Brand Names

Zoloft, Zoloft Concentrate, Zoloft Solution

Indication Specific Dosing

For the treatment of major depression

For the treatment of major depression in adults

Oral dosage

Adults

50 mg PO once daily, initially. May increase the dose by 25 to 50 mg/day at intervals of at least 1 week if inadequate response and depending on tolerability. Usual dose: 50 to 200 mg/day. Max: 200 mg/day.

For the treatment of major depression† in pediatric individuals

Oral dosage

Children† and Adolescents† 12 to 17 years

25 to 50 mg PO once daily, initially. May increase the dose by 12.5 to 50 mg/day at intervals of 1 to 4 weeks if inadequate response and depending on tolerability. Max: 200 mg/day. Individuals with minimal or no response after 4 to 8 weeks of treatment will likely need alternative treatment. Continuation of medication for 6 to 12 months after symptom remission is recommended. Periodically reassess the need for continued treatment. Guidelines suggest that sertraline may be considered in pediatric individuals for whom first-line options (e.g., fluoxetine or escitalopram) cannot be used or are not tolerated.

Children† 6 to 11 years

12.5 to 25 mg PO once daily, initially. May increase the dose by 12.5 to 50 mg/day at intervals of 1 to 4 weeks if inadequate response and depending on tolerability. Max: 200 mg/day. Individuals with minimal or no response after 4 to 8 weeks of

treatment will likely need alternative treatment. Continuation of medication for 6 to 12 months after symptom remission is recommended. Periodically reassess the need for ongoing treatment. Guidelines suggest that sertraline may be considered in pediatric individuals for whom first-line options (e.g., fluoxetine) cannot be used or are not tolerated.

For the treatment of obsessive-compulsive disorder (OCD)

Oral dosage

Adults

50 mg PO once daily, initially. May increase the dose by 25 to 50 mg/day at weekly intervals based on clinical response and tolerability. Max: 200 mg/day.

Adolescents

50 mg PO once daily, initially. May increase the dose by 25 to 50 mg/day at weekly intervals based on clinical response and tolerability. Max: 200 mg/day.

Children 6 to 12 years

25 mg PO once daily, initially. May increase the dose by 25 to 50 mg/day at weekly intervals based on clinical response and tolerability. Usual dose: 50 to 200 mg/day. Max: 200 mg/day.

For the treatment of social phobia (social anxiety disorder)

Oral dosage

Adults

25 mg PO once daily, initially. May increase the dose by 25 or 50 mg/day at weekly intervals based on clinical response and tolerability. Max: 200 mg/day.

Children† and Adolescents† 6 to 17 years

25 mg PO once daily, initially. May increase the dose at weekly intervals based on clinical response and tolerability. Max: 200 mg/day.

For the treatment of posttraumatic stress disorder (PTSD)

Oral dosage

Adults

25 mg PO once daily initially. May increase the dose by 25 to 50 mg/day at intervals of at least 1 week if inadequate response and depending on tolerability. Usual dose: 50 to 200 mg/day. Max: 200 mg/day. Clinical practice guidelines recommend sertraline for the treatment of PTSD in individuals for whom individual psychotherapy is unavailable or prefer medication treatment.

For the treatment of panic disorder

Oral dosage

Adults

25 mg PO once daily initially. After 1 week, increase the dose to 50 mg PO once daily. If necessary, increase by 25 mg/day to 50 mg/day at intervals of not less than 1 week. Therapeutic range: 50 to 200 mg/day. Max: 200 mg/day.

Children† and Adolescents† 6 to 17 years

25 mg PO once daily, initially. May increase the dose at intervals of at least 1 week, if needed. Max: 200 mg/day. Clinical practice guidelines recommend the use of SSRIs (including sertraline) alone or in combination with cognitive behavior therapy (CBT) for children and adolescents with panic disorder. Periodically reassess the need for ongoing maintenance treatment. Further study is needed to evaluate the long-term safety and efficacy of SSRIs in treating childhood anxiety disorders.

For the treatment of premenstrual dysphoric disorder (PMDD)

Oral dosage

Adult females

50 mg/day PO initially, either daily throughout the menstrual cycle or limited to the luteal phase of the menstrual cycle, depending on provider assessment. Patients not responding to a 50 mg/day dose may benefit from dose increases (at 50 mg increments/menstrual cycle) up to 150 mg/day when dosing daily throughout the menstrual cycle, or 100 mg/day when dosing during the luteal phase of the menstrual cycle. If using 100 mg/day with luteal phase dosing, a 50 mg/day titration step for three days should be implemented at the beginning of each luteal phase dosing period. In one study, 62% of women receiving sertraline had at least 30% improvement from baseline versus only 34% of women receiving placebo. The mean effective dosage was 100 mg/day.

For the treatment of generalized anxiety disorder (GAD)†

Oral dosage

Adults

25 mg PO once daily for 1 week, then 50 mg PO once daily for 1 week, and then may increase the dose by 50 mg/day at weekly intervals as needed. Max: 200 mg/day.

Children and Adolescents 6 to 17 years

25 mg PO once daily, initially. May increase the dose at intervals of at least 1 week, if needed. Max: 200 mg/day. Clinical practice guidelines recommend the use of SSRIs (including sertraline) alone or in combination with cognitive behavior therapy (CBT) for children and adolescents with generalized anxiety disorder. Periodically reassess the need for ongoing maintenance treatment. Further study is needed to evaluate the long-term safety and efficacy of SSRIs in treating childhood anxiety disorders.

For the treatment of separation anxiety disorder†

Oral dosage

Children and Adolescents 6 to 17 years

25 mg PO once daily, initially. May increase the dose at intervals of at least 1 week, if needed. Max: 200 mg/day. Clinical practice guidelines recommend the use of SSRIs (including sertraline) alone or in combination with cognitive behavior therapy (CBT) for children and adolescents with separation anxiety disorder. Periodically reassess the need for ongoing maintenance treatment. Further study is needed to evaluate the long-term safety and efficacy of SSRIs in treating childhood anxiety disorders.

For the treatment of hot flashes† due to menopause† or in persons who have been treated for breast cancer†

For treating hot flashes† as a symptom of menopause†

Oral dosage

Adults

50 mg PO once daily, then titrated to 100 mg/day PO, has been used in clinical

studies. The efficacy data from clinical trials are inconsistent and guidelines suggest sertraline as a second or third-line nonhormonal treatment for hot flashes; other SSRIs with more robust efficacy data are preferred.

For hot flashes† in women treated for breast cancer or at increased risk of breast cancer†

Oral dosage

Adults

Clinical trial data regarding efficacy are inconsistent; a dose range of 50 to 100 mg/day PO has been used but may not reduce hot flash frequency or severity. Some guidelines do not recommend the use of sertraline to treat hot flashes in these patients. In a 12-week cross-over, randomized placebo-controlled controlled trial in patients concurrently treated with tamoxifen, hot flash frequency was reduced by 50% in 36% of patients taking sertraline vs. 27% with placebo ($p = 0.7$, NS). Additionally, women who crossed over to sertraline after taking placebo experienced a reduction of 0.9 and 1.7 in hot flash frequency and severity index, respectively, and those who took placebo after sertraline experienced an increase of 1.5 and 3.4 in hot flash frequency and index, respectively ($p = 0.03$). Another trial compared sertraline 100 mg/day to placebo and no significant differences were noted in the frequency or severity of hot flashes between the groups.

For the treatment of premature ejaculation†

Oral dosage

Adult males

Titrate from an initial low dosage (e.g., 25 to 50 mg PO once daily) based on response and tolerability. Guidelines suggest a dose range of 25 to 200 mg/day PO has been shown to increase ejaculatory latency in clinical studies. The lowest effective dose should be utilized, as the benefit of higher doses may be outweighed by increased frequency of erectile dysfunction and decreased libido.

In one study, men with lifelong rapid ejaculation (i.e., an intravaginal ejaculation latency time of 1 minute or less) received sertraline, another SSRI (fluoxetine, fluvoxamine, paroxetine), or placebo for 6 weeks. Mean intravaginal ejaculation latency time (IELT) with placebo was 20 seconds; the IELT in men treated with sertraline 50 mg/day PO increased to approximately 110 seconds. Other studies provide similar support for the use of sertraline or other SSRIs. Alternatively, on-demand administration with 50 mg to 100 mg PO as a single dose 3 to 6 hours

prior to intercourse has also demonstrated modest efficacy and is well-tolerated. However, it has been associated with substantially less ejaculatory delays than daily treatment in studies. On-demand treatment may be combined with an initial trial of daily treatment or concomitant low dose daily medication. The choice of regimen is ultimately defined by clinical judgement and patient preference in light of the frequency of sexual activity.

For the treatment of pruritus† due to cholestatic liver disease

Oral dosage

Adults

Patients treated with sertraline at doses of 50 to 100 mg PO once daily (median dose = 75 mg) reported a significant improvement in itching and decrease in the number of other medications used to treat pruritus (e.g., cholestyramine, antihistamines, phenobarbital). Guidelines and clinical studies suggest sertraline as a fourth-line option when other traditional options (such as cholestyramine, rifampicin, and opioid antagonists) fail or are unable to be tolerated.

For the treatment of binge-eating disorder†

Oral dosage

Adults

25 mg PO once daily for 3 days, initially. Increase the dose by 25 mg/day every 3 days as tolerated. Dose range: 50 to 200 mg/day. Max: 200 mg/day. Clinical practice guidelines suggest that antidepressant therapy (including sertraline) has been shown to be beneficial in reducing binge-eating, independent of whether a comorbid depressive or anxiety disorder is present.

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. Sertraline capsules should be avoided in people who have experienced an allergic-type reaction to FD and C Yellow No. 5 (tartrazine), as tartrazine

may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals. Although the overall incidence of FD and C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

adolescents, children, suicidal ideation

Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies. Prescribe sertraline in the smallest quantity consistent with good patient management to reduce the risk of overdose. Monitor all patients receiving antidepressants closely for clinical worsening, suicidal ideation, and unusual changes in mood or behavior, especially during the first few months of therapy and after any dosage adjustment. Instruct caregivers and patients to immediately notify the prescriber of changes in behavior or suicidal ideation. Consider changing the therapeutic regimen or discontinuing the medication in patients with persistent or worrisome symptoms, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. In a pooled analysis of placebo-controlled trials of antidepressants (n = more than 4,400 pediatric patients and 77,000 adult patients), there was an increased risk for suicidal thoughts and behaviors in patients 24 years of age and younger receiving an antidepressant versus placebo, with considerable variation in the risk of suicidality among drugs. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults older than 24 years; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The difference in absolute risk of suicidal thoughts and behaviors across different indications was highest in those with major depression. No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about the drug effect on suicide. It is unknown if the suicidality risk extends to long-term use (i.e., more than 4 months); however, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression, a known risk factor for suicidal thoughts and behaviors.

bipolar disorder

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

develops symptoms consistent with mania or hypomania, the medication should be discontinued, and appropriate therapy should be initiated.

electroconvulsive therapy, seizures

Sertraline should be used with caution in patients with a history of seizures, a seizure disorder, or other conditions that may lower the seizure threshold. Patients with a history of seizures were excluded from clinical studies with sertraline. Seizures have been reported rarely in patients taking SSRIs. The effects of using sertraline during electroconvulsive therapy (ECT) have not been established in clinical studies; however, there have been rare reports of prolonged seizures in patients taking SSRIs while receiving ECT treatment.

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

Use sertraline with caution in people with baseline QT prolongation or who have conditions that may increase the risk of QT prolongation or torsade de pointes, including bradycardia, congenital long QT syndrome, hypocalcemia, hypokalemia, hypomagnesemia, geriatric adults, females, structural abnormalities that interfere with electrical conduction (e.g., cardiomyopathy, coronary artery disease, ischemic heart disease), or in those who have other additional risk factors for QT prolongation or torsade de pointes. The use of other medications that have been associated with QT prolongation or torsade de pointes may further increase risk.

hypovolemia

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

Child-Pugh class A, Child-Pugh class B, Child-Pugh class C, hepatic failure

Dosage adjustments are recommended when using sertraline in people with hepatic impairment. In studies of patients with chronic mild hepatic disease, sertraline clearance

was reduced. The recommended dose in people with mild hepatic impairment (Child-Pugh class A) is 50% of the normal daily dosage due to increased exposure. The use of sertraline in patients with moderate (Child-Pugh class B) or severe hepatic impairment (Child-Pugh class C) or hepatic failure is not recommended. The use of sertraline capsules is not recommended in patients with hepatic impairment because dosage adjustments are not possible with the available strengths of the capsules.

closed-angle glaucoma, narrow iridocorneal angles

Caution is recommended when prescribing sertraline to people with closed-angle glaucoma. The pupillary dilation that can occur with antidepressants may precipitate a closed-angle glaucoma attack in those with anatomically narrow iridocorneal angles who do not have a patent iridectomy.

obstetric delivery, pregnancy

Available data from published epidemiologic studies and postmarketing reports have not established an increased risk of major birth defects or miscarriage from the use of sertraline during pregnancy. Sertraline oral solution contains 12% alcohol and is not recommended for use during pregnancy because there is no known safe level of alcohol exposure during pregnancy. There are risks to the pregnant person associated with untreated depression (e.g., relapse). Data from published observational studies have reported that exposure to SSRIs, particularly in the month before obstetric delivery, has been associated with a less than 2-fold increase in the risk of postpartum hemorrhage. There is a pregnancy exposure registry that monitors outcomes in pregnant patients exposed to sertraline; information about the registry can be obtained at https://womensmentalhealth.org/research/pregnancyregistry/antidepressants or by calling 1-866-961-2388.

activities requiring coordination and concentration, driving or operating machinery

Sertraline has the potential to cause drowsiness, or 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 sertraline does not affect them adversely. Patients should also be advised to avoid alcohol when taking sertraline.

neonates and infants exposed to this medication in utero

Neonates and infants exposed to this medication in utero during the third trimester may experience poor neonatal adaptation, resulting in complications such as prolonged

hospitalization, respiratory support, and tube feeding upon delivery. Symptoms of poor neonatal adaptation include respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with direct SSRI toxicity, serotonin syndrome, and/or drug discontinuation syndrome. In addition, fetal exposure to SSRIs during late pregnancy has been associated with an increased risk of persistent pulmonary hypertension of the newborn (PPHN). Because PPHN is associated with significant morbidity and mortality, it is important that care teams are aware of SSRI exposure to avoid delays in diagnosis and treatment. In a meta-analysis of 7 studies, there was a small but significant association between SSRI exposure in late pregnancy and PPHN; effects were not significant for other variables examined (e.g., study design, congenital malformations, meconium aspiration). Effects of cesarean delivery, maternal body mass index, and preterm delivery were not assessed. PPHN occurs in approximately 1.9 of 1,000 live births in the general population and is a relatively uncommon event. Based on this analysis, it is estimated that an average of 1 associated case of PPHN would result from 286 to 351 pregnant people being treated with a SSRI during late gestation.

geriatric

The selective serotonin reuptake inhibitors (SSRIs) are often a preferred antidepressant group for treatment of depression or other behavioral symptoms in the geriatric adult, including patients with dementia. The Beers Criteria state that SSRIs are potentially inappropriate medications in older adults with a history of falls or fractures; SSRIs can produce ataxia, impaired psychomotor function, syncope, and additional falls. If an SSRI must be used, consider reducing the use of other CNS-active medications and implement strategies to reduce fall risk. SSRIs may also cause hyponatremia and SIADH; closely monitor sodium concentrations when initiating treatment or changing doses in older adults. The U.S. Omnibus Budget Reconciliation Act (OBRA) regulates antidepressant use in long-term care facilities. When used to manage behavior, stabilize mood, or treat a psychiatric disorder, tapering as outlined in the OBRA guidelines should be attempted unless clinically contraindicated. Dosages and durations of treatment should align with prescribing labels, published literature recommendations, and expert guidelines.

breast-feeding

Sertraline is compatible with breast-feeding; it is usually considered one of the preferred antidepressant medications to use during lactation. Data from published literature demonstrate low levels of sertraline and its metabolites in human milk. There are no data on the effects of sertraline on milk production. Consider the developmental and

health benefits of breast-feeding, along with the clinical need for sertraline therapy and any potential adverse effects on the breast-fed child. In a published pooled analysis of 53 adult-infant pairs, exclusively human milk-fed infants had an average of 2% (range 0% to 15%) of the sertraline serum concentrations measured in the lactating person. No adverse reactions were observed in these infants. Another pooled analysis found that maternal use of sertraline, nortriptyline, and paroxetine usually produced undetectable or low drug concentrations in infant serum.

Pregnancy And Lactation

Sertraline is compatible with breast-feeding; it is usually considered one of the preferred antidepressant medications to use during lactation. Data from published literature demonstrate low levels of sertraline and its metabolites in human milk. There are no data on the effects of sertraline on milk production. Consider the developmental and health benefits of breast-feeding, along with the clinical need for sertraline therapy and any potential adverse effects on the breast-fed child. In a published pooled analysis of 53 adult-infant pairs, exclusively human milk-fed infants had an average of 2% (range 0% to 15%) of the sertraline serum concentrations measured in the lactating person. No adverse reactions were observed in these infants. Another pooled analysis found that maternal use of sertraline, nortriptyline, and paroxetine usually produced undetectable or low drug concentrations in infant serum.

Interactions

Acetaminophen; Aspirin, ASA; Caffeine: (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.

Acetaminophen; Aspirin, ASA; Caffeine: (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.

Acetaminophen; Aspirin: (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.

