increase the risk for serotonin syndrome. Use with caution and monitor for the emergence of excessive sedation or serotonin syndrome. If serotonin syndrome is suspected, serotonergic agents should be discontinued and appropriate medical treatment instituted.
Methadone: (Major) Avoid coadministration of trazodone and methadone due to an additive risk of QT prolongation. Concomitant use of opioid agonists with trazodone may also cause excessive sedation, somnolence, and increase the risk for serotonin syndrome. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Educate patients about the risks and symptoms of serotonin syndrome and excessive CNS depression. Trazodone can prolong the QT/QTc interval at therapeutic doses, and there are postmarketing reports of torsade de pointes (TdP). Methadone is associated with an increased risk for QT prolongation and torsade de pointes (TdP), especially at higher doses (i.e., more than 200 mg/day but averaging approximately 400 mg/day in adult patients). Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction.
Methamphetamine: (Moderate) Coadministration of trazodone and amphetamines may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. The MAOI activity of amphetamines may also be of concern with trazodone. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Serotonergic agents should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.
Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine: (Contraindicated) According to the manufacturer of trazodone, treatment initiation with trazodone is

contraindicated in patients currently receiving intravenous methylene blue due to an increased risk of serotonin syndrome. If urgent psychiatric treatment is required, interventions other than trazodone (e.g., alternative medication, hospitalization) should be considered. Conversely, in patients receiving trazodone and requiring urgent treatment with intravenous methylene blue, trazodone should be discontinued immediately and methylene blue therapy initiated only if acceptable alternatives are not available and the potential benefits of methylene blue outweigh the risks. The patient should be monitored for serotonin syndrome for 2 weeks or until 24 hours after the last dose of methylene blue, whichever comes first. Trazodone may be re-initiated 24 hours after the last dose of methylene blue. Methylene blue is a thiazine dye that is also a potent, reversible inhibitor of the enzyme responsible for the catabolism of serotonin in the brain (MAO-A) and trazodone increases central serotonin effects. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving serotonergic agents such as selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving intravenous methylene blue with other serotonergic psychiatric agents are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. Serotonin syndrome is characterized by rapid development of various symptoms such as hyperthermia, hypertension, myoclonus, rigidity, hyperhidrosis, incoordination, diarrhea, mental status changes (e.g., confusion, delirium, or coma), and in rare cases, death.

Methenamine; Sodium Salicylate: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.

Methohexital: (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and methohexital. Concurrent use may result in additive CNS depression.

Methylene Blue: (Contraindicated) According to the manufacturer of trazodone, treatment initiation with trazodone is contraindicated in patients currently receiving

intravenous methylene blue due to an increased risk of serotonin syndrome. If urgent psychiatric treatment is required, interventions other than trazodone (e.g., alternative medication, hospitalization) should be considered. Conversely, in patients receiving trazodone and requiring urgent treatment with intravenous methylene blue, trazodone should be discontinued immediately and methylene blue therapy initiated only if acceptable alternatives are not available and the potential benefits of methylene blue outweigh the risks. The patient should be monitored for serotonin syndrome for 2 weeks or until 24 hours after the last dose of methylene blue, whichever comes first. Trazodone may be re-initiated 24 hours after the last dose of methylene blue. Methylene blue is a thiazine dye that is also a potent, reversible inhibitor of the enzyme responsible for the catabolism of serotonin in the brain (MAO-A) and trazodone increases central serotonin effects. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent in parathyroid surgery, in patients receiving serotonergic agents such as selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving intravenous methylene blue with other serotonergic psychiatric agents are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. Published interaction reports between intravenously administered methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and/or coma. Serotonin syndrome is characterized by rapid development of various symptoms such as hyperthermia, hypertension, myoclonus, rigidity, hyperhidrosis, incoordination, diarrhea, mental status changes (e.g., confusion, delirium, or coma), and in rare cases, death.
metOLazone: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Metoprolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Metoprolol; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
metroNIDAZOLE: (Major) Concomitant use of metronidazole and trazodone 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.
metyraPONE: (Moderate) Metyrapone may cause dizziness and/or drowsiness. Other drugs that may also cause drowsiness, such as trazodone, should be used with caution. Additive drowsiness and/or dizziness is possible.
Midazolam: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Midostaurin: (Major) Concomitant use of trazodone 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.
miFEPRIStone: (Major) Concomitant use of trazodone and mifepristone increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Concomitant use may also increase the exposure of trazodone, further increasing the risk for adverse effects. Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. If concomitant use is necessary, consider a reduced dose of trazodone based on tolerability and consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring. Trazodone is a CYP3A substrate and mifepristone is a strong CYP3A inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Milnacipran: (Moderate) Coadministration of trazodone and milnacipran may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue milnacipran and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Minoxidil: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Mirtazapine: (Major) Due to the potential for QT prolongation, cautious use and close monitoring are advisable if concurrent use of trazodone and mirtazapine is necessary. Both drugs may cause QT interval prolongation and a risk for torsade de pointes (TdP). In addition, concurrent use of trazodone 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: (Moderate) Consider increasing the trazodone dose based on therapeutic response when coadministered with mitotane. Concurrent use may decrease trazodone exposure. Trazodone is a CYP3A4 substrate; mitotane is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Mobocertinib: (Major) Concomitant use of trazodone 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.
Moexipril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Molindone: (Moderate) Molindone may cause central nervous system (CNS) depression thereby having additive effects with other drugs that can cause CNS depression such as trazodone. Caution is advisable during concurrent use.
Monoamine oxidase inhibitors: (Contraindicated) Due to the risk of serotonin syndrome, monoamine oxidase inhibitors (MAOIs) intended to treat psychiatric disorders are contraindicated for use with trazodone or within 14 days of discontinuing treatment with trazodone. Conversely, trazodone should not be initiated within 14 days of stopping an MAOI.
Morphine: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering morphine with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. For extended-release morphine tablets, start with 15 mg every 12 hours. Morphine; naltrexone should be initiated at 1/3 to 1/2 the recommended starting dosage. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and 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 trazodone 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.
Nabumetone: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Nadolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Nalbuphine: (Moderate) Because of the potential risk and severity of CNS depression, respiratory depression, and serotonin syndrome, caution should be observed when administering nalbuphine with trazodone. 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.
Naproxen: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Naproxen; Esomeprazole: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Naproxen; Pseudoephedrine: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Naratriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant

trazodone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Nebivolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Nefazodone: (Moderate) Coadministration of trazodone and nefazodone may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue nefazodone and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Nelfinavir: (Major) Avoid coadministration of trazodone with nelfinavir due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; nelfinavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Netupitant, Fosnetupitant; Palonosetron: (Moderate) Netupitant is a moderate inhibitor of CYP3A4 and should be used with caution in patients receiving concomitant medications that are primarily metabolized through CYP3A4, such as trazodone. The plasma concentrations of trazodone can increase when co-administered with netupitant; the inhibitory effect on CYP3A4 can last for multiple days.
NiCARdipine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
NIFEdipine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Nilotinib: (Major) Avoid the concomitant use of nilotinib with other agents that prolong the QT interval. Trazodone can prolong the QT interval at therapeutic doses, and torsade de pointes (TdP) has been reported with post-marketing use. Additionally, nilotinib is a moderate CYP3A4 inhibitor and trazodone is a CYP3A4 substrate; administering these drugs together may result in increased trazodone levels. If the use of trazodone is required, hold nilotinib therapy. If the use of nilotinib and trazodone cannot be avoided, a trazodone dose reduction may be necessary; close monitoring of the QT interval is recommended.
niMODipine: (Minor) Due to additive hypotensive effects, patients receiving

antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Nirmatrelvir; Ritonavir: (Major) Avoid coadministration of trazodone with ritonavir due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; ritonavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Nisoldipine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Nitroprusside: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Nonsteroidal antiinflammatory drugs: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Nortriptyline: (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for additive CNS depression and serotonin syndrome.
Ofloxacin: (Major) Concomitant use of ofloxacin and trazodone 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 trazodone 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.
OLANZapine; FLUoxetine: (Major) Concomitant use of trazodone 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. (Major) Trazodone and fluoxetine may both cause QT prolongation. Concurrent use may also increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate appropriate treatment if serotonin syndrome occurs.
OLANZapine; Samidorphan: (Major) Concomitant use of trazodone 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.
Oliceridine: (Major) Concomitant use of oliceridine with trazodone may cause excessive sedation and somnolence. Limit the use of oliceridine with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, reduce initial dosage and titrate to clinical response; use the lowest effective doses and minimum treatment durations. Also 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.
Olmesartan: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Olmesartan; amLODIPine; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Olmesartan; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.

Ondansetron: (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.
Opicapone: (Major) COMT inhibitors should be given cautiously with other agents that cause CNS depression, such as trazodone, due to the possibility of additive sedation. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.
Oritavancin: (Moderate) Trazodone is metabolized by CYP3A4; oritavancin is a weak CYP3A4 inducer. Plasma concentrations and efficacy of trazodone may be reduced if these drugs are administered concurrently.
Orphenadrine: (Moderate) CNS depressants, such as skeletal muscle relaxants, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension. A dose reduction of one or both drugs may be warranted.
Osilodrostat: (Major) Concomitant use of trazodone and osilodrostat 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.
Osimertinib: (Major) Concomitant use of trazodone and osimertinib 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.
Oxaliplatin: (Major) Concomitant use of trazodone and oxaliplatin 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.
Oxaprozin: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be

instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Oxazepam: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
oxyCODONE: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering oxycodone with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and 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 excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering oxymorphone with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and 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 trazodone 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. 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 trazodone 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.
Paliperidone: (Major) Avoid coadministration of trazodone and paliperidone if possible.

Trazodone can prolong the QT/QTc interval at therapeutic doses and there are postmarketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval. Paliperidone has been associated with QT prolongation; torsade de pointes (TdP) and ventricular fibrillation have been reported in the setting of overdose. According to the manufacturer of paliperidone, the drug should be avoided in combination with other agents also known to have this effect. If coadministration is necessary and the patient has known risk factors for cardiac disease or arrhythmias, close monitoring is essential. Concurrent use can also result in additive adverse effects such as drowsiness and dizziness.
Panobinostat: (Major) QT prolongation has been reported with panobinostat therapy in patients with multiple myeloma in a clinical trial; use of panobinostat with other agents that prolong the QT interval is not recommended. Obtain an electrocardiogram at baseline and periodically during treatment. Hold panobinostat if the QTcF increases to >= 480 milliseconds during therapy; permanently discontinue if QT prolongation does not resolve. Drugs with a possible risk for QT prolongation and torsade de pointes that should be used cautiously and with close monitoring with panobinostat include trazodone.
PARoxetine: (Moderate) Coadministration of trazodone and paroxetine may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Pasireotide: (Major) Concomitant use of trazodone and pasireotide 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.
PAZOPanib: (Major) Avoid coadministration of trazodone and pazopanib. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval. Pazopanib has been reported to prolong the QT interval. If pazopanib and the other drug must be continued, closely monitor the patient for QT interval prolongation. Pazopanib is also a weak inhibitor of CYP3A4. Coadministration of pazopanib and trazodone, a CYP3A4 substrate, may cause an increase in systemic concentrations of trazodone.
Pentamidine: (Major) Concomitant use of trazodone and pentamidine 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.
Pentazocine; Naloxone: (Moderate) Because of the potential risk and severity of CNS depression, respiratory depression, and serotonin syndrome, caution should be observed when administering pentazocine with trazodone. 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.
PENTobarbital: (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and pentobarbital. Concurrent use may result in additive CNS depression.
Pentosan: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Perindopril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Perindopril; amLODIPine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Perphenazine: (Minor) Perphenazine, a phenothiazine, is associated with a possible risk for QT prolongation. Theoretically, the risk of QT prolongation may be increased if coadministered with drugs with a possible risk for QT prolongation, such as trazodone. In addition, phenothiazines can potentiate the CNS-depressant action of other drugs such as trazodone. Clinicians should note that additive CNS effects (e.g., oversedation, respiratory depression, and hypotension) may occur if perphenazine is administered concomitantly with trazodone.
Perphenazine; Amitriptyline: (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant

use increases the risk for additive CNS depression and serotonin syndrome. (Minor) Perphenazine, a phenothiazine, is associated with a possible risk for QT prolongation. Theoretically, the risk of QT prolongation may be increased if coadministered with drugs with a possible risk for QT prolongation, such as trazodone. In addition, phenothiazines can potentiate the CNS-depressant action of other drugs such as trazodone. Clinicians should note that additive CNS effects (e.g., oversedation, respiratory depression, and hypotension) may occur if perphenazine is administered concomitantly with trazodone. Phenelzine: (Contraindicated) Due to the risk of serotonin syndrome, monoamine oxidase inhibitors (MAOIs) intended to treat psychiatric disorders are contraindicated for use with trazodone or within 14 days of discontinuing treatment with trazodone. Conversely, trazodone should not be initiated within 14 days of stopping an MAOI. PHENobarbital: (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and phenobarbital. Concurrent use may result in additive CNS depression. Additionally, concurrent use may decrease trazodone exposure; adjust dose as needed based on therapeutic response. Trazodone is a CYP3A4 substrate; phenobarbital is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone. PHENobarbital; Hyoscyamine; Atropine; Scopolamine: (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and phenobarbital. Concurrent use may result in additive CNS depression. Additionally, concurrent use may decrease trazodone exposure; adjust dose as needed based on therapeutic response. Trazodone is a CYP3A4 substrate; phenobarbital is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Phenoxybenzamine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Phentolamine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Phenytoin: (Moderate) Monitor phenytoin concentrations and consider increasing the trazodone dose based on therapeutic response when coadministered with phenytoin; a phenytoin dose adjustment may also be necessary. Concurrent use may increase serum phenytoin concentrations and decrease trazodone exposure. Trazodone is a CYP3A substrate; phenytoin is a strong CYP3A inducer. Coadministration with other strong CYP3A inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Pimavanserin: (Major) Concomitant use of trazodone and pimavanserin 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.
Pimozide: (Contraindicated) Avoid concomitant use of trazodone and pimozide due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation.
Pindolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Piroxicam: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Pitolisant: (Major) Concomitant use of trazodone and pitolisant 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.
Ponesimod: (Major) Concomitant use of trazodone and ponesimod 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. Ponesimod 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.
Posaconazole: (Contraindicated) The concurrent use of posaconazole and trazodone is contraindicated due to the risk of life threatening arrhythmias such as torsades de pointes (TdP). Posaconazole is a potent inhibitor of CYP3A4, an isoenzyme partially responsible for the metabolism of trazodone. These drugs used in combination may result in elevated trazodone plasma concentrations, causing an increased risk for trazodone-related adverse events, such as QT prolongation. Additionally, posaconazole has been associated with prolongation of the QT interval as well as rare cases of TdP; avoid use with other drugs that may prolong the QT interval and are metabolized through CYP3A4, such as trazodone.
Potassium-sparing diuretics: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive

hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Prasugrel: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving platelet inhibitors (e.g., cilostazol, clopidogrel, dipyridamole, ticlopidine, platelet glycoprotein IIb/IIIa inhibitors). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with an antiplatelet medication and to promptly report any bleeding events to the practitioner.
Prazosin: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Pregabalin: (Major) Initiate pregabalin at the lowest recommended dose and monitor patients for symptoms of sedation and somnolence during coadministration of pregabalin and trazodone. Concomitant use of pregabalin with trazodone may cause additive CNS depression. Educate patients about the risks and symptoms of excessive CNS depression.
Primaquine: (Major) Concomitant use of trazodone and primaquine 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.
Primidone: (Moderate) Monitor for excessive sedation and somnolence during coadministration of trazodone and primidone. Concurrent use may result in additive CNS depression. Additionally, concurrent use may decrease trazodone exposure; adjust dose as needed based on therapeutic response. Trazodone is a CYP3A4 substrate; primidone is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Procainamide: (Major) Concomitant use of trazodone and procaonamide 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.
Procarbazine: (Moderate) Coadministration of trazodone and procarbazine may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue procarbazine and trazodone and

initiate symptomatic treatment if serotonin syndrome occurs.
Prochlorperazine: (Minor) Prochlorperazine, a phenothiazine, is associated with a possible risk for QT prolongation. Theoretically, the risk of QT prolongation may be increased if coadministered with drugs with a possible risk for QT prolongation, such as trazodone. In addition, phenothiazines can potentiate the CNS-depressant action of other drugs such as trazodone. Clinicians should note that additive CNS effects (e.g., oversedation, respiratory depression, and hypotension) may occur if prochlorperazine is administered concomitantly with trazodone.
Promethazine: (Major) Concomitant use of promethazine and trazodone 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. Because promethazine causes pronounced sedation, an enhanced CNS depressant effect or additive drowsiness may also occur when it is combined with other CNS depressants including trazodone.
Promethazine; Dextromethorphan: (Major) Concomitant use of promethazine and trazodone 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. Because promethazine causes pronounced sedation, an enhanced CNS depressant effect or additive drowsiness may also occur when it is combined with other CNS depressants including trazodone.
Promethazine; Phenylephrine: (Major) Concomitant use of promethazine and trazodone 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. Because promethazine causes pronounced sedation, an enhanced CNS depressant effect or additive drowsiness may also occur when it is combined with other CNS depressants including trazodone.
Propafenone: (Major) Concomitant use of propafenone and trazodone 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.
Propranolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with

trazodone.
Protriptyline: (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for additive CNS depression and serotonin syndrome.
Pseudoephedrine; Triprolidine: (Moderate) Antihistamines that may cause sedation, such as triprolidine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Quazepam: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
QUEtiapine: (Major) Avoid coadministration of trazodone and quetiapine. Limited data, including some case reports, suggest that quetiapine may be associated with a significant prolongation of the QTc interval in rare instances. According to the manufacturer, use of quetiapine should be avoided in combination with drugs known to increase the QT interval. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are postmarketing reports of TdP. Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval.
Quinapril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Quinapril; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
quiNIDine: (Major) Concomitant use of trazodone and quinidine 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.
Quizartinib: (Major) Concomitant use of quizartinib and trazodone 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.
Ramelteon: (Moderate) CNS depressants should be used cautiously in patients receiving trazodone because of additive CNS depressant effects, including possible respiratory

