# Brand Names

Bucapsol, BuSpar, Buspar Dividose

# Indication Specific Dosing

## For the treatment of generalized anxiety disorder (GAD) or for the short-term relief of the symptoms of anxiety

### Oral dosage

#### Adults

7.5 mg PO twice daily, initially. May increase the dose by 5 mg/day every 2 to 3 days as needed. Usual dosage: 20 to 30 mg/day, in divided doses. Max: 60 mg/day. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

#### Adolescents†

2.5 to 5 mg PO twice daily, initially. May increase by 5 mg/day every 3 to 7 days as needed. Usual dosage: 10 to 30 mg/day, in divided doses. Max: 60 mg/day. Guidelines do not consider buspirone a first-line option for the treatment of anxiety in adolescents due to inconsistent clinical trial results. In a small study of pediatric patients with anxiety disorder, doses of 5 to 30 mg PO twice daily were well-tolerated in adolescents and improved symptoms over 4 to 6 weeks of treatment. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

#### Children† 6 to 12 years

2.5 to 5 mg PO twice daily, initially. May increase by 5 mg/day every 3 to 7 days as needed. Usual dosage: 10 to 15 mg/day, in divided doses. Max: 60 mg/day. Guidelines do not consider buspirone a first-line option for the treatment of anxiety in children. Dosages exceeding 7.5 mg PO twice daily may be poorly

tolerated. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.

# 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.

## benzodiazepine dependence, increased risk for benzodiazepine withdrawal

Buspirone has a slow onset of action and does not exhibit cross-tolerance with benzodiazepines or other common sedative/hypnotic drugs. Buspirone will not block the withdrawal syndrome often seen with cessation of therapy in those with benzodiazepine dependence and should be used cautiously in people that are at increased risk for benzodiazepine withdrawal. People who are being converted from a benzodiazepine to buspirone therapy may need to overlap buspirone initiation with the gradual downward titration of the benzodiazepine to reduce the risk of withdrawal. Rebound or withdrawal symptoms may occur over varying time periods, depending on the type of medication used, the duration of use, and its effective half-life of elimination.

## renal failure, renal impairment

The use of buspirone in people with severe renal impairment or renal failure is not recommended. Buspirone is predominantly excreted by the kidneys, and people with impaired renal function demonstrated increased plasma levels and a prolonged half-life of buspirone compared to healthy individuals.

## Child-Pugh class C, hepatic failure

The use of buspirone in people with severe hepatic impairment (Child-Pugh class C) or hepatic failure is not recommended. A pharmacokinetic study in people with impaired hepatic function demonstrated increased plasma levels and a prolonged half-life of buspirone compared to healthy subjects.

### activities requiring coordination and concentration, driving or operating machinery

Buspirone 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 buspirone does not affect them adversely. While formal interaction studies of buspirone with alcohol indicate that buspirone does not increase alcohol-induced impairment in motor and mental performance, it is prudent to avoid concomitant use of alcohol and buspirone.

## geriatric

The safety and efficacy profiles of buspirone in geriatric adults are similar to those in younger adults; however, a lower initial dosage is recommended in geriatric adults. The U.S. Omnibus Budget Reconciliation Act (OBRA) regulates medication use in long-term care facilities. When buspirone is 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

Clinical studies related to the use of buspirone in pregnancy and subsequent outcomes are limited. In a prospective analysis of data from the Massachusetts General Hospital National Pregnancy Registry for Psychiatric Medications, 68 pregnant people who gave birth to 72 infants reported use of buspirone during the first trimester of pregnancy. No major malformations were reported in any infants who were exposed to buspirone during the first trimester. Additional well-controlled studies with larger populations of pregnant patients are needed to further assess for potential risks related to buspirone exposure in pregnancy. No teratogenic effects have been observed in animal studies when using approximately 30 times the maximum recommended human dose (MRHD); however, animal reproduction studies are not always predictive of human response. The effects of buspirone during labor and delivery are unknown.

## breast-feeding

Use buspirone with caution during breast-feeding. Buspirone and its metabolites are excreted in the milk of lactating rats. Limited information indicates that doses of buspirone up to 45 mg/day produce low levels in human milk; however, there are no data on the long-term use of buspirone during lactation and the FDA-approved label

recommends avoidance if clinically possible. Consider if an alternative would be appropriate. A pooled analysis found that maternal use of paroxetine usually produced undetectable or low drug concentrations in infant serum; this agent may be an option when initiating chronic therapy for generalized anxiety disorder (GAD) in a breast-feeding individual. For acute anxiety requiring a benzodiazepine, short-acting agents such as oxazepam or lorazepam may be considered; however, the breastfed child should be monitored for sedation, feeding difficulties, or other signs of toxicity which would indicate the need to discontinue the benzodiazepine.

## Pregnancy And Lactation

Clinical studies related to the use of buspirone in pregnancy and subsequent outcomes are limited. In a prospective analysis of data from the Massachusetts General Hospital National Pregnancy Registry for Psychiatric Medications, 68 pregnant people who gave birth to 72 infants reported use of buspirone during the first trimester of pregnancy. No major malformations were reported in any infants who were exposed to buspirone during the first trimester. Additional well-controlled studies with larger populations of pregnant patients are needed to further assess for potential risks related to buspirone exposure in pregnancy. No teratogenic effects have been observed in animal studies when using approximately 30 times the maximum recommended human dose (MRHD); however, animal reproduction studies are not always predictive of human response. The effects of buspirone during labor and delivery are unknown.

## Interactions

Acetaminophen; Aspirin, ASA; Caffeine: (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Acetaminophen; Aspirin, ASA; Caffeine: (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Acetaminophen; Aspirin: (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Acetaminophen; Aspirin; diphenhydrAMINE: (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone

by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of dihydrocodeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Acetaminophen; Codeine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Acetaminophen; HYDROcodone: (Moderate) Concomitant use of hydrocodone with other central nervous system depressants, such as buspirone, can potentiate the effects of hydrocodone and may lead to additive CNS or respiratory depression. If hydrocodone is used with buspirone, the dose of one or both drugs should be reduced.
Acetaminophen; oxyCODONE: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of oxycodone, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Adagrasib: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with adagrasib. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering adagrasib with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A; adagrasib is a strong CYP3A inhibitor. Coadministration with another strong CYP3A inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
ALFentanil: (Moderate) If concomitant use of alfentanil and buspirone is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Almotriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant buspirone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
ALPRAZolam: (Moderate) Concomitant administration of benzodiazepines with CNS-depressant drugs, including buspirone, can potentiate the CNS effects (e.g., increased

sedation or respiratory depression) of either agent. It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect.
Amitriptyline: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Amobarbital: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.
Amoxapine: (Moderate) CNS depressants should be combined cautiously with amoxapine because they could cause additive depressant effects and possible respiratory depression or hypotension. This combination is considered to be safe as long as patients are monitored for excessive adverse effects from either agent.
Amoxicillin; Clarithromycin; Omeprazole: (Moderate) Concomitant administration of clarithromycin with buspirone may result in increases in buspirone AUC; the mechanism is probably reduced buspirone metabolism via CYP3A4. A low dose of buspirone is recommended if administered with significant CYP3A4 inhibitors. Subsequent dose adjustments should be based on clinical assessment.
Amphetamine: (Moderate) Coadministration of buspirone with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Buspirone has some serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Amphetamine; Dextroamphetamine: (Moderate) Coadministration of buspirone with amphetamines may increase the risk of serotonin syndrome. At high doses,

amphetamines can increase serotonin release and act as serotonin agonists. Buspirone has some serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Amphetamines: (Moderate) Coadministration of buspirone with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Buspirone has some serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Apalutamide: (Moderate) Monitor for decreased efficacy of buspirone if apalutamide is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A4 substrate and apalutamide is a strong CYP3A4 inducer. Coadministration with another strong CYP3A4 inducer decreased the AUC of buspirone by 89.6%.
Apraclonidine: (Minor) No specific drug interactions were identified with systemic agents and apraclonidine during clinical trials. Theoretically, apraclonidine might potentiate the effects of CNS depressant drugs such as the anxiolytics, sedatives, and hypnotics, including barbiturates or benzodiazepines.
Aprepitant, Fosaprepitant: (Moderate) Use caution if buspirone and aprepitant, fosaprepitant are used concurrently and monitor for an increase in buspirone-related adverse effects for several days after administration of a multi-day aprepitant regimen. In vitro, buspirone 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 buspirone. 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.