Acetaminophen; Aspirin; diphenhydrAMINE: (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.
Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) Because of the potential risk and severity of serotonin syndrome and a potential for additive CNS effects, caution should be observed when coadministering drugs that have additive properties such as sertraline and dihydrocodeine. In addition, sertraline has the potential for clinically relevant CYP2D6 inhibition and may decrease the metabolism of dihydrocodeine to dihydromorphine, increasing the risk of dihydrocodeine-related adverse effects such as CNS or respiratory depression. Inhibition of CYP2D6 by sertraline may also result in reduced effectiveness of dihydrocodeine by inhibiting the conversion of dihydrocodeine to dihydromorphine. If serotonin syndrome occurs, discontinue the serotonergic agents, and institute appropriate treatment.
Acetaminophen; Chlorpheniramine; Dextromethorphan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic

dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Acetaminophen; Codeine: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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.
Acetaminophen; Dextromethorphan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Acetaminophen; Dextromethorphan; Doxylamine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Acetaminophen; Dextromethorphan; guaiFENesin; Phenylephrine: (Moderate) Because

of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Acetaminophen; Dextromethorphan; guaiFENesin; Pseudoephedrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Acetaminophen; Dextromethorphan; Phenylephrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Acetaminophen; Dextromethorphan; Pseudoephedrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Acetaminophen; HYDROcodone: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of hydrocodone and sertraline because of the potential risk of serotonin syndrome and prolonged opioid adverse reactions. Discontinue hydrocodone if serotonin syndrome is suspected. Concomitant use of hydrocodone with sertraline may increase hydrocodone

plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. Monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of sertraline could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If sertraline is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Sertraline is a weak inhibitor of CYP2D6.
Acetaminophen; Ibuprofen: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Acetaminophen; oxyCODONE: (Moderate) If concomitant use of oxycodone and sertraline 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.
Adagrasib: (Major) Concomitant use of adagrasib and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
ALFentanil: (Moderate) If concomitant use of alfentanil and sertraline is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Alfuzosin: (Moderate) Concomitant use of sertraline and alfuzosin may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Aliskiren; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of

hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Almotriptan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering almotriptan with sertraline. Serotonin syndrome has been reported during concurrent use of serotonin-receptor agonists and selective serotonin reuptake inhibitors (SSRIs). Some patients had used the combination previously without incident when serotonin syndrome occurred. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly after a dose increase of the SSRI or the addition of other serotonergic medications to an existing SSRI regimen. Discontinue sertraline and almotriptan and initiate symptomatic treatment if serotonin syndrome occurs.
ALPRAZolam: (Minor) The manufacturer of alprazolam states that in vitro studies suggest sertraline may inhibit the metabolism of alprazolam via inhibition of CYP3A4. The potential for clinical interaction is uncertain. Be alert for any change in psychomotor performance or other benzodiazepine-related side effects when sertraline is combined with alprazolam.
Alteplase: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis, such as thrombolytic agents. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding.
aMILoride: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
aMILoride; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Amiodarone: (Major) Concomitant use of amiodarone and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose. Due to the extremely long half-life of amiodarone, a drug interaction is possible for days to weeks after drug discontinuation.

Amisulpride: (Major) Concomitant use of sertraline and amisulpride increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Amitriptyline: (Moderate) Monitor patients for signs and symptoms of serotonin syndrome during concomitant use of sertraline and amitriptyline, 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.
amLODIPine; Celecoxib: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
amLODIPine; Valsartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Amoxapine: (Moderate) Sertraline is an in vivo inhibitor of CYP2D6, the isoenzyme partially responsible for the metabolism of amoxapine, a tetracyclic antidepressant. In several cases, symptoms of toxicity, including seizures, have been reported when tricyclic antidepressants have been coadministered with an SSRI. At least one case report exists of a death thought to be due to impaired clearance of the tricyclic antidepressant amitriptyline by fluoxetine. Also, this combination may represent duplicative therapy. Patients receiving amoxapine should be monitored closely for toxicity if sertraline is added.
Amoxicillin; Clarithromycin; Omeprazole: (Major) Concomitant use of sertraline and clarithromycin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Amphetamine: (Moderate) Coadministration of selective serotonin reuptake inhibitors

(SSRIs) like sertraline with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. 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.
Amphetamine; Dextroamphetamine: (Moderate) Coadministration of selective serotonin reuptake inhibitors (SSRIs) like sertraline with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. 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.
Amphetamines: (Moderate) Coadministration of selective serotonin reuptake inhibitors (SSRIs) like sertraline with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. 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.
Anagrelide: (Major) Concomitant use of sertraline and anagrelide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Antithrombin III: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and anticoagulants like antithrombin III. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding.
Apixaban: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and anticoagulants like apixaban. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding.
Apomorphine: (Moderate) Concomitant use of sertraline and apomorphine may

increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Argatroban: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and other drugs that affect coagulation like thrombin inhibitors. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding.
ARIPiprazole: (Moderate) Monitor for aripiprazole-related adverse reactions during concomitant use of sertraline and consider taking steps to minimize the risk of QT/QTc interval prolongation and torsade de pointes (TdP), such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. Patients receiving both a CYP3A inhibitor plus sertraline may require an aripiprazole dosage adjustment. Dosing recommendations vary based on aripiprazole dosage form and CYP3A inhibitor strength. See prescribing information for details. Concomitant use may increase aripiprazole exposure and risk for side effects; use may also increase the risk for QT/QTc prolongation ad TdP. Aripiprazole is a CYP2D6 and CYP3A substrate, sertraline is a weak CYP2D6 inhibitor, and both medications have been associated with QT/QTc prolongation.
Arsenic Trioxide: (Major) Concomitant use of sertraline and arsenic trioxide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Artemether; Lumefantrine: (Major) Concomitant use of sertraline and artemether increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose. (Major) Concomitant use of sertraline and lumefantrine increases the risk of QT/QTc prolongation and

torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Asenapine: (Major) Concomitant use of sertraline and asenapine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Aspirin, ASA: (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.
Aspirin, ASA; Butalbital; Caffeine: (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.
Aspirin, ASA; Caffeine: (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.
Aspirin, ASA; Caffeine; Orphenadrine: (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.
Aspirin, ASA; Carisoprodol; Codeine: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite,

morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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. (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.

Aspirin, ASA; Citric Acid; Sodium Bicarbonate: (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.

Aspirin, ASA; Dipyridamole: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis, such as dipyridamole. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding. (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.

Aspirin, ASA; Omeprazole: (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.

Aspirin, ASA; oxyCODONE: (Moderate) If concomitant use of oxycodone and sertraline 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. (Moderate) The combined

use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.
Atazanavir; Cobicistat: (Moderate) Close monitoring for antidepressant response and careful dose titrations of the antidepressant therapy is recommended during coadministration of selective serotonin reuptake inhibitors (SSRIs) and cobicistat. Concurrent use may result in elevated SSRI plasma concentrations. Predictions regarding this interaction can be made based on the metabolic pathways of these drugs. All SSRIs are substrates for the hepatic isoenzyme CYP2D6, while citalopram, escitalopram, and sertraline are also substrates for CYP3A4; cobicistat is an inhibitor of both CYP2D6 and CYP3A4.
Atenolol; Chlorthalidone: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Atomoxetine: (Moderate) Concomitant use of atomoxetine and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Azilsartan; Chlorthalidone: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Azithromycin: (Major) Concomitant use of azithromycin and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Bedaquiline: (Major) Concomitant use of sertraline and bedaquiline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte

monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Benazepril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Benzhydrocodone; Acetaminophen: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of benzhydrocodone and sertraline because of the potential risk of serotonin syndrome. Discontinue benzhydrocodone if serotonin syndrome is suspected. 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.
Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Contraindicated) According to the manufacturer of sertraline, treatment initiation with sertraline is contraindicated in patients currently receiving intravenous (IV) methylene blue due to an increased risk of serotonin syndrome. If urgent psychiatric treatment is required, interventions other than sertraline (e.g., alternative medication, hospitalization) should be considered. Conversely, in patients receiving sertraline and requiring urgent treatment with IV methylene blue, sertraline should be discontinued immediately and methylene blue therapy initiated only if acceptable alternatives are not available and the potential benefits outweigh the risks. The patient should be monitored for serotonin syndrome for 2 weeks or until 24 hours after the last dose of methylene blue, whichever comes first. Sertraline may be re-initiated 24 hours after the last dose of methylene blue. Results from an in vitro study indicate that methylene blue is a potent, reversible inhibitor of the monoamine oxidase type A enzyme (MAO-A). MAO-A is responsible for the metabolism of serotonin; therefore, concurrent use of an MAO-A inhibitor with a serotonergic agent may result in a clinically significant interaction. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent, in patients receiving SSRIs, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents with IV methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. One case describes a patient receiving citalopram who experienced agitation, restlessness, pupil dilation with sluggish response to light, myoclonic movements of the lower limbs, and brisk reflexes following an infusion of methylene blue, while another patient receiving

paroxetine developed tachycardia, agitation, dystonia and abnormal eye movements. During a retrospective study of 193 surgical patients who had received a methylene blue injection, it was found that all 12 of the patients who experienced postoperative neurological sequelae had been taking a serotonin reuptake inhibitor preoperatively. One of the 12 patients experienced cardiopulmonary arrest and died. Of the remaining 181 patients who did not experience neurological sequelae, 8.8% were taking a serotonin reuptake inhibitor. Published interaction reports between IV methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and coma. Signs and symptoms of serotonin syndrome include fever, diaphoresis, shivering, myoclonus, tremor, tachycardia, diarrhea, nausea, headache, incoordination, mental status changes (e.g., agitation, confusion), hyperreflexia, seizures, and coma. (Moderate) The combined use of selective serotonin reuptake inhibitors (SSRIs) and aspirin, ASA or other salicylates which affect hemostasis may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin.
Benzphetamine: (Moderate) Coadministration of selective serotonin reuptake inhibitors (SSRIs) like sertraline with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. 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.
Bismuth Subcitrate Potassium; metroNIDAZOLE; Tetracycline: (Moderate) Concomitant use of metronidazole and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP.
Bismuth Subsalicylate: (Moderate) The combined use of selective serotonin reuptake inhibitors (SSRIs) and aspirin, ASA or other salicylates which affect hemostasis may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin.
Bismuth Subsalicylate; metroNIDAZOLE; Tetracycline: (Moderate) Concomitant use of metronidazole and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP.
(Moderate) The combined use of selective serotonin reuptake inhibitors (SSRIs) and aspirin, ASA or other salicylates which affect hemostasis may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the

antiplatelet effects of aspirin.
Bisoprolol; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Bivalirudin: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and other drugs that affect coagulation like thrombin inhibitors. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding.
Brexpiprazole: (Moderate) Because brexpiprazole is partially metabolized by CYP2D6, increased brexpiprazole plasma concentrations may occur during concurrent use of inhibitors of CYP2D6. Sertraline is generally considered a weak inhibitor of CYP2D6, but has the potential for clinically important interactions with CYP2D6 substrates, particularly those with a narrow therapeutic index. Decreased metabolism of brexpiprazole may lead to clinically important adverse reactions such as sedation or extrapyramidal symptoms.
Brompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Brompheniramine; Pseudoephedrine; Dextromethorphan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Bumetanide: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
BUPivacaine; Meloxicam: (Moderate) Monitor for signs and symptoms of bleeding during

concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Buprenorphine: (Major) Cautious use and close monitoring are advisable if concurrent use of sertraline and buprenorphine is necessary due to possible serotonin syndrome or QT prolongation. Buprenorphine has caused QT prolongation in some patients during clinical trials. The risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease. Concurrent use of opioids with other drugs that modulate serotonergic function, such as SSRIs, has also resulted in serotonin syndrome in some cases. Patients should be carefully observed, particularly during treatment initiation and during dose adjustments. Discontinue the serotonergic medications if serotonin syndrome is suspected.
Buprenorphine; Naloxone: (Major) Cautious use and close monitoring are advisable if concurrent use of sertraline and buprenorphine is necessary due to possible serotonin syndrome or QT prolongation. Buprenorphine has caused QT prolongation in some patients during clinical trials. The risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease. Concurrent use of opioids with other drugs that modulate serotonergic function, such as SSRIs, has also resulted in serotonin syndrome in some cases. Patients should be carefully observed, particularly during treatment initiation and during dose adjustments. Discontinue the serotonergic medications if serotonin syndrome is suspected.
buPROPion: (Minor) Concomitant use of bupropion and sertraline may theoretically increase the risk for sertraline-related adverse effects in some patients. Adjunctive therapy with bupropion plus a selective serotonin reuptake inhibitor (SSRI), like sertraline, is typically associated with improved clinical outcomes, especially in patients with a partial response to monotherapy. In some patients, an increase in exposure to sertraline or its metabolites may occur. Sertraline is metabolized by a variety of CYP enzymes including CYP2D6; bupropion is a strong CYP2D6 inhibitor. The concomitant use of strong CYP2D6 inhibitors, like bupropion, is not expected to have a meaningful effect on concentrations of sertraline or its metabolites in most patients.
buPROPion; Naltrexone: (Minor) Concomitant use of bupropion and sertraline may theoretically increase the risk for sertraline-related adverse effects in some patients. Adjunctive therapy with bupropion plus a selective serotonin reuptake inhibitor (SSRI), like sertraline, is typically associated with improved clinical outcomes, especially in patients with a partial response to monotherapy. In some patients, an increase in exposure to sertraline or its metabolites may occur. Sertraline is metabolized by a

variety of CYP enzymes including CYP2D6; bupropion is a strong CYP2D6 inhibitor. The concomitant use of strong CYP2D6 inhibitors, like bupropion, is not expected to have a meaningful effect on concentrations of sertraline or its metabolites in most patients.
busPIRone: (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.
Butalbital; Acetaminophen; Caffeine; Codeine: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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.
Butalbital; Aspirin; Caffeine; Codeine: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient

carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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. (Moderate) The combined use of selective serotonin reuptake inhibitors and aspirin, ASA may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation.
Cabotegravir; Rilpivirine: (Moderate) Concomitant use of sertraline and rilpivirine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with rilpivirine is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Candesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Cangrelor: (Moderate) Platelet aggregation may be impaired by selective serotonin reuptake inhibitors (SSRIs) due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymosis, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving platelet inhibitors (e.g., cangrelor). Patients should be instructed to monitor for signs and symptoms of bleeding while taking an SSRI concurrently with an antiplatelet medication and to promptly report any bleeding events to the practitioner.
Capsaicin; Metaxalone: (Moderate) Concomitant use of selective serotonin reuptake inhibitors (SSRIs) and metaxalone may increase the risk for serotonin syndrome. Monitor patients for serotonin syndrome if concomitant use is necessary.
Captopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Celecoxib: (Moderate) Monitor for signs and symptoms of bleeding during concomitant

selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Celecoxib; Tramadol: (Moderate) Monitor for reduced efficacy of tramadol, signs of opioid withdrawal, seizures, or serotonin syndrome if coadministration with sertraline is necessary. If sertraline is discontinued, consider a dose reduction of tramadol and frequently monitor for signs of respiratory depression and sedation. Tramadol is a CYP2D6 substrate and sertraline is a CYP2D6 inhibitor. Concomitant use of tramadol with CYP2D6 inhibitors can increase the plasma concentration of tramadol and decrease the plasma concentration of the active metabolite M1. Since M1 is a more potent mu-opioid agonist, decreased M1 exposure could result in decreased therapeutic effects, and may result in signs and symptoms of opioid withdrawal in patients who have developed physical dependence to tramadol. Increased tramadol exposure can result in increased or prolonged therapeutic effects and increased risk for serious adverse events including seizures and serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Ceritinib: (Major) Concomitant use of sertraline and ceritinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
chlordiazePOXIDE; Amitriptyline: (Moderate) Monitor patients for signs and symptoms of serotonin syndrome during concomitant use of sertraline and amitriptyline, 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.
Chloroquine: (Major) Concomitant use of sertraline and chloroquine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to

minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Chlorothiazide: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Chlorpheniramine; Codeine: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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.
Chlorpheniramine; Dextromethorphan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Chlorpheniramine; HYDROcodone: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of hydrocodone and sertraline because of the potential risk of serotonin syndrome and prolonged opioid adverse reactions. Discontinue hydrocodone if serotonin syndrome is suspected. Concomitant use of hydrocodone with sertraline may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. Monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of sertraline could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If sertraline is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Sertraline is a weak inhibitor of CYP2D6.
Chlorpheniramine; Ibuprofen; Pseudoephedrine: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
chlorproMAZINE: (Major) Use caution and monitor patients for QT prolongation when administering chlorpromazine with sertraline. Chlorpromazine, a phenothiazine, is associated with an established risk of QT prolongation and torsade de pointes (TdP). QTc prolongation and TdP have been reported during postmarketing use of sertraline; most cases had confounding risk factors. The risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal

(typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). In addition, sertraline is a CYP2D6 inhibitor and chlorpromazine is a CYP2D6 substrate. Decreased metabolism of chlorpromazine may lead to adverse effects such as arrhythmias, orthostatic hypotension, excessive sedation, or extrapyramidal symptoms.
Chlorthalidone: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Choline Salicylate; Magnesium Salicylate: (Moderate) Monitor for signs and symptoms of bleeding during concomitant magnesium salicylate and selective serotonin reuptake inhibitor (SSRI) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. (Moderate) The combined use of selective serotonin reuptake inhibitors (SSRIs) and aspirin, ASA or other salicylates which affect hemostasis may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation. A cohort study in > 26,000 patients found that SSRI use alone increased the risk for serious GI bleed by 3.6-fold; when an SSRI was combined with aspirin the risk was increased by > 5-fold. The absolute risk of GI bleed from concomitant therapy with aspirin and a SSRI was low (20/2640 patients) in this cohort study and the clinician may determine that the combined use of these drugs is appropriate.
Cilostazol: (Moderate) Platelet aggregation may be impaired by selective serotonin reuptake inhibitors (SSRIs) due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication in patients receiving platelet inhibitors. Monitor for signs and symptoms of bleeding.
Ciprofloxacin: (Moderate) Concomitant use of ciprofloxacin and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Cisapride: (Contraindicated) Avoid concomitant use of sertraline and cisapride due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times

the maximum recommended dose.
Citalopram: (Major) Due to the similarity in pharmacology of sertraline and citalopram and the potential for serious adverse reactions, including serotonin syndrome, these selective serotonin reuptake inhibitors (SSRIs) should not be administered together. Also, both sertraline and citalopram have been associated with QT prolongation and torsade de pointes (TdP), which could theoretically result in additive effects on the QT interval. It is advisable to monitor for signs and symptoms of serotonin syndrome during an overlapping transition from one SSRI to another SSRI.
Clarithromycin: (Major) Concomitant use of sertraline and clarithromycin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Class IC Antiarrhythmics: (Major) Use caution and monitor patients for QT prolongation when administering Class IC Antiarrhythmics with sertraline. Class IC antiarrhythmics increase the QT interval, but largely due to prolongation of the QRS interval. QTc prolongation and torsade de pointes (TdP) have been reported during postmarketing use of sertraline; most cases had confounding risk factors. The risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). In addition, sertraline is a mild to moderate inhibitor of CYP2D6, and inhibition of CYP2D6 can result in increased concentrations of antiarrhythmic drugs metabolized via the same pathway, including flecainide and propafenone.
Clofazimine: (Moderate) Concomitant use of clofazimine and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
clomiPRAMINE: (Major) There have been postmarketing reports of QT prolongation and torsade de pointes (TdP) during treatment with sertraline and the manufacturer of sertraline recommends avoiding concurrent use with drugs known to prolong the QTc interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose

or with higher-dose prescription therapy (elevated serum concentrations). In addition, serotonin syndrome is possible when coadministering drugs that have serotonergic properties such as sertraline and TCAs. 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. Lastly, sertraline is a CYP2D6 inhibitor, one of the isoenzymes responsible for the metabolism of TCAs. During a study evaluating the effects of concurrent use of sertraline and low-dose doxepin (6 mg) in healthy subjects, the doxepin mean AUC and Cmax estimates were about 21% and 32% higher, respectively, during concomitant sertraline administration than in those receiving doxepin alone. Measurements of psychomotor function showed more impairment in the combination group than the group receiving doxepin alone; however, subjective measures of alertness were similar between the two groups. Patients receiving a tricyclic antidepressant should be monitored closely for toxicity if sertraline is added. The American Heart Association has published guidelines regarding cardiovascular monitoring of certain psychotropic drug combinations in children.

Clopidogrel: (Moderate) Carefully monitor patients for signs and symptoms of bleeding during coadministration of sertraline and clopidogrel. Selective serotonin reuptake inhibitors (SSRIs) affect platelet activation; therefore, concomitant use may increase the risk of bleeding.

cloZAPine: (Moderate) Use caution and monitor patients for QT prolongation when administering clozapine with sertraline. Treatment with clozapine has been associated with QT prolongation, torsade de pointes, cardiac arrest, and sudden death. Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). In addition, concurrent use of clozapine, a CYP2D6 substrate, with a CYP2D6 inhibitor, such as sertraline, can increase clozapine plasma concentrations and lead to adverse effects, such as seizures or orthostatic hypotension. Modest (less than 2-fold) elevations in concentrations of clozapine and its metabolites have been reported during concurrent use of sertraline. A case denoting sudden cardiac death has been described in the literature when clozapine was combined with sertraline, but causality was not established.

Cobicistat: (Moderate) Close monitoring for antidepressant response and careful dose titrations of the antidepressant therapy is recommended during coadministration of selective serotonin reuptake inhibitors (SSRIs) and cobicistat. Concurrent use may result in elevated SSRI plasma concentrations. Predictions regarding this interaction can be made based on the metabolic pathways of these drugs. All SSRIs are substrates for the

hepatic isoenzyme CYP2D6, while citalopram, escitalopram, and sertraline are also substrates for CYP3A4; cobicistat is an inhibitor of both CYP2D6 and CYP3A4.
Cocaine: (Major) Concomitant use of cocaine with drugs that have CNS serotonergic properties, such as SSRIs, could potentiate serotonin neurotransmission, and result in the serotonin syndrome. 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. Patients receiving this combination should be monitored for the emergence of serotonin syndrome or neuroleptic malignant syndrome-like reactions. Additionally, citalopram causes dose-dependent QT interval prolongation. Local anesthetics (e.g., cocaine) are associated with a possible risk for QT prolongation and according to the manufacturer of citalopram, concurrent use of citalopram with other drugs that prolong the QT interval is not recommended. If concurrent therapy is considered essential, ECG monitoring is recommended.
Codeine: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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.
Codeine; Dexbrompheniramine: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite,

morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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.
Codeine; guaiFENesin: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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.
Codeine; guaiFENesin; Pseudoephedrine: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine

until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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.
Codeine; Phenylephrine; Promethazine: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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. (Moderate) Concomitant use of promethazine and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Codeine; Promethazine: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of codeine and sertraline because of the potential risk of serotonin syndrome, reduced codeine

efficacy, and potential for opioid withdrawal symptoms. Discontinue codeine if serotonin syndrome is suspected. Concomitant use may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. Monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of sertraline could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If sertraline is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Sertraline is a weak inhibitor of CYP2D6. 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. (Moderate) Concomitant use of promethazine and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Crizotinib: (Major) Concomitant use of sertraline and crizotinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Cyclobenzaprine: (Major) Because of the potential risk and severity of serotonin syndrome, concurrent use of cyclobenzaprine with other drugs that have serotonergic properties, such as the selective serotonin reuptake inhibitors (SSRIs), should generally be avoided. 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. If serotonin syndrome is suspected, sertraline and concurrent serotonergic agents should be discontinued.
cycloSPORINE: (Moderate) Although a causal relationship has not been established, the combination of cyclosporine and sertraline is suspected of causing serotonin syndrome

in a renal transplant patient. Sertraline serum concentrations may have increased due to possible CYP3A4 inhibition by cyclosporine.
Cyproheptadine: (Moderate) Cyproheptadine is a serotonin antagonist in the CNS and can oppose the pharmacologic actions of selective serotonin reuptake inhibitors (SSRIs) such as sertraline. Cyproheptadine has been used for the management of orgasm dysfunction caused by the SSRIs and for the adjunctive treatment of SSRI overdose (i.e., serotonin syndrome) in emergency situations; however, a reversal of antidepressant effects may occur when cyproheptadine is given in a routine manner along with the SSRIs due to the serotonin antagonistic effects of cyproheptadine.
Dabigatran: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and anticoagulants like dabigatran. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding.
Dalteparin: (Moderate) Monitor for signs and symptoms of bleeding during concomitant low molecular weight heparin and selective serotonin reuptake inhibitor (SSRI) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs are coadministered with another anticoagulant.
Darifenacin: (Moderate) Sertraline, an inhibitor of CYP3A4, may decrease the metabolism of darifenacin and increase serum concentrations. Patients should be monitored for increased anticholinergic effects if these drugs are used concomitantly; dosage adjustments of darifenacin may be necessary.
Darunavir: (Moderate) Use caution when coadministering darunavir with sertraline, as decreased SSRI concentrations may be seen. If sertraline is coadministered with darunavir, carefully titrate the dose of sertraline based on a clinical assessment of antidepressant response.
Darunavir; Cobicistat: (Moderate) Close monitoring for antidepressant response and careful dose titrations of the antidepressant therapy is recommended during coadministration of selective serotonin reuptake inhibitors (SSRIs) and cobicistat. Concurrent use may result in elevated SSRI plasma concentrations. Predictions regarding this interaction can be made based on the metabolic pathways of these drugs. All SSRIs are substrates for the hepatic isoenzyme CYP2D6, while citalopram, escitalopram, and sertraline are also substrates for CYP3A4; cobicistat is an inhibitor of both CYP2D6 and CYP3A4. (Moderate) Use caution when coadministering darunavir with sertraline, as decreased SSRI concentrations may be seen. If sertraline is coadministered with darunavir, carefully titrate the dose of sertraline based on a clinical assessment of antidepressant response.

Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Moderate) Close monitoring for antidepressant response and careful dose titrations of the antidepressant therapy is recommended during coadministration of selective serotonin reuptake inhibitors (SSRIs) and cobicistat. Concurrent use may result in elevated SSRI plasma concentrations. Predictions regarding this interaction can be made based on the metabolic pathways of these drugs. All SSRIs are substrates for the hepatic isoenzyme CYP2D6, while citalopram, escitalopram, and sertraline are also substrates for CYP3A4; cobicistat is an inhibitor of both CYP2D6 and CYP3A4. (Moderate) Use caution when coadministering darunavir with sertraline, as decreased SSRI concentrations may be seen. If sertraline is coadministered with darunavir, carefully titrate the dose of sertraline based on a clinical assessment of antidepressant response.
Dasatinib: (Moderate) Concomitant use of sertraline and dasatinib may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Degarelix: (Moderate) Concomitant use of sertraline and androgen deprivation therapy (i.e., degarelix) may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Desflurane: (Major) Concomitant use of sertraline and halogenated anesthetics increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Desipramine: (Major) There have been postmarketing reports of QT prolongation and torsade de pointes (TdP) during treatment with sertraline and the manufacturer of sertraline recommends avoiding concurrent use with drugs known to prolong the QTc interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). In addition,

serotonin syndrome is possible when coadministering drugs that have serotonergic properties such as sertraline and TCAs. 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. Lastly, sertraline is a CYP2D6 inhibitor, one of the isoenzymes responsible for the metabolism of TCAs. During a study evaluating the effects of concurrent use of sertraline and low-dose doxepin (6 mg) in healthy subjects, the doxepin mean AUC and Cmax estimates were about 21% and 32% higher, respectively, during concomitant sertraline administration than in those receiving doxepin alone. Measurements of psychomotor function showed more impairment in the combination group than the group receiving doxepin alone; however, subjective measures of alertness were similar between the two groups. Patients receiving a tricyclic antidepressant should be monitored closely for toxicity if sertraline is added. The American Heart Association has published guidelines regarding cardiovascular monitoring of certain psychotropic drug combinations in children.
Desmopressin: (Minor) Additive hyponatremic effects may be seen in patients treated with desmopressin and drugs associated with water intoxication, hyponatremia, or SIADH including SSRIs. Use combination with caution, and monitor patients for signs and symptoms of hyponatremia, which may include monitoring serum sodium or electrolytes periodically. Ensure the patient is compliant with fluid restrictions and intake.
Desvenlafaxine: (Major) Due to similarity of pharmacology and the potential for additive adverse effects, including serotonin syndrome, selective serotonin reuptake inhibitors (SSRIs) should generally not be administered with serotonin norepinephrine reuptake inhibitors like desvenlafaxine. 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. Discontinuation symptoms have been reported when switching from other antidepressants to desvenlafaxine. It may be advisable to taper the previous antidepressant to minimize discontinuation symptoms.
Deutetrabenazine: (Moderate) Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). If use of sertraline and deutetrabenazine together is necessary, use caution and monitor patients for QT prolongation. Deutetrabenazine may prolong the QT interval, but the degree of QT prolongation is not clinically significant when deutetrabenazine is administered within the recommended dosage range.

Dexbrompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Dexchlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
dexmedeTOMIDine: (Moderate) Concomitant use of dexmedetomidine and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Dexmethylphenidate: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Dextroamphetamine: (Moderate) Coadministration of selective serotonin reuptake inhibitors (SSRIs) like sertraline with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. 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.
Dextromethorphan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Dextromethorphan; buPROPion: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome. (Minor) Concomitant use of bupropion and sertraline may theoretically increase the risk for sertraline-related adverse effects in some patients. Adjunctive therapy with bupropion plus a selective serotonin reuptake inhibitor (SSRI), like sertraline, is typically associated with improved clinical outcomes, especially in patients with a partial response to monotherapy. In some patients, an increase in exposure to sertraline or its metabolites may occur. Sertraline is metabolized by a variety of CYP enzymes including CYP2D6; bupropion is a strong CYP2D6 inhibitor. The concomitant use of strong CYP2D6 inhibitors, like bupropion, is not expected to have a meaningful effect on concentrations of sertraline or its metabolites in most patients.
Dextromethorphan; diphenhydrAMINE; Phenylephrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Dextromethorphan; guaiFENesin: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering

dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Dextromethorphan; guaiFENesin; Phenylephrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Dextromethorphan; guaiFENesin; Pseudoephedrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
Dextromethorphan; quiNIDine: (Major) Concomitant use of sertraline and quinidine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose. (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects

consistent with the serotonin syndrome.
Diclofenac: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Diclofenac; miSOPROStol: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Diflunisal: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Dihydroergotamine: (Moderate) Monitor for serotonin syndrome and symptoms of serotonin excess such as weakness, hyperreflexia, and incoordination during concomitant use of ergotamine and sertraline. Both medications enhance serotonergic activity.
diphenhydrAMINE; Ibuprofen: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
diphenhydrAMINE; Naproxen: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Dipyridamole: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis, such as dipyridamole. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding.
Disopyramide: (Major) Concomitant use of sertraline and disopyramide increases the

risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Disulfiram: (Major) The ingestion of ethanol by patients receiving disulfiram causes an extremely unpleasant reaction that can last from 30 minutes to several hours. Oral sertraline solution contains a high percentage of alcohol (12%) and should not be co-administered with disulfiram. A disulfiram-like reaction is not expected with formulations of sertraline that do not contain alcohol.
Diuretics: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Dofetilide: (Major) Concomitant use of sertraline and dofetilide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Dolasetron: (Moderate) Use caution and monitor patients for QT prolongation and serotonin syndrome when administering dolasetron with sertraline. Dolasetron has been associated with a dose-dependent prolongation in the QT, PR, and QRS intervals on an electrocardiogram. Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). In addition, taking these drugs together may increase the risk for serotonin syndrome. If concurrent use is required and serotonin syndrome occurs, discontinue all serotonergic agents and initiate appropriate medical treatment.
Dolutegravir; Rilpivirine: (Moderate) Concomitant use of sertraline and rilpivirine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated

with rilpivirine is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Donepezil: (Moderate) Concomitant use of sertraline and donepezil may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Donepezil; Memantine: (Moderate) Concomitant use of sertraline and donepezil may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Dordaviprone: (Major) Concomitant use of dordaviprone and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Doxepin: (Moderate) Monitor for an increase in doxepin-related adverse reactions and signs and symptoms of serotonin syndrome during concomitant use, 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. Concomitant use may increase doxepin exposure. During a study evaluating the effects of concurrent use of sertraline and low-dose doxepin (6 mg) in healthy subjects, the doxepin mean AUC and Cmax estimates were about 21% and 32% higher, respectively, during concomitant sertraline administration than in those receiving doxepin alone. Doxepin is a CYP2D6 substrate and sertraline is a CYP2D6 inhibitor.
Doxercalciferol: (Moderate) Doxercalciferol is converted in the liver to 1,25-

dihydroxyergocalciferol, the major active metabolite, and 1-alpha, 24-dihydroxyvitamin D2, a minor metabolite. Although not specifically studied, cytochrome P450 enzyme inhibitors, including selective serotonin reuptake inhibitors (SSRIs), may inhibit the 25-hydroxylation of doxercalciferol, thereby decreasing the formation of the active metabolite and thus, decreasing efficacy. Patients should be monitored for a decrease in efficacy if SSRIs are coadministered with doxercalciferol.
Dronedarone: (Contraindicated) Avoid concomitant use of sertraline and dronedarone due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
droPERidol: (Major) Concomitant use of sertraline and droperidol increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
DULoxetine: (Major) Due to similarity of pharmacology and the potential for additive adverse effects, including serotonin syndrome, selective serotonin reuptake inhibitors (SSRIs) such as sertraline should generally not be administered with serotonin norepinephrine reuptake inhibitors (SNRIs) such as duloxetine.
Edoxaban: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and anticoagulants like edoxaban. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding.
Efavirenz: (Moderate) Concomitant use of sertraline and efavirenz may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Efavirenz; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) Concomitant use of sertraline and efavirenz may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The

degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Efavirenz; lamiVUDine; Tenofovir Disoproxil Fumarate: (Moderate) Concomitant use of sertraline and efavirenz may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Elbasvir; Grazoprevir: (Moderate) Administering sertraline with elbasvir; grazoprevir may result in elevated sertraline plasma concentrations. Sertraline 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) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering eletriptan with sertraline. Serotonin syndrome has been reported during concurrent use of serotonin-receptor agonists and selective serotonin reuptake inhibitors (SSRIs). Some patients had used the combination previously without incident when serotonin syndrome occurred. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly after a dose increase of the SSRI or the addition of other serotonergic medications to an existing SSRI regimen. Discontinue sertraline and eletriptan and initiate symptomatic treatment if serotonin syndrome occurs.
Elexacaftor; tezacaftor; ivacaftor: (Minor) Increased monitoring is recommended if ivacaftor is administered concurrently with CYP2C9 substrates, such as sertraline. Ivacaftor is an inhibitor of CYP3A and a weak inhibitor of CYP2C9; sertraline is metabolized by CYP3A and CYP2C9. Co-administration of ivacaftor with CYP3A and CYP2C9 substrates, such as sertraline, can theoretically increase sertraline exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Eliglustat: (Moderate) Concomitant use of sertraline and eliglustat may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Alafenamide: (Moderate) Close monitoring for antidepressant response and careful dose titrations of the

antidepressant therapy is recommended during coadministration of selective serotonin reuptake inhibitors (SSRIs) and cobicistat. Concurrent use may result in elevated SSRI plasma concentrations. Predictions regarding this interaction can be made based on the metabolic pathways of these drugs. All SSRIs are substrates for the hepatic isoenzyme CYP2D6, while citalopram, escitalopram, and sertraline are also substrates for CYP3A4; cobicistat is an inhibitor of both CYP2D6 and CYP3A4.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) Close monitoring for antidepressant response and careful dose titrations of the antidepressant therapy is recommended during coadministration of selective serotonin reuptake inhibitors (SSRIs) and cobicistat. Concurrent use may result in elevated SSRI plasma concentrations. Predictions regarding this interaction can be made based on the metabolic pathways of these drugs. All SSRIs are substrates for the hepatic isoenzyme CYP2D6, while citalopram, escitalopram, and sertraline are also substrates for CYP3A4; cobicistat is an inhibitor of both CYP2D6 and CYP3A4.
Emtricitabine; Rilpivirine; Tenofovir alafenamide: (Moderate) Concomitant use of sertraline and rilpivirine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with rilpivirine is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Emtricitabine; Rilpivirine; Tenofovir Disoproxil Fumarate: (Moderate) Concomitant use of sertraline and rilpivirine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with rilpivirine is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Enalapril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.