depression or hypotension. A dose reduction of one or both drugs may be warranted.
Ramipril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Ranolazine: (Major) The manufacturer of trazodone recommends avoiding trazodone in patients receiving other drugs that increase the QT interval. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of torsade de pointes (TdP). 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. In addition, ranolazine could impair the metabolism of trazodone through inhibition of CYP3A, thereby increasing the risk of trazodone-related adverse effects, including QT prolongation.
Rasagiline: (Major) The manufacturer of rasagiline recommends against concurrent use with antidepressants, including trazodone, or use of an antidepressant within 14 days of discontinuing rasagiline since serotonin syndrome has been reported in patients treated with antidepressants and rasagiline. If coadministration is necessary, inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue rasagiline and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Relugolix: (Major) Concomitant use of trazodone and relugolix 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.
Relugolix; Estradiol; Norethindrone acetate: (Major) Concomitant use of trazodone and relugolix 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.
Remifentanil: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering remifentanil with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and

dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Remimazolam: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Reteplase, r-PA: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving thrombolytic agents. Patients should be closely monitored for signs and symptoms of bleeding when a thrombolytic agent is administered with trazodone.
Revumenib: (Major) Concomitant use of revumenib and trazodone 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.
Ribociclib: (Major) Avoid coadministration of ribociclib with trazodone due to an increased risk for QT prolongation and torsade de pointes (TdP). Systemic exposure of trazodone may also be increased resulting in increase in treatment-related adverse reactions. Ribociclib is a strong CYP3A4 inhibitor that has been shown to prolong the QT interval in a concentration-dependent manner. Trazodone is a CYP3A4 substrate that can also prolong the QT/QTc interval at therapeutic doses; in addition, there are postmarketing reports of TdP. Concomitant use may increase the risk for QT prolongation.
Ribociclib; Letrozole: (Major) Avoid coadministration of ribociclib with trazodone due to an increased risk for QT prolongation and torsade de pointes (TdP). Systemic exposure of trazodone may also be increased resulting in increase in treatment-related adverse reactions. Ribociclib is a strong CYP3A4 inhibitor that has been shown to prolong the QT interval in a concentration-dependent manner. Trazodone is a CYP3A4 substrate that can also prolong the QT/QTc interval at therapeutic doses; in addition, there are postmarketing reports of TdP. Concomitant use may increase the risk for QT prolongation.
rifAMPin: (Moderate) Consider increasing the trazodone dose based on therapeutic response when coadministered with rifampin. Concurrent use may decrease trazodone exposure. Trazodone is a CYP3A4 substrate; rifampin is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone.
Rifapentine: (Moderate) Consider increasing the trazodone dose based on therapeutic response when coadministered with rifapentine. Concurrent use may decrease trazodone exposure. Trazodone is a CYP3A4 substrate; rifapentine is a strong CYP3A4 inducer. Coadministration with other strong CYP3A4 inducers decreased the exposure

of trazodone compared to the use of trazodone alone.
Rilpivirine: (Major) Concomitant use of trazodone and rilpivirine 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. 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 trazodone and risperidone 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.
Ritonavir: (Major) Avoid coadministration of trazodone with ritonavir due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; ritonavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Rivaroxaban: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Rizatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
romiDEPsin: (Major) Concomitant use of trazodone and romidepsin 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.
Sacubitril; Valsartan: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with

trazodone.
Safinamide: (Contraindicated) Safinamide is contraindicated for use with trazodone due to the risk of serotonin syndrome. 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. At least 14 days should elapse between the discontinuation of safinamide and the initiation of trazodone.
Salicylates: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Salsalate: (Moderate) Monitor for signs and symptoms of bleeding during concomitant trazodone and salicylate use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when serotonin norepinephrine reuptake inhibitors are coadministered with another anticoagulant.
Saquinavir: (Contraindicated) The concurrent use of trazodone and saquinavir boosted with ritonavir is contraindicated due to the risk of life threatening cardiac arrythmias. Saquinavir boosted with ritonavir is a potent inhibitor of CYP3A4, an isoenzyme partially responsible for the metabolism of trazodone. These drugs used together may result in large increases in trazodone serum concentrations, which could cause adverse events such as nausea, dizziness, hypotension, syncope, and cardiac arrhythmias.
Secobarbital: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and secobarbital. Concurrent use may result in additive CNS depression.
Selegiline: (Contraindicated) Trazodone is contraindicated for use with selegiline, a selective monoamine oxidase type B inhibitor (MAO-B inhibitor). At least 14 days should elapse between discontinuation of selegiline and initiation of treatment with trazodone. After stopping treatment with trazodone, a time period of at least 14 days should elapse before starting therapy with selegiline. Serotonin syndrome has occurred in patients receiving selective MAO-B inhibitors and serotonergic antidepressants simultaneously.
Selpercatinib: (Major) Concomitant use of trazodone and selpercatinib 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.
Serotonin-Receptor Agonists: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Sertraline: (Major) Trazodone and sertraline may both cause QT prolongation. Concurrent use may also increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate appropriate treatment if serotonin syndrome occurs.
Sevoflurane: (Major) Concomitant use of trazodone 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.
Siponimod: (Major) Concomitant use of trazodone and siponomod 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.
Solifenacin: (Major) Concomitant use of trazodone and solifenacin 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.
SORAfenib: (Major) Concomitant use of trazodone and sorafenib 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.
Sotalol: (Major) Concomitant use of sotalol and trazodone 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.
Spironolactone: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension.

Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Spironolactone; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
St. John's Wort, Hypericum perforatum: (Moderate) Coadministration of trazodone and St. John's Wort may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Stiripentol: (Moderate) Monitor for excessive sedation and somnolence during coadministration of stiripentol and trazodone. CNS depressants can potentiate the effects of stiripentol.
SUFentanil: (Moderate) Because of the potential risk and severity of excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering sufentanil with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Sulindac: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
SUMAtriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
SUMAtriptan; Naproxen: (Moderate) Monitor for signs and symptoms of serotonin

syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome. (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
SUNItinib: (Major) Concomitant use of trazodone and sunitinib 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.
Suvorexant: (Moderate) CNS depressant drugs may have cumulative effects when administered concurrently and they should be used cautiously with suvorexant. A reduction in dose of the CNS depressant may be needed in some cases.
Tacrolimus: (Major) Concomitant use of trazodone and tacrolimus 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.
Taletrectinib: (Major) Concomitant use of taletrectinib and trazodone 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.
Tamoxifen: (Major) Concomitant use of tamoxifen and trazodone 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 excessive sedation, somnolence, and serotonin syndrome, caution should be observed when administering tapentadol with trazodone. Limit the use of opioid pain medications with trazodone to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. Inform patients taking this combination of the possible increased risks and monitor for the emergence of excessive CNS depression

and serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Tasimelteon: (Moderate) CNS depressants should be used cautiously in patients receiving trazodone because of additive CNS depressant effects, including possible respiratory depression or hypotension. A dose reduction of one or both drugs may be warranted.
Telavancin: (Major) Concomitant use of trazodone and telavancin 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.
Telmisartan: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Telmisartan; amLODIPine: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Telmisartan; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Temazepam: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Tenecteplase: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving thrombolytic agents. Patients should be closely monitored for signs and symptoms of bleeding when a thrombolytic agent is administered with trazodone.
Terazosin: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Tetrabenazine: (Major) Concomitant use of trazodone and tetrabenazine 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.
Thalidomide: (Major) The use of CNS depressants, such as trazodone, concomitantly with thalidomide may cause an additive sedative effect and should be avoided. Thalidomide frequently causes drowsiness and somnolence. Dose reductions may be required. Patients should be instructed to avoid situations where drowsiness may be a problem and not to take other medications that may cause drowsiness without adequate medical advice. Advise patients as to the possible impairment of mental and/or physical abilities required for the performance of hazardous tasks, such as driving a car or operating other complex or dangerous machinery.
Thiazide diuretics: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Thioridazine: (Contraindicated) Avoid concomitant use of trazodone and thioridazine due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation.
Thiothixene: (Moderate) Thiothixene can potentiate the CNS-depressant action of other drugs such as trazodone. Caution should be exercised during simultaneous use of these agents due to potential excessive CNS effects or additive hypotension.
Thrombolytic Agents: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving thrombolytic agents. Patients should be closely monitored for signs and symptoms of bleeding when a thrombolytic agent is administered with trazodone.
Ticagrelor: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving platelet inhibitors (e.g., cilostazol, clopidogrel, dipyridamole, ticlopidine, platelet glycoprotein IIb/IIIa inhibitors). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with an antiplatelet medication and to promptly report any bleeding events to the practitioner.
Timolol: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Tipranavir: (Major) Avoid coadministration of trazodone with tipranavir due to the potential for increased trazodone exposure and associated adverse effects including QT

prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; tipranavir is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Tolcapone: (Major) COMT inhibitors should be given cautiously with other agents that cause CNS depression, such as trazodone, due to the possibility of additive sedation. COMT inhibitors have also been associated with sudden sleep onset during activities of daily living such as driving, which has resulted in accidents in some cases. Prescribers should re-assess patients for drowsiness or sleepiness regularly throughout treatment, especially since events may occur well after the start of treatment. Patients should be advised to avoid driving or other tasks requiring mental alertness until they know how the combination affects them.
Tolmetin: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Tolterodine: (Major) Tolterodine has been associated with dose-dependent prolongation of the QT interval, especially in poor CYP2D6 metabolizers and should be avoided in combination with trazodone. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval.
Toremifene: (Major) Concomitant use of trazodone and toremifene 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.
Torsemide: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
traMADol: (Major) Reserve concomitant prescribing of tramadol and trazodone for use in patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death. If

concomitant use is necessary, also monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue therapy immediately if serotonin syndrome is suspected. Also, the concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system, such as trazodone, has resulted in serotonin syndrome.
Tramadol; Acetaminophen: (Major) Reserve concomitant prescribing of tramadol and trazodone for use in patients in whom alternate treatment options are inadequate. Limit dosages and durations to the minimum required and monitor patients closely for respiratory depression and sedation. If concomitant use is necessary, consider prescribing naloxone for the emergency treatment of opioid overdose. Concomitant use can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death. If concomitant use is necessary, also monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue therapy immediately if serotonin syndrome is suspected. Also, the concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system, such as trazodone, has resulted in serotonin syndrome.
Trandolapril: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Trandolapril; Verapamil: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Tranylcypromine: (Contraindicated) Due to the risk of serotonin syndrome, monoamine oxidase inhibitors (MAOIs) intended to treat psychiatric disorders are contraindicated for use with trazodone or within 14 days of discontinuing treatment with trazodone. Conversely, trazodone should not be initiated within 14 days of stopping an MAOI.
Treprostinil: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Triamterene: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Triamterene; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects,

patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone. (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Triazolam: (Major) Monitor for excessive sedation and somnolence during coadministration of trazodone and benzodiazepines. Concurrent use may result in additive CNS depression.
Triclabendazole: (Major) Concomitant use of triclabendazole and trazodone 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.
Tricyclic antidepressants: (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for additive CNS depression and serotonin syndrome.
Trifluoperazine: (Minor) Trifluoperazine, a phenothiazine, is associated with a possible risk for QT prolongation. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are post-marketing reports of torsade de pointes (TdP). Therefore, the manufacturer recommends avoiding trazodone in patients receiving other drugs that increase the QT interval; if the drugs must be used together, use with caution. In addition, phenothiazines should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects, including possible respiratory depression or hypotension.
Trimipramine: (Moderate) Monitor for unusual drowsiness and excess sedation and signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and tricyclic antidepressant use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for additive CNS depression and serotonin syndrome.
Triprolidine: (Moderate) Antihistamines that may cause sedation, such as triprolidine, should be used cautiously in patients receiving trazodone because of additive CNS-depressant effects.
Triptorelin: (Major) Concomitant use of triptorelin and trazodone 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.