ARIPiprazole: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Asenapine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Aspirin, ASA: (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Aspirin, ASA; Butalbital; Caffeine: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone. (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Aspirin, ASA; Caffeine: (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Aspirin, ASA; Caffeine; Orphenadrine: (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Aspirin, ASA; Carisoprodol; Codeine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs. (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Aspirin, ASA; Citric Acid; Sodium Bicarbonate: (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone

by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Aspirin, ASA; Dipyridamole: (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Aspirin, ASA; Omeprazole: (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Aspirin, ASA; oxyCODONE: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of oxycodone, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs. (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Atazanavir: (Moderate) When buspirone is administered with an inhibitor of CYP3A4 like atazanavir, a lower dose of buspirone is recommended. Dose adjustment of either drug should be based on clinical assessment.
Atazanavir; Cobicistat: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with cobicistat. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering cobicistat with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4. Cobicistat is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects. (Moderate) When buspirone is administered with an inhibitor of CYP3A4 like atazanavir, a lower dose of buspirone is recommended. Dose adjustment of either drug should be based on clinical assessment.
Atropine; Difenoxin: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of diphenoxylate/difenoxin, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
atypical antipsychotic: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Avacopan: (Moderate) Monitor for an increase in buspirone-related adverse reactions if

coadministration with avacopan is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and avacopan is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and avacopan is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Azelastine: (Moderate) Monitor for excessive sedation and somnolence during coadministration of azelastine and buspirone. Concurrent use may result in additive CNS depression.
Azelastine; Fluticasone: (Moderate) Monitor for excessive sedation and somnolence during coadministration of azelastine and buspirone. Concurrent use may result in additive CNS depression.
Barbiturates: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.
Belladonna; Opium: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of opium, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Major) Avoid concomitant use of buspirone and reversible monoamine oxidase inhibitors (MAOIs), such as methylene blue, due to the risk for serotonin syndrome. For patients who are chronically receiving buspirone therapy and require emergency treatment with intravenous (IV) methylene blue, use the lowest possible IV methylene blue dose and hold buspirone until 24 hours after the last dose of IV methylene blue. The risk for serotonin syndrome is greatest with IV methylene blue doses of 1 mg/kg or more. Monitor for serotonin syndrome for 2 weeks or until 24 hours after the last dose of IV methylene blue, whichever comes first. Starting buspirone in a patient who is being treated with IV methylene blue is contraindicated.
Benzphetamine: (Moderate) Coadministration of buspirone with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Buspirone has some serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs

should be discontinued and appropriate medical treatment should be initiated.
Berotralstat: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with berotralstat is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and berotralstat is added or removed from therapy. Buspirone is a sensitive CYP3A4 substrate and berotralstat is a moderate CYP3A4 inhibitor. Coadministration with other moderate CYP3A4 inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Brexpiprazole: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Buprenorphine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant buprenorphine and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Buprenorphine; Naloxone: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant buprenorphine and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Butalbital; Acetaminophen: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.
Butalbital; Acetaminophen; Caffeine: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.
Butalbital; Acetaminophen; Caffeine; Codeine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of

one or both drugs. (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.
Butalbital; Aspirin; Caffeine; Codeine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs. (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone. (Minor) In vitro studies showed that therapeutic levels of aspirin, ASA increased the plasma concentrations of free buspirone by 23% through plasma protein binding displacement. In vivo interaction studies with these drugs have not been performed.
Butorphanol: (Moderate) Concomitant use of butorphanol with other CNS depressants, such as buspirone, can potentiate the effects of butorphanol on respiratory depression, CNS depression, and sedation.
Calcium, Magnesium, Potassium, Sodium Oxybates: (Moderate) Monitor for excessive sedation and somnolence during concomitant use of buspirone and oxybates. Concurrent use may result in additive CNS depression.
carBAMazepine: (Moderate) Monitor for decreased efficacy of buspirone if carbamazepine is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A substrate and carbamazepine is a strong CYP3A inducer. Coadministration with another strong CYP3A inducer decreased buspirone exposure by 89.6%.
Cariprazine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Celecoxib; Tramadol: (Moderate) Tramadol can cause additive CNS depression when used with other agents that are CNS depressants including buspirone.

Cenobamate: (Moderate) If cenobamate is added to a patient receiving a stable buspirone dose, a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A4 substrate and cenobamate is a moderate CYP3A4 inducer. CYP3A4 inducers may increase the rate of buspirone metabolism.
Ceritinib: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with ceritinib. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering ceritinib with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4. Ceritinib is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
chlordiazePOXIDE: (Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
chlordiazePOXIDE; Amitriptyline: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
(Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
chlordiazePOXIDE; Clidinium: (Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence.

Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
Chlorpheniramine; Codeine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Chlorpheniramine; HYDROcodone: (Moderate) Concomitant use of hydrocodone with other central nervous system depressants, such as buspirone, can potentiate the effects of hydrocodone and may lead to additive CNS or respiratory depression. If hydrocodone is used with buspirone, the dose of one or both drugs should be reduced.
Ciprofloxacin: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with ciprofloxacin is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and ciprofloxacin is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and ciprofloxacin is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Citalopram: (Moderate) Coadministration of buspirone with citalopram may increase the risk of serotonin syndrome. Buspirone has some serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Clarithromycin: (Moderate) Concomitant administration of clarithromycin with buspirone may result in increases in buspirone AUC; the mechanism is probably reduced buspirone metabolism via CYP3A4. A low dose of buspirone is recommended if administered with significant CYP3A4 inhibitors. Subsequent dose adjustments should be based on clinical assessment.
cloBAZam: (Moderate) Concomitant administration of benzodiazepines like clobazam with CNS-depressant drugs, including buspirone, may potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
clomiPRAMINE: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose

increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Clorazepate: (Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
cloZAPine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Cobicistat: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with cobicistat. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering cobicistat with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4. Cobicistat is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
Codeine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Codeine; Dexbrompheniramine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Codeine; guaiFENesin: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Codeine; guaiFENesin; Pseudoephedrine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive

responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Codeine; Phenylephrine; Promethazine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Codeine; Promethazine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of codeine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Conivaptan: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with conivaptan is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and conivaptan is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and conivaptan is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Crizotinib: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with crizotinib is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and crizotinib is added or removed from therapy. Buspirone is a sensitive CYP3A4 substrate and crizotinib is a moderate CYP3A inhibitor. Coadministration with a moderate CYP3A4 inhibitor increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Dabrafenib: (Major) The concomitant use of dabrafenib and buspirone may lead to decreased buspirone concentrations and loss of efficacy. Use of an alternative agent is recommended. If concomitant use of these agents together is unavoidable, monitor patients for loss of buspirone efficacy. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. Dabrafenib is a moderate CYP3A4 inducer and buspirone is a sensitive CYP3A4 substrate. Concomitant use of dabrafenib with a single dose of another sensitive CYP3A4 substrate decreased the AUC value of the sensitive CYP3A4 substrate by 65%.
Darunavir: (Moderate) The plasma concentrations of buspirone may be elevated when administered concurrently with darunavir. Close clinical monitoring is recommended during coadministration; buspirone dose reductions may be required. Predictions regarding this interaction can be made based on the metabolic pathways of these drugs. Darunavir is an inhibitor of CYP3A4, an isoenzyme responsible for the metabolism of buspirone. These drugs used in combination may result in elevated buspirone plasma

concentrations, causing an increased risk for buspirone-related adverse events.
Darunavir; Cobicistat: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with cobicistat. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering cobicistat with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4. Cobicistat is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects. (Moderate) The plasma concentrations of buspirone may be elevated when administered concurrently with darunavir. Close clinical monitoring is recommended during coadministration; buspirone dose reductions may be required. Predictions regarding this interaction can be made based on the metabolic pathways of these drugs. Darunavir is an inhibitor of CYP3A4, an isoenzyme responsible for the metabolism of buspirone. These drugs used in combination may result in elevated buspirone plasma concentrations, causing an increased risk for buspirone-related adverse events.
Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with cobicistat. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering cobicistat with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4. Cobicistat is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects. (Moderate) The plasma concentrations of buspirone may be elevated when administered concurrently with darunavir. Close clinical monitoring is recommended during coadministration; buspirone dose reductions may be required. Predictions regarding this interaction can be made based on the metabolic pathways of these drugs. Darunavir is an inhibitor of CYP3A4, an isoenzyme responsible for the metabolism of buspirone. These drugs used in combination may result in elevated buspirone plasma concentrations, causing an increased risk for buspirone-related adverse events.
Desipramine: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Desvenlafaxine: (Moderate) Coadministration of buspirone with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients

taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
dexAMETHasone: (Moderate) Monitor for decreased efficacy of buspirone if dexamethasone is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A substrate and dexamethasone is a CYP3A inducer.
Dextroamphetamine: (Moderate) Coadministration of buspirone with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Buspirone has some serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Dicyclomine: (Moderate) Dicyclomine can cause drowsiness, so it should be used cautiously in patients receiving CNS depressants like buspirone.
Digoxin: (Minor) Buspirone can displace digoxin from plasma proteins, but the clinical significance of this effect has yet to be determined.
dilTIAZem: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with diltiazem is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and diltiazem is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and diltiazem is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Diphenoxylate; Atropine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of diphenoxylate/difenoxin, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Doxepin: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
droNABinol: (Moderate) Use caution if coadministration of dronabinol with buspirone is necessary, and monitor for additive dizziness, confusion, somnolence, and other CNS effects.