Encorafenib: (Major) Concomitant use of sertraline and encorafenib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Enoxaparin: (Moderate) Monitor for signs and symptoms of bleeding during concomitant low molecular weight heparin and selective serotonin reuptake inhibitor (SSRI) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs are coadministered with another anticoagulant.
Entrectinib: (Major) Concomitant use of sertraline and entrectinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Eptifibatide: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis, such as eptifibatide. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding.
Ergoloid Mesylates: (Minor) Monitor for symptoms of serotonergic toxicity during concomitant use of ergoloid mesylates (co-dergocrine mesylate) and a selective serotonin reuptake inhibitor (SSRI). Serotonin receptor agonist and antagonist activity has been observed with ergoloid mesylates. Concomitant use may increase the risk for serotonin syndrome in some patients.
Ergotamine: (Moderate) Monitor for serotonin syndrome and symptoms of serotonin excess such as weakness, hyperreflexia, and incoordination during concomitant use of ergotamine and sertraline. Both medications enhance serotonergic activity.
Ergotamine; Caffeine: (Moderate) Monitor for serotonin syndrome and symptoms of serotonin excess such as weakness, hyperreflexia, and incoordination during concomitant use of ergotamine and sertraline. Both medications enhance serotonergic activity.

eriBULin: (Major) Concomitant use of sertraline and eribulin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Erythromycin: (Major) Concomitant use of sertraline and erythromycin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Escitalopram: (Major) Due to the similarity in pharmacology of sertraline and escitalopram and the potential for serious adverse reactions, including serotonin syndrome, these selective serotonin reuptake inhibitors (SSRIs) should not be administered together. Also, both sertraline and escitalopram have been associated with QT prolongation, which could theoretically result in additive effects on the QT interval. It is advisable to monitor for signs and symptoms of serotonin syndrome during an overlapping transition from one SSRI to another SSRI.
Ethacrynic Acid: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Etodolac: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Etrasimod: (Moderate) Concomitant use of etrasimod and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose. Etrasimod has a limited effect on the QT/QTc interval at therapeutic doses but may cause bradycardia and atrioventricular conduction delays which may increase the risk for TdP in patients with a prolonged QT/QTc interval.

Fenfluramine: (Moderate) Use fenfluramine and sertraline 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.
Fenofibric Acid: (Minor) At therapeutic concentrations, fenofibric acid is a weak inhibitor of CYP2C19. Concomitant use of fenofibric acid with CYP2C19 substrates, such as sertraline, has not been formally studied. Fenofibric acid may theoretically increase plasma concentrations of CYP2C19 substrates and could lead to toxicity for drugs that have a narrow therapeutic range. Monitor the therapeutic effect of sertraline during coadministration with fenofibric acid.
Fenoprofen: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
fentaNYL: (Moderate) If concomitant use of fentanyl and sertraline is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Fexinidazole: (Major) Concomitant use of fexinidazole and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Fingolimod: (Moderate) Concomitant use of sertraline and fingolimod may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Flecainide: (Major) Use caution and monitor patients for QT prolongation when administering Class IC Antiarrhythmics with sertraline. Class IC antiarrhythmics increase the QT interval, but largely due to prolongation of the QRS interval. QTc prolongation and torsade de pointes (TdP) have been reported during postmarketing use of sertraline; most cases had confounding risk factors. The risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc

interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). In addition, sertraline is a mild to moderate inhibitor of CYP2D6, and inhibition of CYP2D6 can result in increased concentrations of antiarrhythmic drugs metabolized via the same pathway, including flecainide and propafenone.
Fluconazole: (Moderate) Concomitant use of fluconazole and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
FLUoxetine: (Major) Due to the similarity in pharmacology of fluoxetine and sertraline and the potential for serious adverse reactions, including serotonin syndrome, these selective serotonin reuptake inhibitors (SSRIs) should not be administered together. Also, both fluoxetine and sertraline have been associated with QT prolongation, which could theoretically result in additive effects on the QT interval. It is advisable to monitor for signs and symptoms of serotonin syndrome during an overlapping transition from one SSRI to another SSRI.
fluPHENAZine: (Minor) Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval, such as fluphenazine; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). If use together is necessary, use caution and monitor patients for QT prolongation. In addition, CYP2D6 substrates such as fluphenazine may require lower doses during concurrent use with sertraline, due to CYP2D6 inhibition by sertraline and the potential for arrhythmias or other adverse reactions associated with antipsychotics such as extrapyramidal symptoms.
Flurbiprofen: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
fluvoxaMINE: (Major) Due to the similarity in pharmacology of sertraline and fluvoxamine and the potential for serious adverse reactions, including serotonin syndrome, these selective serotonin reuptake inhibitors (SSRIs) should not be

administered together. Also, both sertraline and fluvoxamine have been associated with QT prolongation, which could theoretically result in additive effects on the QT interval. It is advisable to monitor for signs and symptoms of serotonin syndrome during an overlapping transition from one SSRI to another SSRI.
Fondaparinux: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and anticoagulants like fondaparinux. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding.
Foscarnet: (Major) Concomitant use of sertraline and foscarnet increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Fosinopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Fosphenytoin: (Moderate) Monitor phenytoin concentrations during concomitant sertraline use; a fosphenytoin dosage adjustment may be necessary. Sertraline may increase phenytoin concentrations.
Fostemsavir: (Moderate) Concomitant use of sertraline and fostemsavir may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with fostemsavir is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 4 times the recommended daily dose. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Frovatriptan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering frovatriptan with selective serotonin reuptake inhibitors (SSRIs). Serotonin syndrome has been reported during concurrent use of serotonin-receptor agonists and SSRIs. Some patients had used the combination previously without incident when serotonin syndrome occurred. Inform patients taking this combination of the possible increased risk and monitor for the

emergence of serotonin syndrome particularly after a dose increase of the SSRI or the addition of other serotonergic medications to an existing SSRI regimen. Discontinue the SSRI and frovatriptan and initiate symptomatic treatment if serotonin syndrome occurs.
Furosemide: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Gemifloxacin: (Moderate) Concomitant use of sertraline and gemifloxacin may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Gemtuzumab Ozogamicin: (Moderate) Concomitant use of sertraline and gemtuzumab ozogamicin may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Gepirone: (Moderate) Concomitant use of gepirone and sertraline may increase the risk of serotonin syndrome and QT/QTc prolongation and torsade de pointes (TdP) in some patients. If concomitant use is necessary, monitor for serotonin syndrome and consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose. QT prolongation with gepirone has also been observed at 2 times the maximum recommended dose.
Gepotidacin: (Major) Concomitant use of gepotidacin and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been

described at 2 times the maximum recommended dose.
Gilteritinib: (Moderate) Use caution and monitor for evidence of QT prolongation if concurrent use of gilteritinib and sertraline is necessary. Gilteritinib has been associated with QT prolongation. Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). Additionally, gilteritinib inhibits human 5HT2B receptor or sigma nonspecific receptors, which may reduce the effects of drugs like sertraline that target these receptors.
Givinostat: (Major) Concomitant use of givinostat and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose. The degree of QT prolongation associated with givinostat is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 5 times the maximum recommended dose.
Glasdegib: (Major) Concomitant use of sertraline and glasdegib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Goserelin: (Moderate) Concomitant use of sertraline and androgen deprivation therapy (i.e., goserelin) may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Granisetron: (Moderate) Use caution and monitor patients for QT prolongation and serotonin syndrome when administering granisetron with sertraline. Granisetron has

been associated with QT prolongation. Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). In addition, taking these drugs together may increase the risk for serotinin syndrome. If serotonin syndrome occurs, discontinue serotonergic agents and initiate appropriate medical treatment.
Grapefruit juice: (Minor) Advise patients to not significantly alter their intake of grapefruit juice while taking sertraline until more data are available. Grapefruit juice has been reported to inhibit the metabolism of sertraline, elevating sertraline trough concentrations. It is not clear if the interaction is clinically significant for patients. The theorized mechanism is the inhibition of sertraline metabolism via CYP3A4; however, sertraline is known to be metabolized by many CYP enzymes, and inhibition of one enzyme is not likely to significantly affect sertraline pharmacokinetics.
Halogenated Anesthetics: (Major) Concomitant use of sertraline and halogenated anesthetics increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Haloperidol: (Moderate) Use caution and monitor patients for QT prolongation and increased haloperidol-related adverse effects when administering haloperidol with sertraline. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). Additionally, sertraline is an inhibitor of CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 may increase the risk of adverse effects, including QT prolongation.
Heparin: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and anticoagulants like heparin. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and

gastrointestinal bleeding.
Histrelin: (Moderate) Concomitant use of sertraline and androgen deprivation therapy (i.e., histrelin) may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Homatropine; HYDROcodone: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of hydrocodone and sertraline because of the potential risk of serotonin syndrome and prolonged opioid adverse reactions. Discontinue hydrocodone if serotonin syndrome is suspected. Concomitant use of hydrocodone with sertraline may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. Monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of sertraline could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If sertraline is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Sertraline is a weak inhibitor of CYP2D6.
hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
hydroCHLOROthiazide, HCTZ; Moexipril: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
HYDROcodone: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of hydrocodone and sertraline because of the potential risk of serotonin syndrome and prolonged opioid adverse reactions. Discontinue hydrocodone if serotonin syndrome is suspected. Concomitant use of hydrocodone with sertraline may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. Monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of sertraline could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome

in those with physical dependence to hydrocodone. If sertraline is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Sertraline is a weak inhibitor of CYP2D6.
HYDROcodone; Ibuprofen: (Moderate) Careful monitoring, particularly during treatment initiation and dose adjustment, is recommended during coadministration of hydrocodone and sertraline because of the potential risk of serotonin syndrome and prolonged opioid adverse reactions. Discontinue hydrocodone if serotonin syndrome is suspected. Concomitant use of hydrocodone with sertraline may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. Monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of sertraline could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If sertraline is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Sertraline is a weak inhibitor of CYP2D6.
(Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
HYDROmorphone: (Moderate) If concomitant use of hydromorphone and sertraline 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.
Hydroxychloroquine: (Major) Concomitant use of hydroxychloroquine and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
hydrOXYzine: (Moderate) Concomitant use of hydroxyzine and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated

with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate; Sodium Biphosphate: (Contraindicated) According to the manufacturer of sertraline, treatment initiation with sertraline is contraindicated in patients currently receiving intravenous (IV) methylene blue due to an increased risk of serotonin syndrome. If urgent psychiatric treatment is required, interventions other than sertraline (e.g., alternative medication, hospitalization) should be considered. Conversely, in patients receiving sertraline and requiring urgent treatment with IV methylene blue, sertraline should be discontinued immediately and methylene blue therapy initiated only if acceptable alternatives are not available and the potential benefits outweigh the risks. The patient should be monitored for serotonin syndrome for 2 weeks or until 24 hours after the last dose of methylene blue, whichever comes first. Sertraline may be re-initiated 24 hours after the last dose of methylene blue. Results from an in vitro study indicate that methylene blue is a potent, reversible inhibitor of the monoamine oxidase type A enzyme (MAO-A). MAO-A is responsible for the metabolism of serotonin; therefore, concurrent use of an MAO-A inhibitor with a serotonergic agent may result in a clinically significant interaction. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent, in patients receiving SSRIs, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents with IV methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. One case describes a patient receiving citalopram who experienced agitation, restlessness, pupil dilation with sluggish response to light, myoclonic movements of the lower limbs, and brisk reflexes following an infusion of methylene blue, while another patient receiving paroxetine developed tachycardia, agitation, dystonia and abnormal eye movements. During a retrospective study of 193 surgical patients who had received a methylene blue injection, it was found that all 12 of the patients who experienced postoperative neurological sequelae had been taking a serotonin reuptake inhibitor preoperatively. One of the 12 patients experienced cardiopulmonary arrest and died. Of the remaining 181 patients who did not experience neurological sequelae, 8.8% were taking a serotonin reuptake inhibitor. Published interaction reports between IV methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and coma. Signs and symptoms of serotonin syndrome include fever, diaphoresis, shivering, myoclonus, tremor, tachycardia, diarrhea, nausea, headache, incoordination, mental status changes (e.g., agitation, confusion), hyperreflexia, seizures, and coma. (Moderate) The combined use

of selective serotonin reuptake inhibitors (SSRIs) and aspirin, ASA or other salicylates which affect hemostasis may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin.
Ibuprofen: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Ibuprofen; Famotidine: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Ibuprofen; Pseudoephedrine: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Ibutilide: (Major) Concomitant use of sertraline and ibutilide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Idelalisib: (Major) Avoid concomitant use of idelalisib, a strong CYP3A inhibitor, with sertraline, a CYP3A substrate, as sertraline toxicities may be significantly increased. The AUC of a sensitive CYP3A substrate was increased 5.4-fold when coadministered with idelalisib.
Iloperidone: (Major) Concomitant use of sertraline and iloperidone increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been

described at 2 times the maximum recommended dose.
Imatinib: (Major) Sertraline is a substrate for the CYP isoenzymes 3A4, 2D6 and 2C19. Imatinib is a potent inhibitor of cytochrome P450 2D6 and 3A4 and might decrease sertraline metabolism leading to increased adverse reactions.
Imipramine: (Major) There have been postmarketing reports of QT prolongation and torsade de pointes (TdP) during treatment with sertraline and the manufacturer of sertraline recommends avoiding concurrent use with drugs known to prolong the QTc interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). In addition, serotonin syndrome is possible when coadministering drugs that have serotonergic properties such as sertraline and TCAs. 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. Lastly, sertraline is a CYP2D6 inhibitor, one of the isoenzymes responsible for the metabolism of TCAs. During a study evaluating the effects of concurrent use of sertraline and low-dose doxepin (6 mg) in healthy subjects, the doxepin mean AUC and Cmax estimates were about 21% and 32% higher, respectively, during concomitant sertraline administration than in those receiving doxepin alone. Measurements of psychomotor function showed more impairment in the combination group than the group receiving doxepin alone; however, subjective measures of alertness were similar between the two groups. Patients receiving a tricyclic antidepressant should be monitored closely for toxicity if sertraline is added. The American Heart Association has published guidelines regarding cardiovascular monitoring of certain psychotropic drug combinations in children.
Indapamide: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Indomethacin: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Inotuzumab Ozogamicin: (Major) Concomitant use of sertraline and inotuzumab increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is

necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Iobenguane I 123: (Major) Discontinue medications that decrease norepinephrine uptake, such as selective serotonin reuptake inhibitors (SSRIs), for at least 5 biological half-lives prior to iobenguane I 123 administration. Consider medication tapering or additional supportive therapy as appropriate to minimize the risk for precipitating SSRI withdrawal symptoms. Medications that decrease the uptake of norepinephrine can cause false negative imaging results. Increasing the dose of iobenguane I 123 will not overcome any potential uptake limiting effect of this medication.
Ioflupane I 123: (Moderate) Selective serotonin reuptake inhibitors (SSRIs) may interfere with dopamine transporter (DAT) imaging that utilizes radiolabeled ioflupane. Observed changes in striatal tracer binding have generally been small and inconsistent. These changes are unlikely to affect the interpretation of visual assessments in routine clinical practice but may be relevant in the research setting.
Irbesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Isocarboxazid: (Contraindicated) Due to the risk of serotonin syndrome, monoamine oxidase inhibitors (MAOIs) intended to treat psychiatric disorders are contraindicated for use with selective serotonin reuptake inhibitors (SSRIs). MAOIs should not be used within 5 weeks of discontinuing treatment with fluoxetine or within 14 days of discontinuing treatment with other SSRIs. Conversely, SSRIs should not be initiated within 14 days of stopping an MAOI. Monitor the patient for serotonin-related effects during therapy transitions.
Isoflurane: (Major) Concomitant use of sertraline and halogenated anesthetics increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Itraconazole: (Moderate) Concomitant use of sertraline and itraconazole may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended

dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Ivacaftor: (Minor) Increased monitoring is recommended if ivacaftor is administered concurrently with CYP2C9 substrates, such as sertraline. Ivacaftor is an inhibitor of CYP3A and a weak inhibitor of CYP2C9; sertraline is metabolized by CYP3A and CYP2C9. Co-administration of ivacaftor with CYP3A and CYP2C9 substrates, such as sertraline, can theoretically increase sertraline exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Ivosidenib: (Major) Concomitant use of sertraline and ivosidenib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Ketoconazole: (Contraindicated) Avoid concomitant use of ketoconazole and sertraline due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. Ketoconazole has a well established risk for QT prolongation and TdP. QTc prolongation and TdP have been reported during postmarketing use of sertraline; most cases had confounding risk factors; the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Sertraline has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure).
Ketoprofen: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Ketorolac: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Lansoprazole; Amoxicillin; Clarithromycin: (Major) Concomitant use of sertraline and clarithromycin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for

TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Lapatinib: (Moderate) Concomitant use of sertraline and lapatinib may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Lasmiditan: (Moderate) Serotonin syndrome may occur during coadministration of lasmiditan and selective serotonin reuptake inhibitors. 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: (Major) Concomitant use of sertraline and lefamulin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Lenvatinib: (Major) Concomitant use of sertraline and lenvatinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Leuprolide: (Moderate) Concomitant use of sertraline and androgen deprivation therapy (i.e., leuprolide) may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered

within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Leuprolide; Norethindrone: (Moderate) Concomitant use of sertraline and androgen deprivation therapy (i.e., leuprolide) may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
levoFLOXacin: (Moderate) Concomitant use of levofloxacin and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Levoketoconazole: (Contraindicated) Avoid concomitant use of ketoconazole and sertraline due to an increased risk for torsade de pointes (TdP) and QT/QTc prolongation. Ketoconazole has a well established risk for QT prolongation and TdP. QTc prolongation and TdP have been reported during postmarketing use of sertraline; most cases had confounding risk factors; the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Sertraline has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure).
Levomilnacipran: (Major) Because of the potential risk and severity of serotonin syndrome, concurrent use of levomilnacipran with other drugs that have serotonergic properties, such as selective serotonin reuptake inhibitors (SSRIs), should generally be avoided. 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. If serotonin syndrome is suspected, levomilnacipran and concurrent serotonergic agents should be discontinued.
Levorphanol: (Moderate) If concomitant use of levorphanol and sertraline 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.
Linezolid: (Contraindicated) According to the manufacturer of sertraline, treatment initiation with sertraline is contraindicated in patients currently receiving linezolid due to

an increased risk of serotonin syndrome. If urgent psychiatric treatment is required, interventions other than sertraline (e.g., alternative medication, hospitalization) should be considered. Conversely, in patients receiving sertraline and requiring urgent treatment with linezolid, sertraline 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. Sertraline may be re-initiated 24 hours after the last dose of linezolid. Linezolid is an antibiotic that is also a non-selective monoamine oxidase (MAO) inhibitor. Since monoamine oxidase type A deaminates serotonin, administration of a non-selective MAO inhibitor concurrently with sertraline can lead to serious reactions including serotonin syndrome or neuroleptic malignant syndrome-like reactions. 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. Serotonin syndrome has been reported in patients receiving either citalopram, escitalopram, fluoxetine, or paroxetine in combination with linezolid.
Lisdexamfetamine: (Moderate) Coadministration of selective serotonin reuptake inhibitors (SSRIs) like sertraline with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. 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.
Lisinopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Lithium: (Moderate) Coadministration of sertraline and lithium may increase the risk for QT prolongation and serotonin syndrome. Lithium has been associated with QT prolongation. However, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. The effect of sertraline on the QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease. Lithium is an effective augmenting agent to antidepressants in treatment-resistant depression; however, lithium has central serotonin-enhancing effects and may increase the risk of serotonin syndrome when combined with selective serotonin reuptake inhibitors (SSRIs) such as sertraline. Inform patients of the possible increased risk and monitor for serotonin syndrome, particularly during treatment initiation and dosage increases. If serotonin syndrome occurs, serotonergic agents

should be discontinued and symptomatic treatment should be initiated.
Lofexidine: (Major) Concomitant use of sertraline and lofexidine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Loperamide: (Moderate) Concomitant use of loperamide and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Loperamide; Simethicone: (Moderate) Concomitant use of loperamide and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Lopinavir; Ritonavir: (Major) Concomitant use of sertraline and lopinavir increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Losartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Low Molecular Weight Heparins: (Moderate) Monitor for signs and symptoms of bleeding during concomitant low molecular weight heparin and selective serotonin reuptake inhibitor (SSRI) use due to increased risk for bleeding. Serotonin release by

platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs are coadministered with another anticoagulant.
Lumacaftor; Ivacaftor: (Minor) Increased monitoring is recommended if ivacaftor is administered concurrently with CYP2C9 substrates, such as sertraline. Ivacaftor is an inhibitor of CYP3A and a weak inhibitor of CYP2C9; sertraline is metabolized by CYP3A and CYP2C9. Co-administration of ivacaftor with CYP3A and CYP2C9 substrates, such as sertraline, can theoretically increase sertraline exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Lumateperone: (Moderate) Monitor for adverse effects suggestive of serotonin excess, such as serotonin syndrome and hyponatremia, during concomitant use of a serotonin reuptake inhibitor, such as sertraline, and lumateperone. Both medications affect the serotonin transporter and concomitant use may increase the risk for adverse effects.
Macimorelin: (Major) Concomitant use of sertraline and macimorelin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Magnesium Salicylate: (Moderate) Monitor for signs and symptoms of bleeding during concomitant magnesium salicylate and selective serotonin reuptake inhibitor (SSRI) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Maprotiline: (Moderate) Concomitant use of sertraline and maprotiline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Mavorixafor: (Moderate) Concomitant use of mavorixafor and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider

taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose. The degree of QT prolongation associated with mavorixafor is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Meclofenamate Sodium: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Mefenamic Acid: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Mefloquine: (Moderate) Concomitant use of sertraline and mefloquine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Meloxicam: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Meloxicam; Rizatriptan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering rizatriptan with selective serotonin reuptake inhibitors (SSRIs). Serotonin syndrome has been reported during concurrent use of serotonin-receptor agonists ("triptans") and SSRIs. Some patients had used the combination previously without incident when serotonin syndrome occurred. Inform patients of the possible increased risk and monitor for the

emergence of serotonin syndrome, particularly after the initiation of the SSRI or dose increases. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Meperidine: (Moderate) If concomitant use of meperidine and sertraline 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.
Metaxalone: (Moderate) Concomitant use of selective serotonin reuptake inhibitors (SSRIs) and metaxalone may increase the risk for serotonin syndrome. Monitor patients for serotonin syndrome if concomitant use is necessary.
Methadone: (Major) Coadministration should be avoided if possible due to the potential risk of serotonin syndrome, QT prolongation or torsade de pointes (TdP), or opioid-related side effects. There have been postmarketing reports of QT prolongation and TdP during treatment with sertraline and the manufacturer of sertraline recommends avoiding concurrent use with drugs known to prolong the QTc interval. The need to coadminister methadone with drugs known to prolong the QT interval should be done with extreme caution and a careful assessment of treatment risks versus benefits. Methadone is associated with an increased risk for QT prolongation and TdP, especially at higher doses (greater than 200 mg/day but averaging approximately 400 mg/day in adult patients). Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction. In addition, both sertraline and methadone have central serotonergic properties and serotonin syndrome is possible. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical treatment should be implemented. Lastly, sertraline is a CYP2D6 inhibitor and methadone is partially metabolized by CYP2D6, which may increase the risk of CNS depressive effects, respiratory depression, QT prolongation, or other adverse effects.
Methamphetamine: (Moderate) Coadministration of selective serotonin reuptake inhibitors (SSRIs) like sertraline with amphetamines may increase the risk of serotonin syndrome. At high doses, amphetamines can increase serotonin release and act as serotonin agonists. 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. Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine: (Contraindicated) According to the manufacturer of sertraline, treatment initiation with sertraline is contraindicated in patients currently receiving intravenous (IV) methylene blue due to an increased risk of serotonin syndrome. If urgent psychiatric treatment is required, interventions other than sertraline (e.g., alternative medication, hospitalization) should be considered. Conversely, in patients receiving sertraline and requiring urgent treatment with IV methylene blue, sertraline should be discontinued immediately and methylene blue therapy initiated only if acceptable alternatives are not available and the potential benefits outweigh the risks. The patient should be monitored for serotonin syndrome for 2 weeks or until 24 hours after the last dose of methylene blue, whichever comes first. Sertraline may be re-initiated 24 hours after the last dose of methylene blue. Results from an in vitro study indicate that methylene blue is a potent, reversible inhibitor of the monoamine oxidase type A enzyme (MAO-A). MAO-A is responsible for the metabolism of serotonin; therefore, concurrent use of an MAO-A inhibitor with a serotonergic agent may result in a clinically significant interaction. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent, in patients receiving SSRIs, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents with IV methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. One case describes a patient receiving citalopram who experienced agitation, restlessness, pupil dilation with sluggish response to light, myoclonic movements of the lower limbs, and brisk reflexes following an infusion of methylene blue, while another patient receiving paroxetine developed tachycardia, agitation, dystonia and abnormal eye movements. During a retrospective study of 193 surgical patients who had received a methylene blue injection, it was found that all 12 of the patients who experienced postoperative neurological sequelae had been taking a serotonin reuptake inhibitor preoperatively. One of the 12 patients experienced cardiopulmonary arrest and died. Of the remaining 181 patients who did not experience neurological sequelae, 8.8% were taking a serotonin reuptake inhibitor. Published interaction reports between IV methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and coma. Signs and symptoms of serotonin syndrome include fever, diaphoresis, shivering, myoclonus, tremor, tachycardia, diarrhea, nausea, headache, incoordination, mental status changes (e.g., agitation, confusion), hyperreflexia, seizures, and coma.

Methylene Blue: (Contraindicated) According to the manufacturer of sertraline, treatment initiation with sertraline is contraindicated in patients currently receiving intravenous (IV) methylene blue due to an increased risk of serotonin syndrome. If urgent psychiatric treatment is required, interventions other than sertraline (e.g., alternative medication, hospitalization) should be considered. Conversely, in patients receiving sertraline and requiring urgent treatment with IV methylene blue, sertraline should be discontinued immediately and methylene blue therapy initiated only if acceptable alternatives are not available and the potential benefits outweigh the risks. The patient should be monitored for serotonin syndrome for 2 weeks or until 24 hours after the last dose of methylene blue, whichever comes first. Sertraline may be re-initiated 24 hours after the last dose of methylene blue. Results from an in vitro study indicate that methylene blue is a potent, reversible inhibitor of the monoamine oxidase type A enzyme (MAO-A). MAO-A is responsible for the metabolism of serotonin; therefore, concurrent use of an MAO-A inhibitor with a serotonergic agent may result in a clinically significant interaction. Cases of serotonin syndrome have been reported, primarily following administration of standard infusions of methylene blue (1 to 8 mg/kg) as a visualizing agent, in patients receiving SSRIs, serotonin/norepinephrine reuptake inhibitors, or clomipramine. It is not known if patients receiving other serotonergic psychiatric agents with IV methylene blue are at a comparable risk or if methylene blue administered by other routes (e.g., orally, local injection) or in doses less than 1 mg/kg IV can produce a similar outcome. One case describes a patient receiving citalopram who experienced agitation, restlessness, pupil dilation with sluggish response to light, myoclonic movements of the lower limbs, and brisk reflexes following an infusion of methylene blue, while another patient receiving paroxetine developed tachycardia, agitation, dystonia and abnormal eye movements. During a retrospective study of 193 surgical patients who had received a methylene blue injection, it was found that all 12 of the patients who experienced postoperative neurological sequelae had been taking a serotonin reuptake inhibitor preoperatively. One of the 12 patients experienced cardiopulmonary arrest and died. Of the remaining 181 patients who did not experience neurological sequelae, 8.8% were taking a serotonin reuptake inhibitor. Published interaction reports between IV methylene blue and serotonergic psychiatric agents have documented symptoms including lethargy, confusion, delirium, agitation, aggression, obtundation, myoclonus, expressive aphasia, hypertonia, pyrexia, elevated blood pressure, seizures, and coma. Signs and symptoms of serotonin syndrome include fever, diaphoresis, shivering, myoclonus, tremor, tachycardia, diarrhea, nausea, headache, incoordination, mental status changes (e.g., agitation, confusion), hyperreflexia, seizures, and coma.
Methylphenidate Derivatives: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during

concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Methylphenidate: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Metoclopramide: (Moderate) Concomitant use of metoclopramide and selective serotonin reuptake inhibitors (SSRIs) such as sertraline may increase the risk for serotonin syndrome. Monitor patients for serotonin syndrome if concomitant use is necessary. In rare cases postmarketing, NMS-like symptoms, which may overlap with serotonin syndrome symptoms, have been reported with metoclopramide when used with serotonergic agents.
metOLazone: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Metoprolol; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
metroNIDAZOLE: (Moderate) Concomitant use of metronidazole and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP.
Mexiletine: (Moderate) Some SSRIs may interact with certain antiarrhythmics. Sertraline is a mild to moderate inhibitor of CYP2D6. Inhibition of CYP2D6 can result in increased concentrations of antiarrhythmic drugs metabolized via the same pathway, including encainide and mexiletine. Clinical data are not always available to document interactions. Increased plasma concentrations may increase the risk of proarrhythmia.
Midostaurin: (Major) Concomitant use of sertraline and midostaurin increases the risk of

QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
miFEPRIStone: (Major) Concomitant use of sertraline and mifepristone increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Milnacipran: (Major) Because of the potential risk and severity of serotonin syndrome, concurrent use of milnacipran with other drugs that have serotonergic properties, such as the selective serotonin reuptake inhibitors (SSRIs), should generally be avoided. 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. If serotonin syndrome is suspected, milnacipran and concurrent serotonergic agents should be discontinued.
Mirabegron: (Moderate) Mirabegron is a moderate CYP2D6 inhibitor. Exposure of drugs metabolized by CYP2D6 such as sertraline may be increased when co-administered with mirabegron. Sertraline has been shown to be a CYP2D6 substrate and a mild to moderate inhibitor of CYP2D6 in vitro. Mirabegron exposure may also increase. Appropriate monitoring and dose adjustment may be necessary.
Mirtazapine: (Moderate) Use sertraline with caution in combination with mirtazapine. Coadministration may increase the risk for QT prolongation, torsade de pointes (TdP), and serotonin syndrome. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical treatment should be implemented. Both drugs have been reported to cause QT prolongation. However, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease.
Mobocertinib: (Major) Concomitant use of mobocertinib and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinical significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.

Modafinil: (Moderate) Dose adjustments of sertraline, a substrate for CYP2C19, may be necessary when used concomitantly with modafinil. Elimination of sertraline may be prolonged by modafinil via inhibition of CYP2C19, with resultant higher systemic exposure. Monitor for adverse effects, such as serotonin excess, and reduce the sertraline dosage if needed.
Monoamine oxidase inhibitors: (Contraindicated) Due to the risk of serotonin syndrome, monoamine oxidase inhibitors (MAOIs) intended to treat psychiatric disorders are contraindicated for use with selective serotonin reuptake inhibitors (SSRIs). MAOIs should not be used within 5 weeks of discontinuing treatment with fluoxetine or within 14 days of discontinuing treatment with other SSRIs. Conversely, SSRIs should not be initiated within 14 days of stopping an MAOI. Monitor the patient for serotonin-related effects during therapy transitions.
Morphine: (Moderate) If concomitant use of morphine and sertraline 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.
Moxifloxacin: (Major) Concomitant use of sertraline and moxifloxacin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Nabumetone: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Nalbuphine: (Moderate) If concomitant use of nalbuphine and sertraline 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.
Naproxen: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association

between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Naproxen; Esomeprazole: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Naproxen; Pseudoephedrine: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Naratriptan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering naratriptan with selective serotonin reuptake inhibitors (SSRIs). Serotonin syndrome has been reported during concurrent use of serotonin-receptor agonists ("triptans") and SSRIs. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly after initiation of SSRI treatment or any dose increases. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Nefazodone: (Major) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering drugs that have serotonergic properties such as nefazodone and sertraline. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. At least one case report of serotonin syndrome from the concurrent use of nefazodone and a selective serotonin reuptake inhibitor (i.e., paroxetine) has been published. Additionally, when a 200 mg dose of nefazodone was administered to subjects who had been receiving fluoxetine for 1 week, there was an increased incidence of transient serotonin-related adverse events. If serotonin syndrome occurs, all serotonergic agents should be discontinued and appropriate medical treatment should be implemented.
Netupitant, Fosnetupitant; Palonosetron: (Major) Because of the potential risk and severity of serotonin syndrome, use caution when administering palonosetron with other drugs that have serotonergic properties such as sertraline. If serotonin syndrome is suspected, discontinue palonosetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.
Nilotinib: (Major) Concomitant use of sertraline and nilotinib increases the risk of

QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Nitroglycerin: (Minor) Nitroglycerin can cause hypotension. This action may be additive with other agents that can cause hypotension such as antidepressants. Patients should be monitored more closely for hypotension if nitroglycerin is used concurrently with antidepressants.
Nonsteroidal antiinflammatory drugs: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Nortriptyline: (Major) Because both sertraline and tricyclic antidepressants are associated with a possible risk of QT prolongation and torsade de pointes (TdP), the combination should be used cautiously and with close monitoring. In addition, because of the potential risk and severity of serotonin syndrome, caution should be observed when administering sertraline with other drugs that have serotonergic properties such as tricyclic antidepressants. 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. Clinicians should also be alert for pharmacokinetic interactions between tricyclic antidepressants and SSRIs. Sertraline is a weak to moderate inhibitor of CYP2D6, the isozyme responsible for metabolism of many of the tricyclic antidepressants. During a study evaluating the effects of concurrent use of sertraline and low-dose doxepin (6 mg) in healthy subjects, the doxepin mean AUC and Cmax estimates were about 21% and 32% higher, respectively, during concomitant sertraline administration than in those receiving doxepin alone. Measurements of psychomotor function showed more impairment in the combination group than the group receiving doxepin alone; however, subjective measures of alertness were similar between the two groups. Patients receiving a tricyclic antidepressant should be monitored closely for toxicity if an SSRI is added. The American Heart Association has published guidelines regarding cardiovascular monitoring of certain psychotropic drug combinations in children.
Ofloxacin: (Moderate) Concomitant use of ofloxacin and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking

steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
OLANZapine: (Moderate) Concomitant use of sertraline and olanzapine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
OLANZapine; FLUoxetine: (Major) Due to the similarity in pharmacology of fluoxetine and sertraline and the potential for serious adverse reactions, including serotonin syndrome, these selective serotonin reuptake inhibitors (SSRIs) should not be administered together. Also, both fluoxetine and sertraline have been associated with QT prolongation, which could theoretically result in additive effects on the QT interval. It is advisable to monitor for signs and symptoms of serotonin syndrome during an overlapping transition from one SSRI to another SSRI. (Moderate) Concomitant use of sertraline and olanzapine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
OLANZapine; Samidorphan: (Moderate) Concomitant use of sertraline and olanzapine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Oliceridine: (Moderate) If concomitant use of oliceridine and sertraline 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.