Tryptophan, 5-Hydroxytryptophan: (Major) Due to the risk of serotonin syndrome, concurrent use of trazodone and other serotonergic medications, such as tryptophan, 5-hydroxytryptophan should be avoided if possible. If concomitant use is clinically warranted, patients should be informed of the increased risk of serotonin syndrome, particularly during treatment initiation and during dose increases. 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. Treatment with trazodone and any concomitant serotonergic agents should be discontinued immediately if signs and symptoms of serotonin syndrome occur, and supportive symptomatic treatment should be initiated.
Tucatinib: (Major) Avoid coadministration of trazodone with tucatinib due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; tucatinib is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Valerian, Valeriana officinalis: (Major) Valerian, Valeriana officinalis may interact with trazodone. These interactions are probably pharmacodynamic in nature, or result from additive mechanisms of action. For example, additive sedation is possible.
Valsartan: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Valsartan; hydroCHLOROthiazide, HCTZ: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Vandetanib: (Major) Concomitant use of vandetanib and trazodone 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.
Vardenafil: (Major) Concomitant use of vardenafil and trazodone 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 trazodone 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.
Venlafaxine: (Major) Due to the potential for QT prolongation, cautious use and close monitoring are advisable if concurrent use of trazodone and venlafaxine is necessary. Both drugs may cause QT interval prolongation and a risk for torsade de pointes (TdP). In addition, concurrent use of trazodone with other drugs that modulate serotonergic function, such as venlafaxine, 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.
Verapamil: (Minor) Due to additive hypotensive effects, patients receiving antihypertensive agents concurrently with trazodone may have excessive hypotension. Decreased dosage of the antihypertensive agent may be required when given with trazodone.
Vilazodone: (Moderate) Vilazodone and trazodone have similar pharmacologic effects and may increase risk for sedation and serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue vilazodone and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Voclosporin: (Major) Concomitant use of voclosporin and trazodone 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. 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) Avoid coadministration of trazodone with clarithromycin due to the potential for increased trazodone exposure and associated adverse effects including QT prolongation. If concurrent use cannot be avoided, consider a reduced dose of trazodone based on tolerability. Trazodone is a CYP3A4 substrate; clarithromycin is a strong CYP3A4 inhibitor. Coadministration of other strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.
Voriconazole: (Major) Avoid coadministration of voriconazole with trazodone due to the potential for additive effects on the QT interval; increased exposure to trazodone may also occur. Both drugs are associated with QT prolongation; there are also postmarketing reports of torsade de pointes (TdP) with trazodone. Voriconazole has also

been associated with rare cases of torsades de pointes, cardiac arrest, and sudden death. In addition, coadministration of voriconazole (a strong CYP3A4 inhibitor) with trazodone (a CYP3A4 substrate) may result in elevated trazodone plasma concentrations and an increased risk for adverse events, including QT prolongation. If these drugs are given together, consider decreasing the dose of trazodone and 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 trazodone 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.
Vortioxetine: (Moderate) Coadministration of trazodone and vortioxetine may increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue vortioxetine and trazodone and initiate symptomatic treatment if serotonin syndrome occurs.
Warfarin: (Moderate) Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with anticoagulants and to promptly report any bleeding events to the practitioner. Serotonergic agents may increase the risk of bleeding when combined with anticoagulants via inhibition of serotonin uptake by platelets; however, the absolute risk is not known. It would be prudent for clinicians to monitor the INR and patient's clinical status closely if trazodone is added to or removed from the regimen of a patient stabilized on anticoagulant therapy.
Zaleplon: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of zaleplon and other CNS depressants, such as trazodone, due to the risk for additive CNS depression and next-day psychomotor impairment; dosage adjustments may be necessary.
Ziconotide: (Moderate) Trazodone is a CNS depressant medication that may increase drowsiness, dizziness, and confusion that are associated with ziconotide.
Ziftomenib: (Major) Concomitant use of ziftomenib and trazodone 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.
Ziprasidone: (Major) Concomitant use of ziprasidone and trazodone 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.
ZOLMitriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant trazodone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Zolpidem: (Moderate) Monitor for unusual drowsiness and sedation during coadministration of trazodone and zolpidem due to the risk for additive CNS depression and next-day psychomotor impairment; dose adjustments may be necessary. Limit the dose of Intermezzo sublingual tablets to 1.75 mg/day.
Zuranolone: (Major) Avoid the use of multiple sedating agents due to the risk for additive CNS depression. If use is necessary, consider a downward dosage adjustment of either or both medications, especially in patients with additional risk factors for sedation-related harm.

Adverse Reaction

abnormal dreams, agitation, anxiety, confusion, dizziness, drowsiness, fatigue, hallucinations, headache, insomnia, memory impairment, paranoia, psychosis

Drowsiness (24% to 41%) and dizziness (20% to 28%) are the most common central nervous system (CNS) side effects of trazodone. Other CNS effects occurring in 2% or more of trazodone recipients in clinical trials included headache (10% to 20%), nervousness (6% to 15%), fatigue (6% to 11%), confusion (5% to 6%), impaired concentration (1% to 3%), and disorientation (0 to 2%). CNS or psychiatric side effects occurring in less than 2% of treated patients included hallucinations/delusions, hypomania, and memory impairment. Abnormal dreams, agitation, anxiety, hallucinations, insomnia, paranoid reaction (paranoia), psychosis, and stupor have been reported postmarketing.

depression, mania, suicidal ideation

Mania can occur in persons predisposed to bipolar disorder during treatment with an antidepressant. Monitor all antidepressant-recipients for worsening of depression and/or the emergence of suicidal behaviors or suicidal ideation, especially during the initial months of drug therapy and after dosage changes. Caregivers and/or trazodone recipients should immediately notify the care team of changes in behavior or suicidal ideation during trazodone treatment. In a pooled analysis of placebo-controlled trials of antidepressants (n = 4,500 pediatrics and 77,000 adults), there was an increased risk for

suicidal thoughts and behaviors in people 24 years of age and younger receiving an antidepressant versus placebo, with considerable variation in the risk of suicidality among drugs. The difference in the absolute risk of suicidal thoughts and behaviors across different indications was highest in those with major depression. No suicides occurred in any of the pediatric trials. These studies did not show an increased risk of suicidal thoughts and behavior with antidepressant use in people over 24 years of age. There was a reduction in risk with antidepressant use in adults 65 years and older.