Dronedarone: (Moderate) Dronedarone is metabolized by and is an inhibitor of CYP3A. Buspirone is a substrate for CYP3A4. The concomitant administration of dronedarone and CYP3A substrates may result in increased exposure of the substrate and should, therefore, be undertaken with caution.
droPERidol: (Major) CNS depressants have additive effects with droperidol. Following administration of droperidol, lower doses of the other CNS depressant should be used.
DULoxetine: (Moderate) Coadministration of buspirone with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Duvelisib: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with duvelisib is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and duvelisib is added or removed from therapy. Buspirone is a sensitive CYP3A4 substrate and duvelisib is a moderate CYP3A4 inhibitor. Coadministration with other moderate CYP3A4 inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Efavirenz: (Moderate) Substances that are inducers of hepatic cytochrome P450 isoenzyme CYP3A4, such as efavirenz, may increase the rate of buspirone metabolism. In a study of healthy volunteers, co-administration of buspirone with rifampin decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect.
Efavirenz; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) Substances that are inducers of hepatic cytochrome P450 isoenzyme CYP3A4, such as efavirenz, may increase the rate of buspirone metabolism. In a study of healthy volunteers, co-administration of buspirone with rifampin decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect.
Efavirenz; lamiVUDine; Tenofovir Disoproxil Fumarate: (Moderate) Substances that are inducers of hepatic cytochrome P450 isoenzyme CYP3A4, such as efavirenz, may increase the rate of buspirone metabolism. In a study of healthy volunteers, co-administration of buspirone with rifampin decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of

buspirone may be necessary to maintain anxiolytic effect.
Elagolix: (Moderate) Monitor for decreased efficacy of buspirone if elagolix is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A4 substrate and elagolix is a weak to moderate CYP3A4 inducer.
Elagolix; Estradiol; Norethindrone acetate: (Moderate) Monitor for decreased efficacy of buspirone if elagolix is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A4 substrate and elagolix is a weak to moderate CYP3A4 inducer.
Elbasvir; Grazoprevir: (Moderate) Administering buspirone with elbasvir; grazoprevir may result in elevated buspirone plasma concentrations. Buspirone 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 buspirone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Alafenamide: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with cobicistat. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering cobicistat with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4. Cobicistat is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with cobicistat. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering cobicistat with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4. Cobicistat is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
Encorafenib: (Moderate) Monitor for decreased efficacy of buspirone if encorafenib is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A substrate and encorafenib is a strong CYP3A inducer. Coadministration with another strong CYP3A inducer decreased buspirone exposure by 89.6%.

Enzalutamide: (Moderate) Monitor for decreased efficacy of buspirone if enzalutamide is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a CYP3A4 substrate and enzalutamide is a strong CYP3A4 inducer. Coadministration with another strong CYP3A4 inducer decreased the AUC of buspirone by 89.6%.
Erythromycin: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with erythromycin is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and erythromycin is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and erythromycin is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Escitalopram: (Moderate) Coadministration of buspirone with escitalopram may increase the risk of serotonin syndrome. Buspirone has some serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Estazolam: (Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
Eszopiclone: (Moderate) The combination of buspirone and other CNS depressants can increase the risk for sedation.
Etomidate: (Moderate) General anesthetics potentiate the effects of CNS depressants.
Fedratinib: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with fedratinib is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and fedratinib is added or removed from therapy. Buspirone is a sensitive CYP3A4 substrate and fedratinib is a moderate CYP3A4 inhibitor. Coadministration with other moderate CYP3A4 inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Fenfluramine: (Moderate) Use fenfluramine and buspirone with caution due to an increased risk of serotonin syndrome. Monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if

serotonin syndrome occurs.
fentaNYL: (Moderate) Monitor patients for signs and symptoms of serotonin syndrome during concomitant use of buspirone and fentanyl, particularly during treatment initiation and dosage increases. If serotonin syndrome occurs, consider discontinuation of therapy. The concomitant use of serotonergic drugs increases the risk of serotonin syndrome.
Fexinidazole: (Moderate) Monitor for decreased efficacy of buspirone if fexinidazole is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A substrate and fexinidazole is a moderate CYP3A inducer.
FLUoxetine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering buspirone and fluoxetine. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Flurazepam: (Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
fluvoxaMINE: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering buspirone and fluvoxamine. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Food: (Major) Buspirone should be taken consistently with or without food because food decreases the presystemic clearance of buspirone.
Fosamprenavir: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with fosamprenavir is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and fosamprenavir is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and fosamprenavir is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.

Fosphenytoin: (Moderate) Monitor for decreased efficacy of buspirone if fosphenytoin is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A substrate and fosphenytoin is a strong CYP3A inducer. Coadministration with another strong CYP3A inducer decreased buspirone exposure by 89.6%.
Frovatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant buspirone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
General anesthetics: (Moderate) General anesthetics potentiate the effects of CNS depressants.
Gepirone: (Moderate) Monitor for serotonin syndrome if concomitant use of gepirone and buspirone is necessary. Both medications affect the serotonergic neurotransmitter system; concomitant use increases the risk for serotonin syndrome.
Grapefruit juice: (Major) Patients receiving buspirone should be advised to avoid drinking large amounts of grapefruit juice. In a study in healthy volunteers, coadministration of buspirone (10 mg single dose) with grapefruit juice (200 mL double-strength three times daily for 2 days) increased plasma buspirone concentrations significantly (4.3-fold increase in Cmax; 9.2-fold increase in AUC). Subjective drowsiness and other side effects of buspirone, like dizziness, nausea, headache, nervousness, or restlessness. may be increased with grapefruit juice ingestion.
Haloperidol: (Moderate) Monitor for adverse effects, such as excess sedation and QT prolongation, during coadministration of buspirone and haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and buspirone. Elevated haloperidol concentrations may increase the risk of adverse effects, including QT prolongation.
Homatropine; HYDROcodone: (Moderate) Concomitant use of hydrocodone with other central nervous system depressants, such as buspirone, can potentiate the effects of hydrocodone and may lead to additive CNS or respiratory depression. If hydrocodone is used with buspirone, the dose of one or both drugs should be reduced.
HYDROcodone: (Moderate) Concomitant use of hydrocodone with other central nervous system depressants, such as buspirone, can potentiate the effects of hydrocodone and may lead to additive CNS or respiratory depression. If hydrocodone is used with buspirone, the dose of one or both drugs should be reduced.
HYDROcodone; Ibuprofen: (Moderate) Concomitant use of hydrocodone with other central nervous system depressants, such as buspirone, can potentiate the effects of hydrocodone and may lead to additive CNS or respiratory depression. If hydrocodone is used with buspirone, the dose of one or both drugs should be reduced.
HYDROmorphone: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of hydromorphone, which may potentially lead to respiratory

depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate; Sodium Biphosphate: (Major) Avoid concomitant use of buspirone and reversible monoamine oxidase inhibitors (MAOIs), such as methylene blue, due to the risk for serotonin syndrome. For patients who are chronically receiving buspirone therapy and require emergency treatment with intravenous (IV) methylene blue, use the lowest possible IV methylene blue dose and hold buspirone until 24 hours after the last dose of IV methylene blue. The risk for serotonin syndrome is greatest with IV methylene blue doses of 1 mg/kg or more. Monitor for serotonin syndrome for 2 weeks or until 24 hours after the last dose of IV methylene blue, whichever comes first. Starting buspirone in a patient who is being treated with IV methylene blue is contraindicated.
Idelalisib: (Major) Avoid concomitant use of idelalisib, a strong CYP3A inhibitor, with buspirone, a CYP3A substrate, as buspirone toxicities may be significantly increased. The AUC of a sensitive CYP3A substrate was increased 5.4-fold when coadministered with idelalisib.
Iloperidone: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Imatinib: (Moderate) CYP3A4 inhibitors, such as imatinib, may decrease systemic clearance of buspirone leading to increased or prolonged effects. If buspirone is to be administered concurrently with significant CYP3A4 inhibitors, a low dose of buspirone is recommended initially.
Imipramine: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Ioflupane I 123: (Moderate) Buspirone binds to the dopamine transporter and may interfere with dopamine transporter (DAT) imaging that utilizes radiolabeled ioflupane.
Isavuconazonium: (Moderate) Concomitant use of isavuconazonium with buspirone may result in increased serum concentrations of buspirone. Buspirone 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) Concomitant use of monoamine oxidase inhibitors (MAOIs) and buspirone is contraindicated because several cases of elevated blood pressure have been reported in patients taking MAO inhibitors who were then given