Olmesartan; amLODIPine; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Olmesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Ondansetron: (Major) Due to the potential for QT prolongation, cautious use and close monitoring are advisable if concurrent use of sertraline and ondansetron is necessary. Both medications may cause QT interval prolongation. The risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease. ECG monitoring has been recommended for at-risk patients. In addition, concurrent use of ondansetron with other drugs that modulate serotonergic function, such as SSRIs, has resulted in serotonin syndrome in some cases. Patients should be carefully observed, particularly during treatment initiation and during dose adjustments. Discontinue the serotonergic medications if serotonin syndrome is suspected.
Osilodrostat: (Moderate) Concomitant use of sertraline and osilodrostat may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Osimertinib: (Major) Concomitant use of sertraline and osimertinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Oxaliplatin: (Major) Concomitant use of sertraline and oxaliplatin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte

monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Oxaprozin: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
oxyCODONE: (Moderate) If concomitant use of oxycodone and sertraline 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.
oxyMORphone: (Moderate) If concomitant use of oxymorphone and sertraline 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.
Ozanimod: (Major) Concomitant use of ozanimod and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose. Ozanimod has a limited effect on the QT/QTc interval at therapeutic doses but may cause bradycardia and atrioventricular conduction delays which may increase the risk for TdP in patients with a prolonged QT/QTc interval.
Pacritinib: (Major) Concomitant use of pacritinib and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Paliperidone: (Major) Concomitant use of sertraline and paliperidone increases the risk

of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Palonosetron: (Major) Because of the potential risk and severity of serotonin syndrome, use caution when administering palonosetron with other drugs that have serotonergic properties such as sertraline. If serotonin syndrome is suspected, discontinue palonosetron and concurrent serotonergic agents and initiate appropriate medical treatment. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death.
Panobinostat: (Major) Concomitant use of sertraline and panobinostat increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
PARoxetine: (Moderate) Monitor patients for an increase in paroxetine-related adverse reactions and signs and symptoms of serotonin syndrome during concomitant use of paroxetine and sertraline, 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. Concomitant use may increase paroxetine exposure. Paroxetine is a CYP2D6 substrate and sertraline is a weak CYP2D6 inhibitor.
Pasireotide: (Moderate) Concomitant use of sertraline and pasireotide may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
PAZOPanib: (Major) Concomitant use of sertraline and pazopanib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to

minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Peginterferon Alfa-2b: (Moderate) Monitor for adverse effects associated with increased exposure to sertraline if peginterferon alfa-2b is coadministered. Peginterferon alfa-2b is a CYP2D6 inhibitor, while sertraline is partially metabolized by the CYP2D6 isoenzyme.
Pentamidine: (Major) Concomitant use of sertraline and pentamidine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Pentazocine; Naloxone: (Major) Because of the potential risk and severity of serotonin syndrome reactions, caution should be observed when administering selective serotonin reuptake inhibitors (SSRIs) with other drugs that have serotonergic properties such as pentazocine. 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 occurs, discontinue the offending agent(s) and institute appropriate therapy.
Pentosan: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and pentosan, which has weak anticoagulant properties. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding.
Perphenazine: (Minor) Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval, such as perphenazine; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). If use together is necessary, use caution and monitor patients for QT prolongation. In addition, CYP2D6 substrates such as perphenazine may require lower doses during concurrent use with sertraline, due to CYP2D6 inhibition by sertraline and the potential for arrhythmias or other adverse reactions associated with antipsychotics such as extrapyramidal symptoms.

Perphenazine; Amitriptyline: (Moderate) Monitor patients for signs and symptoms of serotonin syndrome during concomitant use of sertraline and amitriptyline, 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. (Minor) Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval, such as perphenazine; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). If use together is necessary, use caution and monitor patients for QT prolongation. In addition, CYP2D6 substrates such as perphenazine may require lower doses during concurrent use with sertraline, due to CYP2D6 inhibition by sertraline and the potential for arrhythmias or other adverse reactions associated with antipsychotics such as extrapyramidal symptoms.
Phenelzine: (Contraindicated) Due to the risk of serotonin syndrome, monoamine oxidase inhibitors (MAOIs) intended to treat psychiatric disorders are contraindicated for use with selective serotonin reuptake inhibitors (SSRIs). MAOIs should not be used within 5 weeks of discontinuing treatment with fluoxetine or within 14 days of discontinuing treatment with other SSRIs. Conversely, SSRIs should not be initiated within 14 days of stopping an MAOI. Monitor the patient for serotonin-related effects during therapy transitions.
Phentermine: (Moderate) Use phentermine and selective serotonin reuptake inhibitors (SSRIs) together with caution due to a potential for serotonin syndrome. Monitor weight, cardiovascular status, and for potential serotonergic adverse effects. Phentermine is related to the amphetamines, and there has been historical concern that phentermine might exhibit potential to cause serotonin syndrome when combined with serotonergic agents. However, recent data suggest that phentermine's effect on MAO inhibition and serotonin augmentation is minimal at therapeutic doses and some large controlled clinical studies have allowed patients to start phentermine-based therapy for obesity along with their SSRI as long as the antidepressant dose had been stable for at least 3 months prior. Such therapy was generally well-tolerated, especially at lower phentermine doses. Because depression and obesity often coexist, the study data may be important to providing optimal co-therapies.
Phentermine; Topiramate: (Moderate) Use phentermine and selective serotonin reuptake inhibitors (SSRIs) together with caution due to a potential for serotonin syndrome. Monitor weight, cardiovascular status, and for potential serotonergic adverse effects. Phentermine is related to the amphetamines, and there has been historical concern that phentermine might exhibit potential to cause serotonin syndrome when combined with serotonergic agents. However, recent data suggest that phentermine's

effect on MAO inhibition and serotonin augmentation is minimal at therapeutic doses and some large controlled clinical studies have allowed patients to start phentermine-based therapy for obesity along with their SSRI as long as the antidepressant dose had been stable for at least 3 months prior. Such therapy was generally well-tolerated, especially at lower phentermine doses. Because depression and obesity often coexist, the study data may be important to providing optimal co-therapies.
Phenytoin: (Moderate) Monitor phenytoin concentrations during concomitant sertraline use; a phenytoin dosage adjustment may be necessary. Sertraline may increase phenytoin concentrations.
Pimavanserin: (Major) Concomitant use of sertraline and pimavanserin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Pimozide: (Contraindicated) Pimozide is contraindicated for use with selective serotonin reuptake inhibitors (SSRIs) due to an increased risk of QT prolongation and torsade de pointes (TdP). Pimozide is thought to be primarily metabolized through CYP3A4, and to a lesser extent, CYP1A2 and CYP2D6. Elevated plasma concentrations of pimozide occurring through inhibition of one or more of these isoenzymes by SSRIs can lead to QT prolongation, ventricular arrhythmias, and sudden death. Additionally, most SSRIs are also associated with QT prolongation, further increasing the risk of additive QT prolongation.
Piroxicam: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Pitolisant: (Major) Concomitant use of sertraline and pitolisant increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Ponesimod: (Major) In general, do not initiate ponesimod in patients taking sertraline

due to the risk of additive bradycardia, QT prolongation, and torsade de pointes (TdP). If treatment initiation is considered, seek advice from a cardiologist. Ponesimod initiation may result in a transient decrease in heart rate and atrioventricular conduction delays. Ponesimod has not been studied in patients taking concurrent QT prolonging drugs; however, QT prolonging drugs have been associated with TdP in patients with bradycardia. The risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure.
Posaconazole: (Moderate) Concomitant use of sertraline and posaconazole may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Prasugrel: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis, such as prasugrel. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding.
Primaquine: (Moderate) Concomitant use of sertraline and primaquine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Procainamide: (Major) Concomitant use of sertraline and procainamide increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Procarbazine: (Major) Procarbazine is a weak monoamine oxidase inhibitor (MAOI). Although procarbazine appears to be less likely than other MAOIs to produce serious drug interactions, clinicians should avoid the use of selective serotonin reuptake

inhibitors (SSRIs) in patients receiving MAOIs. Fatalities have been reported when fluoxetine was administered to patients receiving MAOIs. Confusion, seizures, severe hypertension, and other, less severe symptoms have also been reported with this drug combination. Non-selective MAOIs inhibit both MAO types A and B. Since serotonin is metabolized by MAO type A, it is thought that this drug interaction may lead to serotonin syndrome or neuroleptic malignant syndrome-like reactions. 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. At least 2 weeks should elapse between the discontinuation of MAOI therapy and the start of therapy with an SSRI except fluoxetine. At least 5 weeks should elapse between the discontinuation of fluoxetine therapy and commencement of MAOI therapy. This 5-week period is needed because of the long half-lives of fluoxetine and its principle metabolite norfluoxetine.
Prochlorperazine: (Minor) Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval, such as prochlorperazine; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). If use together is necessary, use caution and monitor patients for QT prolongation.
Promethazine: (Moderate) Concomitant use of promethazine and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Promethazine; Dextromethorphan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with 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 adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome. (Moderate) Concomitant use of promethazine and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval

prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Promethazine; Phenylephrine: (Moderate) Concomitant use of promethazine and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Propafenone: (Major) Use caution and monitor patients for QT prolongation when administering Class IC Antiarrhythmics with sertraline. Class IC antiarrhythmics increase the QT interval, but largely due to prolongation of the QRS interval. QTc prolongation and torsade de pointes (TdP) have been reported during postmarketing use of sertraline; most cases had confounding risk factors. The risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). In addition, sertraline is a mild to moderate inhibitor of CYP2D6, and inhibition of CYP2D6 can result in increased concentrations of antiarrhythmic drugs metabolized via the same pathway, including flecainide and propafenone.
Protriptyline: (Major) There have been postmarketing reports of QT prolongation and torsade de pointes (TdP) during treatment with sertraline and the manufacturer of sertraline recommends avoiding concurrent use with drugs known to prolong the QTc interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). In addition, serotonin syndrome is possible when coadministering drugs that have serotonergic properties such as sertraline and TCAs. 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. Lastly, sertraline is a CYP2D6 inhibitor, one of the isoenzymes responsible for the metabolism of TCAs. During a study evaluating the effects of concurrent use of sertraline and low-dose doxepin (6 mg) in healthy subjects, the doxepin mean AUC and Cmax estimates were about 21% and 32% higher, respectively, during concomitant sertraline administration than in those receiving doxepin alone. Measurements of psychomotor function showed more impairment in the combination group than the group receiving

doxepin alone; however, subjective measures of alertness were similar between the two groups. Patients receiving a tricyclic antidepressant should be monitored closely for toxicity if sertraline is added. The American Heart Association has published guidelines regarding cardiovascular monitoring of certain psychotropic drug combinations in children.
QUEtiapine: (Major) Avoid coadministration of quetiapine with sertraline due to the potential for additive QT prolongation. Limited data, including some case reports, suggest that quetiapine may be associated with a significant prolongation of the QTc interval in rare instances. QTc prolongation and torsade de pointes (TdP) have been reported during postmarketing use of sertraline; most cases had confounding risk factors. The risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure).
Quinapril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
quiNIDine: (Major) Concomitant use of sertraline and quinidine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
quiNINE: (Major) Concomitant use of sertraline and quinine increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Quizartinib: (Major) Concomitant use of quizartinib and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when

administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Ranolazine: (Moderate) Concomitant use of sertraline and ranolazine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Rasagiline: (Major) It is recommended to avoid concurrent use of rasagiline and selective serotonin reuptake inhibitors (SSRIs). Severe CNS toxicity with hyperpyrexia has been reported during concurrent use of antidepressants and selective or non-selective MAOIs. During postmarketing use of rasagiline, non-fatal cases of serotonin syndrome have been reported during concomitant antidepressant administration. At least 2 weeks should elapse between stopping rasagiline treatment and beginning therapy with any SSRI. Conversely, when discontinuing an SSRI, it is advisable to wait the length of 4 to 5 half-lives of the individual agent being discontinued prior to initiation with rasagiline. At least 5 weeks should elapse between the discontinuation of fluoxetine therapy and initiation of rasagiline. If coadministration of rasagiline and fluvoxamine is required, do not exceed a rasagiline dose of 0.5 mg once daily. Rasagiline is primarily metabolized by CYP1A2; fluvoxamine is a strong CYP1A2 inhibitor. When rasagiline was administered with another strong CYP1A2 inhibitor, the AUC of rasagiline increased by 83%.
Relugolix: (Moderate) Concomitant use of sertraline and androgen deprivation therapy (i.e., relugolix) may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Relugolix; Estradiol; Norethindrone acetate: (Moderate) Concomitant use of sertraline and androgen deprivation therapy (i.e., relugolix) may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Remifentanil: (Moderate) If concomitant use of remifentanil and selective serotonin

reuptake inhibitors (SSRIs) 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.
Reteplase, r-PA: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis, such as thrombolytic agents. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding.
Revumenib: (Major) Concomitant use of revumenib and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Ribociclib: (Major) Concomitant use of sertraline and ribociclib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Ribociclib; Letrozole: (Major) Concomitant use of sertraline and ribociclib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
rifAMPin: (Minor) Concurrent use of rifampin and sertraline can decrease sertraline exposure which may result in decreased sertraline efficacy and symptoms suggestive of antidepressant discontinuation syndrome in some patients. Sertraline is a substrate of CYP2B6, CYP2C9, CYP2C19, and CYP3A; rifampin is an inducer of CYP2B6, a moderate inducer of CYP2C9, and a strong inducer of both CYP2C19 and CYP3A. Data regarding the clinical relevance of this interaction are limited to postmarketing case reports and case series, but the possibility of an interaction cannot be dismissed.