AV block, cardiac arrest, chest pain (unspecified), heart failure, hypertension, hypotension, myocardial infarction, orthostatic hypotension, stroke, syncope

Hypotension (4% to 7%), including orthostatic hypotension, and syncope (3% to 5%), have occurred with trazodone use. Other cardiovascular-related adverse effects associated with trazodone include hypertension (1% to 2%), and shortness of breath (1.3%). Postmarketing reports have also included cases of chest pain (unspecified), cardiospasm, congestive heart failure, cerebrovascular accident (stroke), AV block or other conduction block, myocardial infarction, cardiac arrest.

arrhythmia exacerbation, atrial fibrillation, bradycardia, palpitations, premature ventricular contractions (PVCs), QT prolongation, torsade de pointes, ventricular tachycardia

Cardiac arrhythmias (i.e., arrhythmia exacerbation) and palpitations (up to 7% of outpatients in clinical data) have been reported with trazodone at rates lower than what has been documented with tricyclic antidepressants. Isolated premature ventricular contractions (PVCs), ventricular couplets and short episodes (3 to 4 beats) of ventricular tachycardia have also occurred. Bradycardia and atrial fibrillation have been noted in postmarketing reports with trazodone use. Additionally, there have been postmarketing reports of QT prolongation, Torsade de Pointes, and ventricular tachycardia; some events occurred with trazodone at doses of 100 mg per day or less.

akathisia, aphasia, ataxia, dysarthria, myalgia, paresthesias, seizures, tardive dyskinesia, tremor, vertigo

Various neurologic and musculoskeletal complaints have been reported with trazodone use. Myalgia (more than 1% and up to 6%), tremor (3% to 5%), incoordination or abnormal coordination (2% to 5%) have been reported. Other adverse reactions occurring at an incidence of less than 2% with the use of trazodone in clinical studies included: akathisia, impaired speech (dysarthria), muscle twitches, numbness, and paresthesias. Postmarketing reports have included aphasia, ataxia, extrapyramidal symptoms, grand mal seizures, paresthesias, tardive dyskinesia, and vertigo.

acne vulgaris, alopecia, flushing, hirsutism, hyperhidrosis, night sweats, photosensitivity, pruritus, psoriasis, rash, urticaria

Various skin, skin structure, hypersenstivitiy, and subcutaneous tissue adverse reactions have been reported with trazodone use. Photosensitivity was reported in less than 1% of patients during clinical trials; the mechanism of this reaction is not known. Night sweats (more than 1%), acne vulgaris (less than 1%), hyperhidrosis (less than 1%), alopecia, flushing or vasodilation, psoriasis, rash, urticaria, pruritus, leukonychia, hirsutism, drug eruption, and sweating/clamminess (up to 1.4%) have also been reported. Hypersensitivity has been reported in less than 1% of patients receiving trazodone.

abdominal pain, constipation, diarrhea, dysgeusia, flatulence, gastroesophageal reflux, hypersalivation, nausea, vomiting, xerostomia

Gastrointestinal (GI) adverse reactions have been reported with trazodone use. Xerostomia (15% to 34%) is a common side effect during therapy with trazodone and is believed to be due to alpha-1 adrenergic blocking effects of the drug. Increased salivation and hypersalivation have also been reported with trazodone use. Other GI-related adverse effects include abdominal pain (more than 1%), constipation (7% to 8%), diarrhea (0% to 9%), dysgeusia (up to 1.4%), flatulence, gastroesophageal reflux (less than 1%), increased amylase, nausea (10% to 21%), and vomiting (up to 12.7%).

cholestasis, hyperbilirubinemia, jaundice

Hepatic-related adverse events noted in postmarketing reports of trazodone include cholestasis, hyperbilirubinemia, jaundice, and altered hepatic enzymes.

appetite stimulation, weight gain, weight loss

Appetite stimulation, weight gain (1% to 5%), and weight loss (up to 6%) have been reported in people receiving trazodone.

blurred vision, diplopia

Blurred vision (6% to 15%) may occur with trazodone therapy. Other ophthalmic effects reported with trazodone use include red, tired, or itchy eyes (0% to 3%). Diplopia has been reported postmarketing. The pupillary dilation that occurs following use of many antidepressant drugs including trazodone may trigger an attack of closed-angle glaucoma in a person with anatomically narrow angles who does not have a patent

iridectomy. Trazodone recipients experiencing visual changes, ocular symptoms, or eye pain should have an ophthalmologic examination.

hearing loss, tinnitus

Ear and labyrinth disorders reported with trazodone use include hypoacusis/hearing loss (less than 1%) and tinnitus (less than 1.4%).

bladder discomfort, hematuria, increased urinary frequency, urinary incontinence, urinary retention, urinary urgency

Urinary adverse effects that have been reported with trazodone use include delayed urine flow, increased urinary frequency (less than 2%), urinary incontinence, urinary retention, urinary urgency (greater than 1%), urinary incontinence (less than 1%), bladder discomfort or pain (less than 1%), and hematuria.

ejaculation dysfunction, impotence (erectile dysfunction), libido decrease, libido increase, orgasm dysfunction, priapism

Cases of priapism (painful erections greater than 6 hours in duration) have been reported in males receiving trazodone. Priapism, if not treated promptly, can result in irreversible damage to the erectile tissue. Males who have an erection lasting more than 4 hours, whether painful or not, should immediately discontinue the drug and seek emergency medical attention. Other reproductive and sexual adverse reactions included clitorism (clitoral priapism in females), impotence (erectile dysfunction) (less than 1%), ejaculation dysfunction (retrograde or no ejaculation) (1.5%), orgasm dysfunction (less than 1%), libido increase (less than 2%), and libido decrease (1.3 to 1.5%).

breast discharge, breast enlargement, menstrual irregularity

Adverse endocrine effects associated with trazodone use in females include early menses and missed periods (i.e., menstrual irregularity), breast enlargement or engorgement, and breast discharge or lactation.

anemia, hemolytic anemia, leukocytosis, methemoglobinemia

Hematologic lab abnormalities reported in controlled clinical trials include anemia (less than 2%). Postmarketing reports of hemolytic anemia, leukocytosis, and methemoglobinemia have also been associated with the use of trazodone.