buspirone; serotonin syndrome may also occur. A 10-day interval after discontinuing isocarboxazid is recommended before initiating buspirone treatment. At least 14 days should elapse between the discontinuation of phenelzine and initiating buspirone, At least a 7-day interval should elapse after discontinuing tranylcypromine before initiating buspirone treatment. Monitor for serotonin-related effects during therapy transitions.
Isoflurane: (Moderate) General anesthetics potentiate the effects of CNS depressants.
Itraconazole: (Major) A low dose of buspirone is recommended (e.g., 2.5 mg daily) if used in combination with itraconazole. Subsequent dose adjustment of either drug should be based on clinical assessment. Buspirone is a sensitive CYP3A4 substrate; itraconazole is a strong CYP3A4 inhibitor. In a study in healthy volunteers, coadministration of buspirone with itraconazole increased the AUC and Cmax of buspirone by 19-fold and 13-fold, respectively. These pharmacokinetic interactions were accompanied by an increased incidence of side effects attributable to buspirone.
Ivosidenib: (Moderate) Monitor for loss of efficacy of buspirone during coadministration of ivosidenib; a buspirone dose adjustment may be necessary. Buspirone is a sensitive substrate of CYP3A4; ivosidenib induces CYP3A4 and may lead to decreased buspirone concentrations.
Ketamine: (Moderate) General anesthetics potentiate the effects of CNS depressants.
Ketoconazole: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with ketoconazole. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering ketoconazole with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4; ketoconazole is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
Lansoprazole; Amoxicillin; Clarithromycin: (Moderate) Concomitant administration of clarithromycin with buspirone may result in increases in buspirone AUC; the mechanism is probably reduced buspirone metabolism via CYP3A4. A low dose of buspirone is recommended if administered with significant CYP3A4 inhibitors. Subsequent dose adjustments should be based on clinical assessment.
Lasmiditan: (Moderate) Serotonin syndrome may occur during coadministration of lasmiditan and buspirone. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly after a dose increase or the addition of other serotonergic medications to an existing regimen. Discontinue all serotonergic agents if serotonin syndrome occurs and implement appropriate medical management.
Lefamulin: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with oral lefamulin is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and oral lefamulin is added

or removed from therapy. Buspirone is a sensitive CYP3A4 substrate and oral lefamulin is a moderate CYP3A4 inhibitor; an interaction is not expected with intravenous lefamulin. Coadministration with other moderate CYP3A4 inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Lenacapavir: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with lenacapavir is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and lenacapavir is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and lenacapavir is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Letermovir: (Moderate) Administering letermovir with buspirone may increase buspirone concentration and risk for adverse events. The magnitude of this interaction may be increased in patients who are also receiving cyclosporine. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Consequently, when administered with both letermovir and cyclosporine, a low dose of buspirone used cautiously is recommended. Buspirone is a sensitive substrate of CYP3A4. Letermovir is a moderate CYP3A4 inhibitor. The combined effect of letermovir and cyclosporine on CYP3A4 substrates may be similar to a strong CYP3A4 inhibitor.
Levoketoconazole: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with ketoconazole. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering ketoconazole with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4; ketoconazole is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
Levomilnacipran: (Moderate) Coadministration of buspirone with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Levorphanol: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of levorphanol, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.

Linezolid: (Contraindicated) Due to an increased risk of serotonin syndrome, treatment initiation with buspirone is contraindicated in patients currently receiving linezolid, an antibiotic that is also a non-selective monoamine oxidase (MAO) inhibitor. If urgent psychiatric treatment is required, interventions other than buspirone (e.g., alternative medication, hospitalization) should be considered. In patients receiving buspirone and requiring urgent treatment with linezolid, buspirone 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 two weeks or until 24 hours after the last dose of linezolid, whichever comes first. Buspirone may be re-initiated 24 hours after the last dose of linezolid.
Lisdexamfetamine: (Moderate) Coadministration of buspirone with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Buspirone has some serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Lithium: (Moderate) Coadministration of buspirone with lithium may increase the risk of serotonin syndrome. Both medications have central serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome is suspected, all serotonergic agents should be discontinued and appropriate medical treatment should be implemented.
Lonafarnib: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with lonafarnib. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering lonafarnib with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4; lonafarnib is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
Lopinavir; Ritonavir: (Major) When buspirone is administered with a potent inhibitor of CYP3A4 like ritonavir, a low dose of buspirone used cautiously is recommended. Some patients receiving drugs that are potent inhibitors of CYP3A4 with buspirone have reported lightheadedness, asthenia, dizziness, and drowsiness. If the two drugs are to be used in combination, a low dose of buspirone (e.g., 2.5 mg PO twice daily) is recommended. Subsequent dose adjustment of either drug should be based on clinical assessment. Several other anti-retroviral protease inhibitors also inhibit CYP3A4, and these may interact with buspirone in a similar manner.

Lorlatinib: (Moderate) Monitor for decreased efficacy of buspirone if lorlatinib is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A4 substrate and lorlatinib is a moderate CYP3A4 inducer.
Loxapine: (Moderate) The combination of buspirone and CNS depressants like the antipsychotics can increase the risk for sedation.
Lumacaftor; Ivacaftor: (Moderate) Lumacaftor; ivacaftor may reduce the efficacy of buspirone by decreasing its systemic exposure. A buspirone dosage adjustment may be necessary to maintain anxiolytic activity. Lumacaftor is a strong CYP3A inducer. Buspirone has been shown in vitro to be metabolized via CYP3A4; this finding is consistent with in vivo interactions observed. When coadministered with rifampin, another strong CYP3A inducer, buspirone Cmax and AUC decreased by 84% and 90%, respectively.
Lumacaftor; Ivacaftor: (Moderate) Lumacaftor; ivacaftor may reduce the efficacy of buspirone by decreasing its systemic exposure. A buspirone dosage adjustment may be necessary to maintain anxiolytic activity. Lumacaftor is a strong CYP3A inducer. Buspirone has been shown in vitro to be metabolized via CYP3A4; this finding is consistent with in vivo interactions observed. When coadministered with rifampin, another strong CYP3A inducer, buspirone Cmax and AUC decreased by 84% and 90%, respectively.
Lumateperone: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Lurasidone: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Maprotiline: (Moderate) CNS depressants should be combined cautiously with maprotiline because they could cause additive depressant effects and possible respiratory depression or hypotension.
Meloxicam; Rizatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant buspirone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Meperidine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of meperidine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Meprobamate: (Moderate) The combination of buspirone and other CNS depressants

can increase the risk for sedation.
Methadone: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of methadone, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Methamphetamine: (Moderate) Coadministration of buspirone with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. Buspirone has some serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine: (Major) Avoid concomitant use of buspirone and reversible monoamine oxidase inhibitors (MAOIs), such as methylene blue, due to the risk for serotonin syndrome. For patients who are chronically receiving buspirone therapy and require emergency treatment with intravenous (IV) methylene blue, use the lowest possible IV methylene blue dose and hold buspirone until 24 hours after the last dose of IV methylene blue. The risk for serotonin syndrome is greatest with IV methylene blue doses of 1 mg/kg or more. Monitor for serotonin syndrome for 2 weeks or until 24 hours after the last dose of IV methylene blue, whichever comes first. Starting buspirone in a patient who is being treated with IV methylene blue is contraindicated.
Methohexital: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.
Methscopolamine: (Moderate) CNS depression can be increased when methscopolamine is combined with other CNS depressants such as any anxiolytics, sedatives, and hypnotics.
Methylene Blue: (Major) Avoid concomitant use of buspirone and reversible monoamine oxidase inhibitors (MAOIs), such as methylene blue, due to the risk for serotonin syndrome. For patients who are chronically receiving buspirone therapy and require emergency treatment with intravenous (IV) methylene blue, use the lowest possible IV methylene blue dose and hold buspirone until 24 hours after the last dose of IV methylene blue. The risk for serotonin syndrome is greatest with IV methylene blue doses of 1 mg/kg or more. Monitor for serotonin syndrome for 2 weeks or until 24 hours

after the last dose of IV methylene blue, whichever comes first. Starting buspirone in a patient who is being treated with IV methylene blue is contraindicated.
Metoclopramide: (Minor) Combined use of metoclopramide and other CNS depressants, such as anxiolytics, sedatives, and hypnotics, can increase possible sedation.
Midazolam: (Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
miFEPRIStone: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with mifepristone. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering mifepristone with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A; mifepristone is a strong CYP3A inhibitor. Coadministration with another strong CYP3A inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
Milnacipran: (Moderate) Coadministration of buspirone with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Mirtazapine: (Moderate) The use of mirtazapine with buspirone may increase the risk for serotonin syndrome. Both medications have serotonergic effects. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome.
Mitotane: (Major) Use caution if mitotane and buspirone are used concomitantly, and monitor for decreased efficacy of buspirone and a possible change in dosage requirements. Mitotane is a strong CYP3A4 inducer and buspirone is a CYP3A4 substrate in vitro; coadministration may result in decreased plasma concentrations of buspirone. Coadministration with another strong CYP3A inducer, rifampin, decreased the buspirone Cmax by 83.7% and AUC by 89.6%.
Molindone: (Moderate) The combination of buspirone and CNS depressants like the antipsychotics can increase the risk for sedation.