Rilpivirine: (Moderate) Concomitant use of sertraline and rilpivirine may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with rilpivirine is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
risperiDONE: (Moderate) Concomitant use of sertraline and risperidone may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Rivaroxaban: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and anticoagulants like rivaroxaban. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding.
Rizatriptan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering rizatriptan with selective serotonin reuptake inhibitors (SSRIs). Serotonin syndrome has been reported during concurrent use of serotonin-receptor agonists ("triptans") and SSRIs. Some patients had used the combination previously without incident when serotonin syndrome occurred. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly after the initiation of the SSRI or dose increases. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Rolapitant: (Major) Use caution if sertraline and rolapitant are used concurrently, and monitor for sertraline-related adverse effects. Sertraline is a CYP2D6 substrate and rolapitant is a moderate CYP2D6 inhibitor; the inhibitory effect of rolapitant is expected to persist beyond 28 days for an unknown duration. Exposure to another CYP2D6 substrate, following a single dose of rolapitant increased about 3-fold on Days 8 and Day 22. The inhibition of CYP2D6 persisted on Day 28 with a 2.3-fold increase in the CYP2D6 substrate concentrations, the last time point measured.
romiDEPsin: (Moderate) Concomitant use of sertraline and romidepsin may increase the

risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Safinamide: (Major) The concurrent use of selective serotonin reuptake inhibitors (SSRIs) and monoamine oxidase inhibitors (MAOIs) is generally avoided; however, the manufacturer of safinamide recommends monitoring for serotonin syndrome and using the lowest effective dose of the SSRI during concurrent use. During clinical trial evaluation of safinamide, 1 case of serotonin syndrome occurred during co-administration with an SSRI. 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.
Salsalate: (Moderate) The combined use of selective serotonin reuptake inhibitors (SSRIs) and aspirin, or other salicylates which affect, hemostasis may elevate the risk for an upper GI bleed. SSRIs may inhibit serotonin uptake by platelets, augmenting the antiplatelet effects of aspirin. Additionally, aspirin impairs the gastric mucosa defenses by inhibiting prostaglandin formation. A cohort study in over 26,000 patients found that SSRI use alone increased the risk for serious GI bleed by 3.6-fold; when an SSRI was combined with aspirin the risk was increased by over 5-fold. The absolute risk of GI bleed from concomitant therapy with aspirin and a SSRI was low (20/2640 patients) in this cohort study and the clinician may determine that the combined use of these drugs is appropriate.
Saquinavir: (Major) Concomitant use of sertraline and saquinavir increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Selegiline: (Contraindicated) Selective serotonin reuptake inhibitors (SSRIs) are contraindicated for use with selegiline, a selective monoamine oxidase type B inhibitor (MAO-B inhibitor). At least 14 days should elapse between discontinuation of selegiline and initiation of treatment with an SSRI. With the exception of fluoxetine, a time period equal to 4 to 5 half-lives of the SSRI or any active metabolite should elapse after discontinuing treatment with the SSRI and before starting therapy with selegiline. Because of the long half-life of fluoxetine and its active metabolite, at least 5 weeks

should elapse between discontinuation of fluoxetine and initiation of treatment with selegiline. Serotonin syndrome has occurred in patients receiving selective MAO-B inhibitors and serotonin-augmenting antidepressants simultaneously. Monitor for serotonergic side effects during therapy transitions.
Selpercatinib: (Major) Concomitant use of sertraline and selpercatinib increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Serdexmethylphenidate; Dexmethylphenidate: (Moderate) Caution should be observed when coadministering methylphenidate derivatives and the selective serotonin reuptake inhibitors (SSRIs). There are postmarketing reports of serotonin syndrome during concurrent use of methylphenidate derivatives with other serotonergic medications. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of some SSRIs and downward dose adjustment of the SSRI may be required in some patients. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome. If serotonin syndrome occurs, serotonergic agents should be discontinued and appropriate medical management should be implemented.
Sevoflurane: (Major) Concomitant use of sertraline and halogenated anesthetics increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Siponimod: (Major) Concomitant use of siponimod and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Solifenacin: (Moderate) Concomitant use of sertraline and solifenacin may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as

avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
SORAfenib: (Major) Concomitant use of sorafenib and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Sotalol: (Major) Concomitant use of sertraline and sotalol increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.
Spironolactone: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Spironolactone; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
St. John's Wort, Hypericum perforatum: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when coadministering sertraline and St. John's Wort. 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.
Stiripentol: (Moderate) Consider a dose adjustment of sertraline when coadministered with stiripentol. Coadministration may alter plasma concentrations of sertraline resulting in an increased risk of adverse reactions and/or decreased efficacy. Sertraline is a CYP2B6 substrate. In vitro data predicts inhibition or induction of CYP2B6 by stiripentol potentially resulting in clinically significant interactions.
SUFentanil: (Moderate) If concomitant use of sufentanil and sertraline 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.
Sulindac: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
SUMAtriptan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering sumatriptan with selective serotonin reuptake inhibitors (SSRIs). Serotonin syndrome has been reported during concurrent use of serotonin-receptor agonists ("triptans") and SSRIs. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly after initiation of SSRI treatment or any dose increases. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
SUMAtriptan; Naproxen: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering sumatriptan with selective serotonin reuptake inhibitors (SSRIs). Serotonin syndrome has been reported during concurrent use of serotonin-receptor agonists ("triptans") and SSRIs. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly after initiation of SSRI treatment or any dose increases. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
SUNItinib: (Moderate) Concomitant use of sertraline and sunitinib may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Tacrolimus: (Moderate) Concomitant use of sertraline and tacrolimus may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in

patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Taletrectinib: (Major) Concomitant use of taletrectinib and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Tamoxifen: (Moderate) Concomitant use of tamoxifen and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Tapentadol: (Moderate) If concomitant use of tapentadol and selective serotonin reuptake inhibitors (SSRIs) 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.
Telavancin: (Moderate) Concomitant use of sertraline and telavancin may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Telmisartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Tenecteplase: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis,

such as thrombolytic agents. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding.
Tetrabenazine: (Major) Concomitant use of tetrabenazine and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Tezacaftor; Ivacaftor: (Minor) Increased monitoring is recommended if ivacaftor is administered concurrently with CYP2C9 substrates, such as sertraline. Ivacaftor is an inhibitor of CYP3A and a weak inhibitor of CYP2C9; sertraline is metabolized by CYP3A and CYP2C9. Co-administration of ivacaftor with CYP3A and CYP2C9 substrates, such as sertraline, can theoretically increase sertraline exposure leading to increased or prolonged therapeutic effects and adverse events; however, the clinical impact of this has not yet been determined.
Thioridazine: (Contraindicated) Coadministration of thioridazine and sertraline is contraindicated due to the potential for QT prolongation and torsade de pointes (TdP). Thioridazine is associated with a well-established risk of QT prolongation and TdP and is considered contraindicated for use along with agents associated with QT interval and TdP. QT prolongation and TdP have been reported during postmarketing use of sertraline. Additionally, thioridazine is a CYP2D6 substrate and use with a CYP2D6 inhibitor such as sertraline may increase the risk of thioridazine-induced arrhythmias.
Thrombin Inhibitors: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of selective serotonin reuptake inhibitors (SSRIs) and other drugs that affect coagulation like thrombin inhibitors. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding.
Thrombolytic Agents: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis, such as thrombolytic agents. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding.
Ticagrelor: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis, such as ticagrelor. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding.
Tipranavir: (Moderate) Use caution when coadministering sertraline with a combination of tipranavir plus ritonavir because increased sertraline concentrations may occur. Tipranavir and ritonavir are potent CYP3A4 inhibitors and sertraline is a substrate of

CYP3A4. Patients should be monitored for sertraline-induced adverse effects, including nausea, vomiting, diarrhea, and QT prolongation.
Tirofiban: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis, such as tirofiban. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding.
Tolmetin: (Moderate) Monitor for signs and symptoms of bleeding during concomitant selective serotonin reuptake inhibitor (SSRI) and nonsteroidal antiinflammatory drug (NSAID) use due to increased risk for bleeding. Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.
Tolterodine: (Moderate) Use caution and monitor patients for QT prolongation when administering tolterodine with sertraline. Tolterodine has been associated with dose-dependent prolongation of the QT interval, especially in poor CYP2D6 metabolizers. Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure).
Toremifene: (Major) Concomitant use of toremifene and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Torsemide: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
traMADol: (Moderate) Monitor for reduced efficacy of tramadol, signs of opioid withdrawal, seizures, or serotonin syndrome if coadministration with sertraline is necessary. If sertraline is discontinued, consider a dose reduction of tramadol and frequently monitor for signs of respiratory depression and sedation. Tramadol is a CYP2D6 substrate and sertraline is a CYP2D6 inhibitor. Concomitant use of tramadol with CYP2D6 inhibitors can increase the plasma concentration of tramadol and decrease the plasma concentration of the active metabolite M1. Since M1 is a more potent mu-

opioid agonist, decreased M1 exposure could result in decreased therapeutic effects, and may result in signs and symptoms of opioid withdrawal in patients who have developed physical dependence to tramadol. Increased tramadol exposure can result in increased or prolonged therapeutic effects and increased risk for serious adverse events including seizures and serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Tramadol; Acetaminophen: (Moderate) Monitor for reduced efficacy of tramadol, signs of opioid withdrawal, seizures, or serotonin syndrome if coadministration with sertraline is necessary. If sertraline is discontinued, consider a dose reduction of tramadol and frequently monitor for signs of respiratory depression and sedation. Tramadol is a CYP2D6 substrate and sertraline is a CYP2D6 inhibitor. Concomitant use of tramadol with CYP2D6 inhibitors can increase the plasma concentration of tramadol and decrease the plasma concentration of the active metabolite M1. Since M1 is a more potent mu-opioid agonist, decreased M1 exposure could result in decreased therapeutic effects, and may result in signs and symptoms of opioid withdrawal in patients who have developed physical dependence to tramadol. Increased tramadol exposure can result in increased or prolonged therapeutic effects and increased risk for serious adverse events including seizures and serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Tranylcypromine: (Contraindicated) Due to the risk of serotonin syndrome, monoamine oxidase inhibitors (MAOIs) intended to treat psychiatric disorders are contraindicated for use with selective serotonin reuptake inhibitors (SSRIs). MAOIs should not be used within 5 weeks of discontinuing treatment with fluoxetine or within 14 days of discontinuing treatment with other SSRIs. Conversely, SSRIs should not be initiated within 14 days of stopping an MAOI. Monitor the patient for serotonin-related effects during therapy transitions.
traZODone: (Major) Trazodone and sertraline may both cause QT prolongation. Concurrent use may also increase the risk of serotonin syndrome. Serotonin syndrome has been reported with both drugs when taken alone, but especially when coadministered with other serotonergic agents. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate appropriate treatment if serotonin syndrome occurs.
Triamterene: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Triamterene; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical

intervention. Concomitant use increases the risk for developing hyponatremia.
Triclabendazole: (Moderate) Concomitant use of triclabendazole and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Trifluoperazine: (Minor) Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval, such as trifluoperazine; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). If use together is necessary, use caution and monitor patients for QT prolongation. In addition, CYP2D6 substrates such as trifluoperazine may require lower doses during concurrent use with sertraline, due to CYP2D6 inhibition by sertraline and the potential for arrhythmias or other adverse reactions associated with antipsychotics such as extrapyramidal symptoms.
Trimipramine: (Major) There have been postmarketing reports of QT prolongation and torsade de pointes (TdP) during treatment with sertraline and the manufacturer of sertraline recommends avoiding concurrent use with drugs known to prolong the QTc interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). In addition, serotonin syndrome is possible when coadministering drugs that have serotonergic properties such as sertraline and TCAs. 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. Lastly, sertraline is a CYP2D6 inhibitor, one of the isoenzymes responsible for the metabolism of TCAs. During a study evaluating the effects of concurrent use of sertraline and low-dose doxepin (6 mg) in healthy subjects, the doxepin mean AUC and Cmax estimates were about 21% and 32% higher, respectively, during concomitant sertraline administration than in those receiving doxepin alone. Measurements of psychomotor function showed more impairment in the combination group than the group receiving doxepin alone; however, subjective measures of alertness were similar between the two groups. Patients receiving a tricyclic antidepressant should be monitored closely for toxicity if sertraline is added. The American Heart Association has published guidelines regarding cardiovascular monitoring of certain psychotropic drug combinations in

children.
Triptorelin: (Moderate) Concomitant use of sertraline and androgen deprivation therapy (i.e., triptorelin) may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Tryptophan, 5-Hydroxytryptophan: (Major) Concurrent use of tryptophan and a selective serotonin reuptake inhibitor (SSRI) is not recommended. Since tryptophan is converted to serotonin, the use of tryptophan in patients receiving SSRIs could lead to serotonin excess and, potentially, serotonin syndrome. Discontinuation of tryptophan usually resolves symptoms.
Valerian, Valeriana officinalis: (Moderate) Substances that act on the CNS, including psychoactive drugs, may theoretically interact with valerian, Valeriana officinalis. These interactions are probably pharmacodynamic in nature, or result from additive mechanisms of action. Persons taking medications such as SSRIs should discuss the use of herbal supplements with their health care professional prior to consuming these herbs. Patients should not abruptly stop taking their prescribed psychoactive medication.
Valsartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor for signs and symptoms of hyponatremia during concomitant diuretic and sertraline use; consider discontinuing sertraline if symptomatic hyponatremia occurs and institute appropriate medical intervention. Concomitant use increases the risk for developing hyponatremia.
Vandetanib: (Major) Concomitant use of vandetanib and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Vardenafil: (Moderate) Concomitant use of vardenafil and sertraline may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum

recommended dose.
Vasopressin, ADH: (Moderate) Monitor hemodynamics and adjust the dose of vasopressin as needed when used concomitantly with drugs suspected of causing syndrome of inappropriate antidiuretic hormone (SIADH), such as selective serotonin reuptake inhibitors. Use together may increase the pressor and antidiuretic effects of vasopressin.
Vemurafenib: (Major) Concomitant use of vemurafenib and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Venlafaxine: (Major) Due to similarity of pharmacology and the potential for additive adverse effects, including serotonin syndrome, selective serotonin reuptake inhibitors (SSRIs) should generally not be administered with serotonin norepinephrine reuptake inhibitors like venlafaxine. If serotonin syndrome is suspected, venlafaxine and concurrent serotonergic agents should be discontinued. Also, both sertraline and venlafaxine have been associated with QT prolongation, which could theoretically result in additive effects on the QT interval.
Vilazodone: (Major) Due to possible additive effects on serotonin concentrations, it is advisable to avoid combining selective serotonin reuptake inhibitors (SSRIs) with vilazodone. Interactions between vilazodone and serotonergic agents can lead to serotonin syndrome. Serotonin syndrome is characterized by the rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. Patients receiving vilazodone and sertraline should be monitored for the emergence of serotonin syndrome, particularly during treatment initiation and during dosage increases. Vilazodone and sertraline should be discontinued if serotonin syndrome occurs and supportive symptomatic treatment should be initiated.
Voclosporin: (Moderate) Concomitant use of sertraline and voclosporin may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with voclosporin is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 3 times the maximum recommended dose. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT

prolongation has been described at 2 times the maximum recommended dose.
Vonoprazan; Amoxicillin; Clarithromycin: (Major) Concomitant use of sertraline and clarithromycin increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Vorapaxar: (Moderate) Monitor for bleeding during concomitant use of selective serotonin reuptake inhibitors (SSRIs) and medications that interfere with hemostasis, such as vorapaxar. SSRIs affect platelet activation and may interfere with clot formation increasing the risk for bleeding.
Voriconazole: (Moderate) Concomitant use of sertraline and voriconazole may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Vorinostat: (Moderate) Concomitant use of sertraline and vorinostat may increase the risk of QT/QTc prolongation and torsade de pointes (TdP) in some patients. Consider taking steps to minimize the risk of QT/QTc interval prolongation and TdP, such as avoidance, electrolyte monitoring and repletion, and ECG monitoring, especially in patients with additional risk factors for TdP. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Vortioxetine: (Major) Due to similarity of pharmacology and the potential for additive adverse effects, including serotonin syndrome, vortioxetine should generally not be co-administered with selective serotonin reuptake inhibitors (SSRIs). 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.
Warfarin: (Moderate) Advise patients of the increased bleeding risk associated with the concomitant use of sertraline and warfarin. Carefully monitor the INR. Case reports and epidemiological studies have demonstrated an association between use of drugs that interfere with serotonin reuptake and gastrointestinal bleeding. Additionally, monitor for

sertraline-related adverse effects. Reduce the sertraline or warfarin dose as necessary. Sertraline is highly bound to plasma protein and concomitant use with another drug that is highly bound to plasma protein, like warfarin, may increase free plasma concentrations of sertraline or the other tightly bound drug.
Ziftomenib: (Major) Concomitant use of ziftomenib and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
Ziprasidone: (Major) Concomitant use of ziprasidone and sertraline increases the risk of QT/QTc prolongation and torsade de pointes (TdP). Avoid concomitant use if possible, especially in patients with additional risk factors for TdP. Consider taking steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary. The degree of QT prolongation associated with sertraline is not clinically significant when administered within the recommended dosage range; QT prolongation has been described at 2 times the maximum recommended dose.
ZOLMitriptan: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering zolmitriptan with selective serotonin reuptake inhibitors (SSRIs). Serotonin syndrome has been reported during concurrent use of serotonin-receptor agonists ("triptans") and SSRIs. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly after initiation of SSRI treatment or any dose increases. Discontinue serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Zolpidem: (Moderate) Disorientation, delusions, or hallucinations have been reported rarely during co-administration of zolpidem and SSRIs including sertraline. The duration of the visual hallucinations ranged from 30 minutes to 7 hours. Data from a clinical study in which SSRI-treated patients were given immediate-release zolpidem revealed that four of the seven discontinuations during double-blind treatment with zolpidem (n = 95) were associated with impaired concentration, continuing or aggravated depression, and manic reaction. The mechanism for the interaction is thought to be pharmacodynamic in nature. In one study with sertraline, inhibition of zolpidem metabolism occurred when sertraline was chronically coadministered; zolpidem Cmax was significantly higher (43%) and Tmax was significantly decreased (53%).