hyponatremia, SIADH

Hyponatremia may occur as a result of treatment with serotonergic antidepressants, including trazodone. Cases with serum sodium lower than 110 mmol/L have been reported. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which can lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Geriatric adults, people taking diuretics, and those who are volume-depleted may be at greater risk of developing hyponatremia. In people with symptomatic hyponatremia, discontinue trazodone and institute appropriate medical intervention.

apnea, chills, dyspnea, edema, malaise, nasal congestion, weakness

Sinus/nasal congestion (3% to 6%), malaise (0% to 3%), and shortness of breath or dyspnea (less than 2%) were reported as adverse reactions during clinical trials with trazodone. Other general adverse effects reported in postmarketing use have included chills, edema, unexplained death, and weakness. Respiratory disorders reported in postmarketing use include apnea.

serotonin syndrome

The use of serotonergic antidepressants, including trazodone, can precipitate serotonin syndrome, a potentially life-threatening condition. The coadministration of trazodone with other serotonergic medications can increase the risk of serotonin syndrome. Symptoms may include nausea, vomiting, sedation, dizziness, diaphoresis (sweating), facial flush, mental status changes, myoclonia, restlessness, shivering, and elevated blood pressure. If serotonin syndrome becomes evident during treatment, trazodone and any other serotonergic agents should be discontinued and appropriate supportive symptomatic medical treatment should be initiated.

Description

Trazodone is an oral selective serotonin reuptake inhibitor and a serotonin type 2 receptor antagonist. It is approved for the treatment of major depressive disorder in adults. Due to its sedating effects, trazodone is also commonly used off-label at low doses for the treatment of insomnia. Due to a higher side effect burden versus traditional first-line agents such as the selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs), trazodone is typically used as a second-line agent for depression in adults and may be particularly helpful for

depressed patients with concomitant insomnia. All product labels for antidepressants contain a boxed warning related to an increased risk of suicidality in children, adolescents, and young adults during the initial stages of therapy when treating depression or other conditions; therefore, the necessity of pharmacologic therapy versus the potential risks should be carefully considered in these populations. Trazodone was initially FDA approved in 1981.

Mechanism Of Action

Trazodone has a unique mechanism of action via activity at a variety of receptors, making it distinct from other traditional antidepressant medications. At low doses, trazodone has antagonistic effects at alpha-1 adrenergic receptors and histamine H1 receptors, leading to an increased risk for postural hypotension, syncope, and sedation. Unlike other sedating antidepressants, trazodone has minimal effects on REM sleep while improving sleep efficiency and subjective sleep quality. At increased doses, trazodone exerts antidepressant effects by selectively inhibiting reuptake of serotonin (5-HT) while also acting as an antagonist at 5-HT2 receptors. Trazodone is also a partial agonist at 5-HT1A receptors, which may provide mild anxiolytic activity.

Pharmacokinetics

Trazodone is administered orally. The drug is 89% to 95% protein bound. In vitro studies show that trazodone undergoes metabolism via oxidation to an active metabolite, m-chlorophenylpiperazine (mCPP), by CYP3A4. Other metabolic pathways that may be involved in the metabolism of trazodone have not been well characterized. Less than 1% of an oral dose is excreted unchanged in the urine. Elimination is mainly through the urine, with about 70% to 75% of a dose excreted (mainly as metabolites) within 72 hours. The average terminal elimination half-life of trazodone under fed state is 18 hours.

Affected cytochrome P450 isoenzymes and drug transporters: CYP3A4
Trazodone is extensively metabolized in the liver, primarily by CYP3A4. The concomitant use of trazodone and strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone, and a lower dosage of trazodone may be needed.

Route-Specific Pharmacokinetics

- **Oral Route**

Tablets (immediate-release): Trazodone is well absorbed after oral administration, without selective localization in any tissue. Food affects absorption. When taken with or

shortly after a meal, there may be an increase in the amount of drug absorbed, a decrease in peak plasma concentrations, and an increase in the time to reach peak concentrations. Peak concentrations are achieved 1 hour after dosing on an empty stomach or 2 hours after dosing when taken with food.
Oral Solution: No clinically significant difference in pharmacokinetic parameters were observed between the oral solution and the immediate-release trazodone tablet administered under fed conditions. Peak plasma levels occur approximately 1 hour after administration under fed conditions. Ingestion of a high-fat meal with the oral solution lowers the mean Cmax of trazodone by 31% and increases the mean AUC by 8%. Median Tmax was similar between fed and fasted conditions.

- **Hepatic Impairment**

Trazodone has not been studied in people with hepatic impairment but is metabolized extensively in the liver.

- **Renal Impairment**

Trazodone has not been studied in people with renal impairment. The primary route of excretion for trazodone metabolites, active and inactive, is via the kidney.

Administration

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

Oral Administration

Oral Solid Formulations

Immediate-release tablets
Administer shortly after a meal or light snack.
The occurrence of drowsiness may require the administration of a major portion of the daily dose at bedtime.

Oral Liquid Formulations

Oral solution
Use a calibrated oral dosage device to measure the dose.
Administer shortly after a meal or light snack.
The occurrence of drowsiness may require the administration of a major portion of the daily dose at bedtime.

Maximum Dosage Limits

- **Adults**

600 mg/day PO for immediate-release dosage forms.

- **Geriatric**
  600 mg/day PO for immediate-release dosage forms.
- **Adolescents**
  Safety and efficacy have not been established; off-label doses have not exceeded 150 mg/day PO.
- **Children**
  6 to 12 years: Safety and efficacy have not been established; off-label max: 6 mg/kg/day PO; off-label doses have not exceeded 150 mg/day PO for those 12 years and older.
  1 to 5 years: Safety and efficacy have not been established.
- **Infants**
  Safety and efficacy have not been established.
- **Neonates**
  Safety and efficacy have not been established.

Dosage Forms

- RALDESY 10mg/mL Solution
- Trazodone Hydrochloride 100mg Oral tablet
- Trazodone Hydrochloride 150mg Oral tablet
- Trazodone Hydrochloride 300mg Oral tablet
- Trazodone Hydrochloride 50mg Oral tablet
- Trazodone Hydrochloride Bulk powder

Dosage Adjustment Guidelines

Hepatic Impairment

Use with caution since trazodone is extensively metabolized in the liver and has not been studied in people with hepatic impairment.

Renal Impairment

Use with caution since trazodone has not been studied in people with renal impairment.