Monoamine oxidase inhibitors: (Contraindicated) Concomitant use of monoamine oxidase inhibitors (MAOIs) and buspirone is contraindicated because several cases of elevated blood pressure have been reported in patients taking MAO inhibitors who were then given buspirone; serotonin syndrome may also occur. A 10-day interval after discontinuing isocarboxazid is recommended before initiating buspirone treatment. At least 14 days should elapse between the discontinuation of phenelzine and initiating buspirone, At least a 7-day interval should elapse after discontinuing tranylcypromine before initiating buspirone treatment. Monitor for serotonin-related effects during therapy transitions.
Morphine: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of morphine, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of morphine and buspirone is imperative, reduce the dose of one or both drugs.
Nalbuphine: (Moderate) Concomitant use of nalbuphine with other CNS depressants, such as buspirone, can potentiate the effects of nalbuphine on respiratory depression, CNS depression, and sedation.
Naratriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant buspirone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Nefazodone: (Major) The administration of nefazodone with buspirone has resulted in marked increases in plasma buspirone concentrations most likely due to CYP3A4 inhibition by nefazodone. Some patients receiving both drugs concurrently have reported lightheadedness, asthenia, dizziness, and drowsiness. If buspirone is to be administered concurrently with nefazodone, a low dose of buspirone, such as 2.5 mg PO twice daily, is recommended. Subsequent dosage adjustments should be based on clinical response.
Nelfinavir: (Moderate) When buspirone is administered with an inhibitor of CYP3A4 like nelfinavir, a lower dose of buspirone is recommended. Dose adjustment of either drug should be based on clinical assessment.
NiCARdipine: (Minor) Nicardipine is an inhibitor of CYP3A4 isoenzymes. Co-administration with nicardipine may lead to an increase in serum levels of drugs that are CYP3A4 substrates including buspirone.
Nilotinib: (Moderate) Concomitant use of nilotinib, a moderate CYP3A4 inhibitor, and buspirone, a CYP3A4 substrate, may result in increased buspirone levels. A buspirone dose reduction may be necessary if these drugs are used together.
Nirmatrelvir; Ritonavir: (Major) When buspirone is administered with a potent inhibitor of CYP3A4 like ritonavir, a low dose of buspirone used cautiously is recommended. Some patients receiving drugs that are potent inhibitors of CYP3A4 with buspirone have reported lightheadedness, asthenia, dizziness, and drowsiness. If the two drugs are to

be used in combination, a low dose of buspirone (e.g., 2.5 mg PO twice daily) is recommended. Subsequent dose adjustment of either drug should be based on clinical assessment. Several other anti-retroviral protease inhibitors also inhibit CYP3A4, and these may interact with buspirone in a similar manner.
Nirogacestat: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with nirogacestat is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and nirogacestat is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and nirogacestat is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Nortriptyline: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
OLANZapine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
OLANZapine; FLUoxetine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering buspirone and fluoxetine. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated. (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
OLANZapine; Samidorphan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Oliceridine: (Moderate) If concomitant use of oliceridine and buspirone is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.

Oritavancin: (Moderate) Buspirone is metabolized by CYP3A4; oritavancin is a weak CYP3A4 inducer. Plasma concentrations and efficacy of buspirone may be reduced if these drugs are administered concurrently.
Oxazepam: (Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
oxyCODONE: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of oxycodone, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
oxyMORphone: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of oxymorphone, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use of codeine and buspirone is imperative, reduce the dose of one or both drugs.
Pacritinib: (Moderate) Monitor for decreased efficacy of buspirone if pacritinib is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A substrate and pacritinib is a moderate CYP3A inducer.
Palbociclib: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with palbociclib is necessary. If palbociclib is added to a patient stabilized on buspirone, a buspirone dose adjustment may be necessary to avoid adverse events. Palbociclib is a weak time-dependent inhibitor of CYP3A while buspirone is a sensitive CYP3A4 substrate.
Paliperidone: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Papaverine: (Moderate) Concurrent use of papaverine with potent CNS depressants such as buspirone could lead to enhanced sedation.
PARoxetine: (Moderate) Coadministration of buspirone 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.
PAZOPanib: (Moderate) Pazopanib is a weak inhibitor of CYP3A4. Coadministration of pazopanib and buspirone, a CYP3A4 substrate, may cause an increase in systemic concentrations of buspirone. Use caution when administering these drugs concomitantly.
Pentazocine; Naloxone: (Moderate) Concomitant use of pentazocine with other CNS depressants can potentiate respiratory depression, CNS depression, and sedation. Pentazocine should be used cautiously in any patient receiving these agents, which may include buspirone.
PENTobarbital: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.
Perampanel: (Moderate) Co-administration of perampanel with CNS depressants, including ethanol, may increase CNS depression. The combination of perampanel (particularly at high doses) with ethanol has led to decreased mental alertness and ability to perform complex tasks (such as driving), as well as increased levels of anger, confusion, and depression; similar reactions should be expected with concomitant use of other CNS depressants, such as buspirone.
Perphenazine; Amitriptyline: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Pexidartinib: (Moderate) Monitor for decreased efficacy of buspirone if pexidartinib is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A4 substrate and pexidartinib is a moderate CYP3A4 inducer.
Phenelzine: (Contraindicated) Concomitant use of monoamine oxidase inhibitors (MAOIs) and buspirone is contraindicated because several cases of elevated blood pressure have been reported in patients taking MAO inhibitors who were then given buspirone; serotonin syndrome may also occur. A 10-day interval after discontinuing isocarboxazid is recommended before initiating buspirone treatment. At least 14 days should elapse between the discontinuation of phenelzine and initiating buspirone, At least a 7-day interval should elapse after discontinuing tranylcypromine before initiating

buspirone treatment. Monitor for serotonin-related effects during therapy transitions.
PHENobarbital: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.
PHENobarbital; Hyoscyamine; Atropine; Scopolamine: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.
Phenytoin: (Moderate) Monitor for decreased efficacy of buspirone if phenytoin is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A substrate and phenytoin is a strong CYP3A inducer. Coadministration with another strong CYP3A inducer decreased buspirone exposure by 89.6%.
Pimozide: (Moderate) The combination of buspirone and CNS depressants like the antipsychotics can increase the risk for sedation.
Posaconazole: (Moderate) Posaconazole and buspirone should be coadministered with caution due to an increased potential for buspirone-related adverse events. Posaconazole is a potent inhibitor of CYP3A4, an isoenzyme responsible for the metabolism of buspirone. These drugs used in combination may result in elevated buspirone plasma concentrations, causing an increased risk for buspirone-related adverse events.
Primidone: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.
Procarbazine: (Contraindicated) Simultaneous use of buspirone with drugs that possess

monoamine oxidase inhibitor activity, such as procarbazine, can increase blood pressure, so it is recommended that this combination be avoided. When switching drug therapy, there should be a 14-day delay after discontinuing a drug with MAOI-like actions before initiating a serotonergic drug like buspirone treatment.
Propofol: (Moderate) General anesthetics potentiate the effects of CNS depressants.
Protriptyline: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Quazepam: (Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
QUEtiapine: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Ramelteon: (Moderate) Due to pharmacodynamic additive effects, also use caution when combining ramelteon with buspirone.
Ranolazine: (Moderate) Although data are not available, CYP3A4 inhibitors, such as ranolazine, may decrease systemic clearance of buspirone leading to increased or prolonged effects. If buspirone is to be administered concurrently with significant CYP3A4 inhibitors, a low dose of buspirone (i.e., 2.5 mg PO twice daily) is recommended initially. Subsequent dosage adjustments should be based on clinical response.
Rasagiline: (Major) Monitor blood pressure for hypertension during concomitant use of rasagiline, a selective monoamine oxidase type B inhibitor (MAO-B inhibitor) and buspirone. If a hypertensive crisis occurs, rasagiline should be discontinued immediately and therapy to lower blood pressure should be instituted immediately. Concomitant use of non-selective MAOIs and buspirone is contraindicated because several cases of elevated blood pressure have been reported when the drugs were used together or in succession.
Remifentanil: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of remifentnil, which may potentially lead to respiratory

depression, CNS depression, sedation, or hypotensive responses. If concurrent use is imperative, reduce the dose of one or both drugs if clinically indicated.
Repotrectinib: (Moderate) Monitor for decreased efficacy of buspirone if repotrectinib is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A substrate and repotrectinib is a moderate CYP3A inducer.
Ribociclib: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with ribociclib. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering ribociclib with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4. Ribociclib is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
Ribociclib; Letrozole: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with ribociclib. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering ribociclib with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4. Ribociclib is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
rifAMPin: (Major) Substances that are potent inducers of hepatic cytochrome P450 isoenzyme CYP3A4, such as rifampin, may increase the rate of buspirone metabolism. In a study of healthy volunteers, co-administration of buspirone with rifampin decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone. An in vitro study indicated that buspirone did not displace highly protein-bound drugs such as phenytoin. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect.
Rifapentine: (Moderate) Monitor for decreased efficacy of buspirone if rifapentine is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A4 substrate and rifapentine is a strong CYP3A4 inducer. Coadministration with another strong CYP3A4 inducer decreased buspirone exposure by 89.6%.
Rilzabrutinib: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with rilzabrutinib is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and rilzabrutinib is added or removed from therapy. Buspirone is a CYP3A substrate and rilzabrutinib is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased

buspirone exposure by 3.4- to 6-fold and was accompanied by increased buspirone-related adverse reactions.
risperiDONE: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Ritlecitinib: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with ritlecitinib is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and ritlecitinib is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and ritlecitinib is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Ritonavir: (Major) When buspirone is administered with a potent inhibitor of CYP3A4 like ritonavir, a low dose of buspirone used cautiously is recommended. Some patients receiving drugs that are potent inhibitors of CYP3A4 with buspirone have reported lightheadedness, asthenia, dizziness, and drowsiness. If the two drugs are to be used in combination, a low dose of buspirone (e.g., 2.5 mg PO twice daily) is recommended. Subsequent dose adjustment of either drug should be based on clinical assessment. Several other anti-retroviral protease inhibitors also inhibit CYP3A4, and these may interact with buspirone in a similar manner.
Rizatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant buspirone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
rOPINIRole: (Moderate) The combination of buspirone and other CNS depressants, such as ropinirole, can increase the risk for sedation.
Rotigotine: (Major) Concomitant use of rotigotine with other CNS depressants, such as buspirone, can potentiate the sedation effects of rotigotine.
Saquinavir: (Moderate) When buspirone is administered with an inhibitor of CYP3A4 like saquinavir, a lower dose of buspirone is recommended. Dose adjustment of either drug should be based on clinical assessment.
Secobarbital: (Moderate) Monitor for reduced anxiolytic effect of buspirone. Potent inducers of CYP3A4, such as the barbiturates, may increase the rate of buspirone metabolism. If a patient has been titrated to a stable dosage on buspirone, a dose adjustment of buspirone may be necessary to maintain anxiolytic effect. There is also a risk of additive CNS depression (drowsiness) when buspirone is given concomitantly with barbiturates. In a study in healthy volunteers, co-administration of buspirone with a potent CYP3A4 inducer decreased the plasma concentrations (83.7% decrease in Cmax; 89.6% decrease in AUC) and pharmacodynamic effects of buspirone.

Selegiline: (Contraindicated) Concomitant use of transdermal selegiline with buspirone or within 14 days after discontinuation of treatment with either agent is contraindicated due to the risk of serotonin syndrome; buspirone has serotonergic activity. The use of buspirone with selegiline may also produce substantial elevations in blood pressure. For selegiline oral formulations, monitor blood pressure for hypertension if use with buspirone is necessary. If a hypertensive crisis occurs, selegiline should be discontinued and therapy to lower blood pressure should be instituted immediately.
Serotonin norepinephrine reuptake inhibitors: (Moderate) Coadministration of buspirone with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Serotonin-Receptor Agonists: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant buspirone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Sertraline: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering buspirone and sertraline. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Sevoflurane: (Moderate) General anesthetics potentiate the effects of CNS depressants.
Sodium Oxybate: (Moderate) Monitor for excessive sedation and somnolence during concomitant use of buspirone and oxybates. Concurrent use may result in additive CNS depression.
Sotorasib: (Moderate) Monitor for decreased efficacy of buspirone if sotorasib is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a sensitive CYP3A4 substrate and sotorasib is a moderate CYP3A4 inducer.
Stiripentol: (Moderate) Consider a dose adjustment of buspirone when coadministered with stiripentol. Coadministration may alter plasma concentrations of buspirone resulting in an increased risk of adverse reactions and/or decreased efficacy. Buspirone is a sensitive CYP3A4 substrate. In vitro data predicts inhibition or induction of CYP3A4 by stiripentol potentially resulting in clinically significant interactions.
SUFentanil: (Moderate) Concomitant use of CNS depressants, such as buspirone, can potentiate the effects of sufentanil, which may potentially lead to respiratory depression, CNS depression, sedation, or hypotensive responses. If concurrent use is

imperative, reduce the dose of one or both drugs if clinically indicated.
SUMAtriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant buspirone 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 buspirone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Tapentadol: (Moderate) Additive CNS depressive effects are expected if tapentadol is used in conjunction with other CNS depressants including anxiolytics, sedatives, and hypnotics. When such combined therapy is contemplated, a dose reduction of one or both agents should be considered.
Telotristat Ethyl: (Moderate) Use caution if coadministration of telotristat ethyl and buspirone is necessary, as the systemic exposure of buspirone may be decreased resulting in reduced efficacy. If these drugs are used together, monitor patients for suboptimal efficacy of buspirone; consider increasing the dose of buspirone if necessary. Buspirone is a CYP3A4 substrate. The mean Cmax and AUC of another sensitive CYP3A4 substrate was decreased by 25% and 48%, respectively, when coadministered with telotristat ethyl; the mechanism of this interaction appears to be that telotristat ethyl increases the glucuronidation of the CYP3A4 substrate.
Temazepam: (Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
Tetrabenazine: (Moderate) Concurrent use of tetrabenazine and drugs that can cause CNS depression, such as buspirone, can increase both the frequency and the intensity of adverse effects such as drowsiness, sedation, dizziness, and orthostatic hypotension.
Thalidomide: (Major) Avoid the concomitant use of thalidomide with anxiolytics, sedatives, and hypnotics due to the potential for additive sedative effects.
Thiothixene: (Moderate) The combination of buspirone and CNS depressants like thiothixene can increase the risk for sedation.
Tipranavir: (Moderate) When buspirone is administered with an inhibitor of CYP3A4 like tipranavir, a lower dose of buspirone is recommended. Dose adjustment of either drug should be based on clinical assessment.

traMADol: (Moderate) Tramadol can cause additive CNS depression when used with other agents that are CNS depressants including buspirone.
Tramadol; Acetaminophen: (Moderate) Tramadol can cause additive CNS depression when used with other agents that are CNS depressants including buspirone.
Trandolapril; Verapamil: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with verapamil is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and verapamil is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and verapamil is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Tranylcypromine: (Contraindicated) Concomitant use of monoamine oxidase inhibitors (MAOIs) and buspirone is contraindicated because several cases of elevated blood pressure have been reported in patients taking MAO inhibitors who were then given buspirone; serotonin syndrome may also occur. A 10-day interval after discontinuing isocarboxazid is recommended before initiating buspirone treatment. At least 14 days should elapse between the discontinuation of phenelzine and initiating buspirone, At least a 7-day interval should elapse after discontinuing tranylcypromine before initiating buspirone treatment. Monitor for serotonin-related effects during therapy transitions.
traZODone: (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.
Triazolam: (Moderate) It is common for patients to overlap anxiety treatment when switching from benzodiazepines to buspirone. Buspirone has a slow onset of action and the drug will not block the withdrawal syndrome often seen with cessation of benzodiazepine therapy in those with benzodiazepine dependence. Therefore, before starting therapy with buspirone, withdraw patients gradually from the benzodiazepine. Alternatively, conversion to buspirone therapy may require treatment overlap to allow for the downward titration of the benzodiazepine while buspirone takes effect. It should be noted that the combination of buspirone and benzodiazepines can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent.
Tricyclic antidepressants: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.

Trihexyphenidyl: (Moderate) CNS depressants, such as anxiolytics, sedatives, and hypnotics, can increase the sedative effects of trihexyphenidyl.
Trimethobenzamide: (Moderate) The concurrent use of trimethobenzamide with other medications that cause CNS depression, like buspirone, may potentiate the effects of either trimethobenzamide or buspirone.
Trimipramine: (Moderate) Coadministration of buspirone with tricyclic antidepressants (TCAs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Tucatinib: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with tucatinib. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering tucatinib with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4; tucatinib is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
Vemurafenib: (Moderate) Monitor for decreased efficacy of buspirone if vemurafenib is added to a patient on a stable dosage of buspirone; a dose increase of buspirone may be needed to maintain anxiolytic activity. Buspirone is a CYP3A substrate and vemurafenib is a CYP3A inducer.
Venlafaxine: (Moderate) Coadministration of buspirone with serotonin norepinephrine reuptake inhibitors (SNRIs) may increase the risk of serotonin syndrome. Both types of medications have serotonergic properties. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, all serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Verapamil: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with verapamil is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and verapamil is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and verapamil is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Vigabatrin: (Moderate) Vigabatrin may cause somnolence and fatigue. Drugs that can cause CNS depression, if used concomitantly with vigabatrin, may increase both the frequency and the intensity of adverse effects such as drowsiness, sedation, and

dizziness. Caution should be used when vigabatrin is given with buspirone.
Vilazodone: (Major) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering vilazodone with other drugs that have serotonergic properties such as buspirone. 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. Patients receiving vilazodone and buspirone should be monitored for the emergence of serotonin syndrome, particularly during treatment initiation and during dosage increases. Vilazodone and buspirone should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.
Vonoprazan; Amoxicillin; Clarithromycin: (Moderate) Concomitant administration of clarithromycin with buspirone may result in increases in buspirone AUC; the mechanism is probably reduced buspirone metabolism via CYP3A4. A low dose of buspirone is recommended if administered with significant CYP3A4 inhibitors. Subsequent dose adjustments should be based on clinical assessment.
Voriconazole: (Moderate) A low dose of buspirone used cautiously is recommended when coadministered with voriconazole. If a patient has been titrated to a stable dosage of buspirone, a dose adjustment of buspirone may be necessary to avoid adverse events attributable to buspirone. Administering voriconazole with buspirone may increase buspirone concentration and risk for adverse events. Buspirone is a sensitive substrate of CYP3A4. Voriconazole is a strong CYP3A4 inhibitor. Coadministration with another strong CYP3A4 inhibitor increased the buspirone AUC by 19-fold with an increased incidence of buspirone-related adverse effects.
Vortioxetine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering vortioxetine with other drugs that have serotonergic properties such as buspirone. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome. If serotonin syndrome is suspected, vortioxetine and concurrent serotonergic agents should be discontinued.
Voxelotor: (Moderate) Monitor for an increase in buspirone-related adverse reactions if coadministration with voxelotor is necessary; the effect may be more pronounced if the patient has been titrated to a stable dose of buspirone and voxelotor is added or removed from therapy. Buspirone is a sensitive CYP3A substrate and voxelotor is a moderate CYP3A inhibitor. Coadministration with other moderate CYP3A inhibitors increased buspirone exposure by 3.4 to 6-fold and was accompanied by increased buspirone-related adverse reactions.
Zafirlukast: (Moderate) In vitro data indicate that zafirlukast inhibits the CYP2C9 and CYP3A4 isoenzymes at concentrations close to the clinically achieved total plasma

concentrations. Until more clinical data are available, zafirlukast should be used cautiously in patients stabilized on drugs metabolized by CYP3A4, such as buspirone.
Zaleplon: (Moderate) The combination of buspirone and other CNS depressants, such as sedative hypnotics including zaleplon, may increase the risk for drowsiness or sedation. Because the effects of the use of buspirone with most other psychotropic drugs have not been studied, the concomitant use of buspirone with other CNS-active drugs should be approached with caution.
Ziconotide: (Moderate) CNS depressant medications, such as buspirone, may increase drowsiness, dizziness, and confusion that are associated with ziconotide. Dosage adjustments may be necessary if ziconotide is used with buspirone.
Ziprasidone: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant atypical antipsychotic and buspirone use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
ZOLMitriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant buspirone and serotonin-receptor agonist use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.

## Adverse Reaction

### abnormal dreams, akathisia, ataxia, confusion, dizziness, drowsiness, dysarthria, dysphoria, dystonic reaction, emotional lability, euphoria, excitability, hallucinations, headache, hostility, insomnia, involuntary movements, paresthesias, pseudoparkinsonism, psychosis, restless legs syndrome (RLS), restlessness, seizures, serotonin syndrome, suicidal ideation, tremor, vertigo

Centrally-mediated (CNS) adverse effects were the most frequently occurring reactions during buspirone clinical trials and were among the most common events resulting in discontinuation of therapy (3.4%). Common causes of treatment discontinuation included dizziness, insomnia, nervousness, drowsiness, and lightheadedness. During clinical trials of buspirone in the treatment of anxiety, the following CNS effects occurred in at least 1% of subjects receiving buspirone and with a frequency greater than in placebo subjects: dizziness (12%), drowsiness (10%), nervousness (5%), lightheadedness (3%), excitability (2%), anger/hostility (2%), confusion (2%), numbness (2%), paresthesias (1%), incoordination (1%), tremor (1%), and headache (6%). During other premarketing evaluations, dream disturbances (abnormal dreams) were reported in at least 1% of subjects. CNS effects reported in 0.1% to 1% of subjects included depersonalization, dysphoria, noise intolerance, euphoria, akathisia, fearfulness, loss of interest,

dissociative reaction, hallucinations, involuntary movements, slowed reaction time, suicidal ideation, and seizures. Rarely reported effects (less than 0.1%) included claustrophobia, cold intolerance, stupor, dysarthria, psychosis, and roaring sensation in the head. During postmarketing use, extrapyramidal symptoms (EPS) including pseudoparkinsonism (i.e., cogwheel rigidity, dyskinesia), dystonic reaction, akathisia, and tardive dyskinesia have been reported. Although causality has not been established, buspirone affects central dopamine receptors which may be a contributing factor in the development of extrapyramidal reactions. Other postmarketing events include dizziness/vertigo, ataxia, emotional lability, serotonin syndrome, transient difficulty with recall, restless legs syndrome (RLS), and restlessness. Unlike many other anxiolytics, buspirone does not appear to cause physical or psychological dependence.

## arthralgia, muscle cramps, musculoskeletal pain, myalgia, myasthenia

During clinical trials of buspirone in the treatment of anxiety, musculoskeletal pain or aches (myalgia) occurred in 1% of subjects receiving buspirone and more frequently than in subjects receiving placebo. During other premarketing evaluations, musculoskeletal effects reported in 0.1% to 1% of subjects included muscle cramps, muscle spasms, rigid/stiff muscles, and arthralgia. Myasthenia was reported rarely (less than 0.1%).

## acne vulgaris, alopecia, angioedema, ecchymosis, edema, flushing, hematoma, hyperhidrosis, pruritus, rash, urticaria, xerosis

During clinical trials of buspirone in the treatment of anxiety, the following dermatologic effects occurred in at least 1% of subjects receiving buspirone and more frequently than in subjects receiving placebo: skin rash (1%) and hyperhidrosis or clamminess (1%). During other premarketing evaluations, adverse dermatologic effects reported in 0.1% to 1% of subjects included edema, pruritus, flushing, easy bruising (hematoma), hair loss (alopecia), xerosis, facial edema, and blisters. Acne vulgaris and thinning of nails were reported rarely (less than 0.1%). During postmarketing use, allergic reactions (e.g., urticaria, angioedema) and ecchymosis have been reported. Because of the uncontrolled nature of these spontaneous postmarketing reports, a causal relationship to buspirone has not been determined.

## bleeding, eosinophilia, leukopenia, thrombocytopenia

During premarketing evaluation of buspirone, adverse hematologic effects including eosinophilia, leukopenia, bleeding disturbance (unspecified), and thrombocytopenia were reported in less than 0.1% of buspirone-treated subjects.

## anorexia, appetite stimulation, diarrhea, elevated hepatic enzymes, flatulence, GI bleeding, hypersalivation, nausea, weight gain, weight loss

During clinical trials of buspirone in the treatment of anxiety, gastrointestinal (GI) disturbances, primarily nausea, were one of the most common adverse events causing discontinuation of treatment. In these clinical trials, the following adverse GI effects occurred in at least 1% of subjects receiving buspirone and more frequently than with placebo: nausea (8%) and diarrhea (2%). During other premarketing evaluations, adverse GI effects reported in 0.1% to 1% of buspirone recipients included elevated hepatic enzymes, flatulence, anorexia, appetite stimulation, hypersalivation, irritable colon, weight gain, weight loss, and rectal GI bleeding. Burning of the tongue was reported rarely (less than 0.1%).

## dyspnea, epistaxis, fever, hiccups, hyperventilation, nasal congestion, pharyngitis

During premarketing evaluation of buspirone, the following adverse respiratory effects or infections were reported in at least 1% of treated subjects: sore throat (pharyngitis) and nasal congestion. Adverse effects reported in 0.1% to 1% of buspirone recipients included hyperventilation, dyspnea, chest congestion, and fever. Epistaxis and hiccups were reported rarely (less than 0.1%).

## bradycardia, cardiomyopathy, chest pain (unspecified), heart failure, hypertension, hypotension, myocardial infarction, stroke, syncope

During premarketing evaluation of buspirone, chest pain (unspecified) was reported in at least 1% of drug recipients. Adverse cardiovascular effects reported in 0.1% to 1% of treated subjects included syncope, hypotension, and hypertension. Rarely reported cardiovascular or cerebrovascular effects (less than 0.1%) included stroke, congestive heart failure, myocardial infarction, cardiomyopathy, and bradycardia.

## blurred vision, conjunctivitis, dysgeusia, ocular pain, ocular pruritus, parosmia, photophobia, tinnitus, visual impairment

During clinical trials of buspirone in the treatment of anxiety, blurred vision occurred in 2% of buspirone-treated subjects and more frequently than with placebo. During other premarketing evaluations, adverse effects related to the special senses reported in 0.1% to 1% of buspirone-treated subjects included tinnitus, redness of the eyes, ocular pruritus, dysgeusia, parosmia, and conjunctivitis. Inner ear abnormality, ocular pain, photophobia, pressure on the eyes, and loss of voice were reported rarely (less than

0.1%). Visual impairment (including tunnel vision) has been reported during postmarketing use. Because of the uncontrolled nature of spontaneous postmarketing reports, a causal relationship to buspirone treatment has not been determined.

### galactorrhea

During premarketing evaluation of buspirone, adverse endocrine effects including galactorrhea and thyroid abnormality (unspecified) were reported in less than 0.1% of subjects.

### amenorrhea, dysuria, ejaculation dysfunction, impotence (erectile dysfunction), increased urinary frequency, libido decrease, libido increase, menstrual irregularity, nocturia, urinary retention

During premarketing evaluation of buspirone, the following adverse genitourinary effects or changes in sexual functioning were reported in 0.1% to 1% of buspirone recipients: increased urinary frequency, urinary hesitancy, menstrual irregularity and spotting, dysuria, libido decrease, and libido increase. Rarely reported effects (less than 0.1%) included amenorrhea, pelvic inflammatory disease, enuresis, nocturia, ejaculation dysfunction (delayed ejaculation), and impotence (erectile dysfunction). Urinary retention has been reported during postmarketing use.

### malaise, weakness

During clinical trials of buspirone in the treatment of anxiety, weakness occurred in 2% of subjects receiving buspirone and more frequently than with placebo. During other premarketing evaluations, malaise was reported in 0.1% to 1% of subjects. Alcohol abuse was reported rarely (less than 0.1%).

## Description

Buspirone is an oral anxiolytic that is structurally and pharmacologically distinct from all other anxiolytics. The clinical use of buspirone is limited to the treatment of generalized anxiety disorder (GAD) in adults. While used clinically off-label in pediatrics 6 years of age and older with anxiety, the efficacy of buspirone in pediatric patients with GAD has not been formally established, and guidelines do not recommend it as a first-line treatment in this population due to inconsistent study data. Results from clinical trials of buspirone for panic disorder in adults are generally unfavorable, and data on its use in social anxiety disorder and obsessive-compulsive disorder have produced mixed results. Evidence on the use of buspirone for post-traumatic stress disorder is too limited to be informative. Buspirone differs from other anxiolytics in that it does not possess anticonvulsant or muscle-relaxant properties, does not impair psychomotor function,

and does not cause physical or psychological dependence. Unlike benzodiazepine anxiolytics, buspirone should not be used for the acute relief of anxiety because its onset of effect is delayed by 2 weeks or more. Buspirone was initially FDA-approved in 1986.

## Mechanism Of Action

The mechanism of action of buspirone is not clearly understood since anxiety may be mediated by more than one neuropathway. Buspirone is distinct from typical benzodiazepine anxiolytics in that it does not exert anticonvulsive or muscle relaxant effects. It also lacks a prominent sedative effect that is associated with more traditional anxiolytics. It has no affinity for benzodiazepine receptors and does not affect GABA binding in vitro or in vivo. Buspirone has a high affinity for serotonin 5-HT1A receptors which are found in high quantities in the dorsal raphe and the hippocampus. Buspirone binding to type 1A serotonin receptors occurs on presynaptic neurons in the dorsal raphe and on postsynaptic neurons in the hippocampus. Animal studies reveal that buspirone inhibits the firing rate of 5-HT-containing neurons in the dorsal raphe. The dominant action of buspirone is partial agonism or mixed agonism/antagonism at 5-HT type 1A receptors. Buspirone also has moderate affinity for brain dopamine D2 receptors and is believed to enhance noradrenergic and dopaminergic neuronal activity. The combination of these effects leads to relief of anxiety symptoms without significant sedation or psychomotor impairment.

## Pharmacokinetics

Buspirone is administered orally. Buspirone undergoes extensive first-pass metabolism, leaving only 1% of unchanged drug in plasma. Approximately 86% of buspirone is bound to plasma proteins. Buspirone is oxidized in the liver primarily by CYP3A4. Animal models indicate that the major active metabolite, 1-pyrimidinylpiperazine (1-PP), has one-fourth of the activity of buspirone. In addition, blood samples from humans chronically exposed to buspirone hydrochloride do not exhibit high levels of 1-PP. Other hydroxylated metabolites are inactive. The average elimination half-life of buspirone is about 2 to 3 hours in healthy adults. In a single-dose study, 29% to 63% of a buspirone dose was excreted in the urine within 24 hours, primarily as metabolites. Fecal excretion accounted for 18% to 38% of the dose.

Affected cytochrome P450 (CYP450) isoenzymes and drug transporters: CYP3A4
Buspirone is metabolized primarily by CYP3A4. When administered with a potent inhibitor of CYP3A4, a low dose of buspirone and caution are recommended. Low doses of buspirone, as well as subsequent dose adjustments, may be required during

coadministration of moderate CYP3A4 inhibitors. When used in combination with a potent inducer of CYP3A4, an increased dose of buspirone may be needed to maintain the anxiolytic effect.

## Route-Specific Pharmacokinetics

- **Oral Route**

Buspirone capsule and tablet formulations are bioequivalent. After oral administration, buspirone is rapidly absorbed. Extensive first-pass metabolism results in plasma concentrations of buspirone that are low and variable between individuals. Because buspirone exhibits non-linear pharmacokinetics, dose increases and repeated dosing may lead to somewhat higher blood levels of unchanged buspirone than would be predicted from results of single-dose studies. When given with food, the AUC and Cmax of buspirone increase by roughly 84% and 116%, respectively; however, the total amount of buspirone does not change. Therefore, food may decrease the pre-systemic clearance of buspirone. For this reason, buspirone should be taken in a consistent manner with regard to the timing of dosing; either always with or always without food. When given with food, the AUC and Cmax of buspirone capsules increased by 84% and 17%, respectively. The Cmax of 1-PP decreased 33% while the AUC did not differ significantly. When the capsule was opened and its contents administered in 1 ounce (30 mL) of applesauce following a meal, the AUC and Cmax of buspirone increased by 100% and 40%, respectively, compared to the intact capsule in the fasted state. The Cmax of 1-PP decreased 34% while AUC was unaffected.

- **Hepatic Impairment**

A pharmacokinetic study in individuals with impaired hepatic function demonstrated increased plasma levels and a prolonged half-life of buspirone. After multiple-dose administration to individuals with hepatic impairment, steady-state AUC of buspirone increased 13-fold, compared with healthy adults. Therefore, the administration of buspirone to individuals with severe hepatic impairment is not recommended.

- **Renal Impairment**

A pharmacokinetic study in individuals with impaired renal function demonstrated increased plasma levels and a prolonged half-life of buspirone. After multiple-dose administration to individuals with renal impairment (i.e., CrCl 10 to 70 mL/minute), the steady-state AUC of buspirone increased 4-fold compared with healthy adults. Therefore, the administration of buspirone to individuals with severe renal impairment is not recommended.

- **Pediatrics**

Pharmacokinetic studies have shown that, for identical doses (i.e., 7.5 to 30 mg twice daily), plasma exposure to buspirone and its active metabolite, 1-PP, are equal to or

higher in pediatric patients (age 6 to 17 years) than adults. No unexpected safety findings were associated with buspirone in these trials.

- **Geriatric**

After single or multiple doses in adults, no significant differences in buspirone pharmacokinetics (AUC and Cmax) were observed between elderly and younger adult subjects.

- **Gender Differences**

After single or multiple doses in adults, no significant differences in buspirone pharmacokinetics (AUC and Cmax) were observed between men and women.

- **Ethnic Differences**

The effects of race or ethnicity on the pharmacokinetics of buspirone have not been studied.

# Administration

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

### Oral Administration

Tablets
Administer consistently with regard to food, either always with or always without food.

Capsules (e.g., Bucapsol)
Administer capsules consistently with regard to food, either always with or always without food.
If needed, the capsule contents may be sprinkled on a small amount of applesauce [about 1 to 2 tablespoons (15 to 30 mL)]. The mixture should be swallowed immediately.

# Maximum Dosage Limits

- **Adults**
  60 mg/day PO.
- **Geriatric**
  60 mg/day PO.
- **Adolescents**
  Safety and efficacy have not been established; dosages up to 60 mg/day PO have been used off-label.
- **Children**

6 to 12 years: Safety and efficacy have not been established. Up to 60 mg/day PO has been used off label, but dosages above 15 mg/day PO may be poorly tolerated.
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

- Bucapsol 10mg Capsule
- Bucapsol 15mg Capsule
- Bucapsol 7.5mg Capsule
- Buspirone Hydrochloride 10mg Oral tablet
- Buspirone Hydrochloride 15mg Oral tablet
- Buspirone Hydrochloride 30mg Oral tablet
- Buspirone Hydrochloride 5mg Oral tablet
- Buspirone Hydrochloride 7.5mg Oral tablet
- Buspirone Hydrochloride Bulk powder

## Dosage Adjustment Guidelines

### Hepatic Impairment

Buspirone is not recommended for use in individuals with severe hepatic impairment.

### Renal Impairment

CrCl less than 30 mL/minute: Buspirone is not recommended for use in individuals with severe renal impairment or renal failure.

Intermittent hemodialysis
Buspirone is not recommended in individuals with renal failure.