Adverse Reaction

General Information

The overall adverse reaction profile of sertraline during pediatric clinical trials (n = 281) was generally similar to those seen in adult studies, and side effects occurred at similar incidence rates except where noted.

appetite stimulation, constipation, diarrhea, dyspepsia, melena, nausea, vomiting, xerostomia

Gastrointestinal (GI) effects are among the most common adverse events of sertraline and are the most common side effects associated with discontinuation of sertraline. Combined clinical trial data indicate that the most frequently reported gastrointestinal (GI) effects in adult patients receiving sertraline compared to rates reported with placebo include decreased appetite (7%), constipation (6%), diarrhea/loose stools (20%), dyspepsia (8%), nausea (26%), vomiting (4%), and xerostomia (14%). Other adverse GI effects observed during premarketing evaluation and occurring in less than 2% of patients treated with sertraline included hematochezia, melena, rectal hemorrhage, and appetite stimulation. Common reasons for drug discontinuation during clinical trials included diarrhea (2%), nausea (3%), vomiting (greater than 2%), and decreased appetite (more than 2%).

akathisia, ataxia, coma, dizziness, drowsiness, dystonic reaction, headache, hyperactivity, hyperkinesis, hypoesthesia, insomnia, lethargy, syncope, tremor

Autonomic, central, and peripheral nervous system side effects are fairly common with sertraline. Combined clinical trial data indicate that the most frequently reported autonomic, central, or peripheral effects in adult patients receiving sertraline compared to placebo rates included drowsiness (somnolence 11%), dizziness (12%), tremor (9%), and insomnia (20%). CNS effects leading to discontinuation in more than 2% of patients and at twice the rate of placebo included dizziness, headache, somnolence, and tremor; insomnia led to discontinuation in 2% of patients. Adverse reactions reported in at least 2% of pediatric patients and at a rate of at least twice the placebo rate include hyperkinesis. Other centrally-mediated effects reported during premarketing evaluation and occurring in less than 2% of patients receiving sertraline included ataxia, coma, decreased alertness, hypoesthesia, syncope, lethargy, and psychomotor hyperactivity. During postmarketing use, extrapyramidal symptoms (i.e., akathisia, dystonic reaction including oculogyric crisis) have been reported.

abnormal dreams, agitation, anxiety, confusion, depression, euphoria, hallucinations, irritability, mania, nightmares, psychosis, suicidal ideation, teeth grinding (bruxism)

Combined clinical trial data indicate that the most frequently reported psychiatric effect in adult patients receiving sertraline was agitation (8%). Psychiatric effects occurring in less than 2% of patients receiving sertraline during premarketing evaluation included aggression, teeth grinding (bruxism), confusion (confusional state), irritability, euphoria, and hallucinations. Psychiatric effects including agitation (2%), anxiety, and nervousness were among the most common events associated with discontinuation of sertraline. Adverse reactions reported in at least 2% of pediatric patients and at least twice the rate of placebo included aggression and anxiety. Antidepressants can precipitate mania in susceptible individuals. In a study of 52 pediatric and young adult patients (mean age: 15 years; range: 7 to 22 years) with bipolar disorder or subthreshold mania symptoms, 25.5% had new-onset suicidal ideation within the first 3 months of antidepressant use. Psychosis and paroniria (abnormal dreams and nightmares) have been reported during postmarketing use. Suicidal ideation appears to be more prevalent in pediatric patients with or at high risk for bipolar disorder on antidepressants. Monitor all antidepressant-treated patients for any indication for worsening of depression or the condition being treated and the emergence of suicidal behaviors or suicidal ideation, especially during the initial few months of drug therapy and after dosage changes. In a pooled analysis of placebo-controlled trials of antidepressants (n = 4,500 pediatrics and 77,000 adults), there was an increased risk for suicidal thoughts and behaviors in patients 24 years of age and younger receiving an antidepressant versus placebo, with considerable variation in the risk of suicidality among drugs. The difference in the absolute risk of suicidal thoughts and behaviors across different indications was highest in those with major depression. No suicides occurred in any of the pediatric trials. These studies did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in patients over 24 years of age; there was a reduction in risk with antidepressant use in older adult patients aged 65 years and older. Caregivers and/or patients should immediately notify the prescriber of changes in behavior or suicidal ideation.

seizures

Seizures were reported in less than 2% of patients during premarketing evaluation of sertraline. During a study of sertraline for obsessive-compulsive disorder, seizures occurred in roughly 0.2% (4/1,800) of patients; 3 of these patients were adolescents with a personal or family history of seizure disorder, none of whom were receiving anticonvulsant therapy. No seizures were reported among 3,000 patients during premarketing evaluation for major depressive disorder. Sertraline should be introduced cautiously in patients with a seizure disorder and promptly discontinued if seizures develop. Cerebrovascular spasm, including reversible cerebral vasoconstriction syndrome and Call-Fleming syndrome, have been reported during postmarketing use of sertraline; however, causality has not been established.

hyponatremia, SIADH

Selective serotonin reuptake inhibitors (SSRIs), such as sertraline, may cause hyponatremia, which is frequently the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). In some cases, serum sodium levels less than 110 mmol/L have been reported; however, the adverse effect appeared reversible upon discontinuation of the causative SSRI. Elderly patients, those receiving diuretics or prone to dehydration, and those who are otherwise volume depleted (e.g., hypovolemia) appear to be at greatest risk. Hyponatremia may manifest as headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness which may result in falls. Severe manifestations include hallucinations, fainting, seizure, coma, respiratory arrest, and death. Symptomatic hyponatremia may require discontinuation of the SSRI, as well as implementation of the appropriate medical interventions.

AV block, bradycardia, hypercholesterolemia, hypertension, palpitations, peripheral vasodilation, QT prolongation, sinus tachycardia, torsade de pointes, vasculitis, ventricular tachycardia

Combined clinical trial data indicate that palpitations (4%) were the most frequently reported cardiovascular effect in adult patients receiving sertraline and occurred at a rate twice that of placebo. Sinus tachycardia, vascular hemorrhage, hypertension, peripheral vasodilation, and hypercholesterolemia occurred in less than 2% of patients receiving sertraline during premarketing evaluation. During postmarketing use of the drug, the following cardiovascular or related effects have been reported, although the frequencies are unknown and causality to the drug has not been established: bradycardia, AV block, atrial arrhythmias, QT prolongation, ventricular tachycardia, torsade de pointes (TdP), and vasculitis. Most reports of QT prolongation and TdP have been confounded by other risk factors. In one placebo- and positive-controlled QTc study in 54 adult subjects, the largest mean change in QTc was 10 milliseconds at 2-fold the maximum recommended daily dose of sertraline (about 3-fold the steady-state exposure for sertraline and N-desmethylsertraline). There was a positive relationship between the length of the rate-adjusted QTc interval and serum sertraline concentrations.

agranulocytosis, aplastic anemia, bleeding, ecchymosis, epistaxis, GI bleeding, hematoma, leukopenia, lupus-like symptoms, pancytopenia, petechiae, platelet dysfunction, purpura, serum sickness, thrombocytopenia

Platelet dysfunction (i.e., impaired platelet aggregation) may occur during treatment with selective serotonin reuptake inhibitors (SSRIs) due to platelet serotonin depletion,

possibly increasing the risk of a bleeding complication (e.g., GI bleeding, ecchymosis, epistaxis, hematoma, petechiae, hemorrhage). An increased risk of bleeding complications is possible in patients receiving antiplatelet or anticoagulant medications concurrently with sertraline. Epistaxis and purpura were reported in less than 2% of adult patients receiving sertraline during premarketing evaluation. Epistaxis and purpura were reported in at least 2% of pediatric patients and at a rate of at least twice the placebo rate. Hematologic and lymphatic effects reported during postmarketing use include increased coagulation times (altered platelet function), agranulocytosis, aplastic anemia, pancytopenia, leukopenia, thrombocytopenia, lupus-like symptoms, and serum sickness.

alopecia, anaphylactoid reactions, angioedema, bullous rash, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), hyperhidrosis, maculopapular rash, photosensitivity, pruritus, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria

Combined clinical trial data indicate that hyperhidrosis (increased sweating) occurred in 7% of adult patients receiving sertraline and with an incidence twice that in placebo-treated patients. Adverse dermatologic or hypersensitivity reactions observed during premarketing evaluation of sertraline and occurring in less than 2% of patients included alopecia, cold sweat, dermatitis (unspecified), bullous rash, pruritus, urticaria, anaphylaxis (anaphylactoid reactions), and erythematous, follicular, or maculopapular rash. During postmarketing use of the drug, the following effects have been reported, although the frequencies are unknown and causality to the drug has not been established: photosensitivity and other severe cutaneous disorders, and potentially fatal reactions including angioedema, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN). Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported during postmarketing use of sertraline according to the Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS). Manifestations of DRESS typically include pyrexia, rash, facial swelling, and/or lymph node involvement in conjunction with other organ system abnormalities including hepatitis, nephritis, hematologic abnormalities, myocarditis, or myositis. Eosinophilia is often present. Early manifestations of DRESS such as pyrexia and lymph node involvement may be present without evidence of a rash. Sertraline should be promptly discontinued and appropriate medical treatment should be initiated in patients presenting with a rash or symptoms indicative of DRESS in whom an unrelated etiology cannot be identified.

arthralgia, muscle cramps, rhabdomyolysis, trismus

Musculoskeletal and connective tissue effects reported during premarketing evaluation of sertraline and occurring in less than 2% of adult patients included arthralgia and

muscle spasms (muscle cramps), tightness, or twitching. Muscle spasms/twitching were reported in at least 2% of pediatric patients receiving sertraline at a rate of at least twice the placebo rate. Trismus and rhabdomyolysis have been reported during postmarketing use.

blurred vision, cataracts, mydriasis, ocular hypertension, optic neuritis, tinnitus, visual impairment

Combined clinical trial data indicate that the most frequently reported ophthalmic effect in adult patients receiving sertraline was visual impairment (4%); this effect occurred at a rate twice that of placebo. Rare effects (less than 0.1%) include ocular hypertension (glaucoma or increased intraocular pressure). Ophthalmic or otic effects occurring in less than 2% of patients receiving sertraline during premarketing evaluation included mydriasis, blurred vision, and tinnitus. During postmarketing use, blindness, optic neuritis, and cataracts have been reported; however, the frequencies are unknown and causality to the drug has not been established.

elevated hepatic enzymes, hepatic failure, hepatitis, jaundice, pancreatitis

Elevated hepatic enzymes were reported in less than 2% of patients receiving sertraline during premarketing evaluation. Pancreatitis, hepatitis, jaundice, and hepatic failure with some fatal outcomes have been reported during postmarketing use; although the frequencies are unknown and causality to the drug has not been established.

anosmia, bronchospasm, eosinophilic pneumonia, pulmonary hypertension, yawning

Adverse respiratory and related effects reported during premarketing evaluation of sertraline and occurring in less than 2% of patients included bronchospasm and yawning. Pulmonary hypertension, eosinophilic pneumonia, anosmia, and hyposmia have been reported during postmarketing use.

edema, fatigue, fever, malaise

Combined clinical trial data indicate that fatigue (12%) was reported more frequently in adult patients receiving sertraline than with placebo. Fatigue led to discontinuation in more than 2% of patients receiving sertraline and at twice the rate of placebo-treated patients. General disorders that were reported in less than 2% of patients receiving sertraline during premarketing evaluation included edema, gait disturbance, and fever. Fever occurred in at least 2% of pediatric patients and at a rate twice that of the placebo rate. Malaise was reported in some adult clinical trials.

ejaculation dysfunction, hematuria, impotence (erectile dysfunction), libido decrease, nocturia, orgasm dysfunction, priapism, renal failure (unspecified), urinary incontinence, vaginal bleeding

Combined clinical trial data indicate that the following types of sexual dysfunction were reported more frequently in adult male patients receiving sertraline than placebo: ejaculation dysfunction (ejaculation failure 8%), impotence (erectile dysfunction) (4%), unspecified ejaculation disorder (3%), libido decrease (7%), and unspecified male sexual dysfunction (2%). In adult female patients, libido decrease was reported in 4% of patients receiving sertraline, and the incidence of unspecified female sexual dysfunction was reported as 1%. Postmarketing experience has suggested that the frequency of sexual-related adverse events, including orgasm dysfunction in males and females, during use of SSRIs may be higher than that reported in clinical trials, in part because of underreporting by patients. Prescribers should discuss sexual function prior to initiating treatment with sertraline and throughout treatment and obtain a detailed history and timeline of any changes in sexual function to determine whether the changes are medication-related or may be attributed to the underlying psychiatric disorder. Clinicians should also discuss management strategies and treatment options with patients. Urinary incontinence was reported in at least 2% of pediatric patients and at a rate at least twice the placebo rate during clinical trials of sertraline. Adverse genitourinary (GU) effects that were reported in less than 2% of patients receiving sertraline during premarketing evaluation included hematuria, vaginal bleeding (hemorrhage), and priapism. Priapism is a medical emergency that has been reported rarely with all of the SSRIs; discontinue sertraline if priapism develops and promptly initiate appropriate medical treatment. Acute renal failure (unspecified) and enuresis (nocturia or other involuntary urination) have been reported during postmarketing use; however, the frequencies are unknown and causality to the drug has not been established.

diabetes mellitus, galactorrhea, gynecomastia, hyperglycemia, hyperprolactinemia, hypoglycemia, hypothyroidism, menstrual irregularity

During premarketing evaluation, endocrine effects including galactorrhea, diabetes mellitus, hypoglycemia, and hypothyroidism were reported in less than 2% of patients receiving sertraline. Endocrine effects that have been reported during postmarketing use of sertraline include hyperprolactinemia, gynecomastia, menstrual irregularity, and hyperglycemia; however, the frequencies are unknown and causality to the drug has not been established.

serotonin syndrome

Serotonin syndrome has been reported during postmarketing use of sertraline, although the frequency is unknown and causality has not been established. Serotonin syndrome has been reported during use of SSRIs alone or during SSRI overdose, but primarily during concurrent use of other medications known to increase CNS serotonin levels. Symptoms may include nausea/vomiting, sedation, dizziness, diaphoresis (sweating), facial flush, mental status changes, myoclonia, restlessness, shivering, and elevated blood pressure. If serotonin syndrome becomes evident during sertraline treatment, the SSRI and any other serotonergic agents should be discontinued and appropriate medical treatment should be initiated.

bone fractures, osteopenia

Use selective serotonin reuptake inhibitors (SSRIs) with caution in patients with osteopenia or risk factors for osteopenia. Epidemiological studies suggest an association between the use of SSRIs and bone fractures. Some data suggest that chronic treatment with SSRIs, such as sertraline, may be associated with reduced bone density. Serotonin (5-HT) receptors and the serotonin reuptake transporter (5-HTT) have been found in osteoblasts and osteoclasts, and 5-HT functioning appears to be involved in bone architecture, bone mass, and bone density. Results of an observational retrospective study assessing the association between the degree of 5-HTT inhibition among antidepressants and the risk of osteoporotic and non-osteoporotic fractures indicated that use of antidepressants considered to have a high affinity for 5-HTT was associated with a higher risk of osteoporotic fractures than antidepressants with a moderate or low affinity for 5-HTT (OR 1.86, CI 1.63 to 2.13). There was no trend with increasing affinity for 5-HTT in non-osteoporotic fractures, although antidepressant use in general resulted in a 50% increase in this fracture type. In a separate prospective population-based cohort study, the risk of non-vertebral fractures was 2.35 in users of SSRIs compared to nonusers of antidepressants. A sub-analysis was conducted, which included current and prior antidepressant users only. The results showed that current users of SSRIs had a 2.07-fold increased risk of fracture compared to past users of tricyclic antidepressants or SSRIs, and this risk further increased with prolonged use.

neonatal abstinence syndrome, persistent pulmonary hypertension of the newborn

A neonatal abstinence syndrome has been reported in infants exposed to serotonergic agents in utero. After birth, symptoms consistent with withdrawal (i.e., poor feeding, hypoglycemia, hypothermia, lethargy or irritability, vomiting, etc.) were noted. Such complications can arise immediately upon delivery. Other symptoms have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty,

hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, and constant crying. Serum concentrations of the serotonergic agent were measurable in the infants affected. Several other symptoms (bloody stools, necrotizing enterocolitis) may have been attributable to rebound platelet activation on withdrawal of the exposure to the SSRI. Neonatal symptoms generally improved over several days. A cohort study of 55 women revealed that 22% (12/55) of neonates exposed to an SSRI in the third trimester had complications requiring treatment or extended hospitalization compared with 6% in comparison groups. Complications included respiratory distress (n = 9), hypoglycemia (n = 2), and jaundice (n = 1). The incidence of prematurity in the third trimester SSRI group was significant at 20% vs. 3.7% of controls. These features are consistent with either a direct toxic effect of serotonergic agents, or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome. When treating a pregnant woman with an SSRI or other serotonergic agent during the third trimester, the physician should carefully consider the potential risks and benefits of treatment. If clinically feasible, and taking the drug half-life into consideration, tapering of the serotonergic agent prior to delivery may be considered as an alternative. A case-controlled epidemiologic report has been published that suggests a significant association between maternal use of SSRIs after 20 weeks of pregnancy and the development of persistent pulmonary hypertension of the newborn (PPHN) (odds ratio (OR) 5.1; 95% CI, 1.9 to 13.3). The study population consisted of 377 women whose infants had PPHN and 836 matched control women and their infants. There was no increased risk of PPHN when SSRI use was restricted to the first half of the pregnancy (OR = 0.3; 95% CI, 0.1 to 1.1). Additionally, the use of non-SSRI antidepressant drugs at any time during pregnancy was not associated with an increased risk of PPHN. The SSRIs that were used by women more than 20 weeks gestation in the study included fluoxetine, paroxetine, and sertraline. However, the numbers were too small to permit examination of the effects of dose size, specific SSRI used, or reduction of the length of exposure before delivery. More recent retrospective studies have not shown an increased risk of PPHN with SSRI exposure. In December 2011, the FDA issued a safety announcement stating that based on conflicting data an increased risk of PPHN from SSRI exposure cannot be determined. The FDA advises that healthcare professionals should not alter their current practice of treating depression in pregnancy at this time.

growth inhibition, weight loss

In pediatric clinical trials of sertraline, weight loss (decreased weight) was reported in at least 2% and at a rate of at least twice the placebo rate. As with other SSRIs, decreased weight gain has also been observed in children and adolescents receiving sertraline. Data are inadequate to determine whether the chronic use of SSRIs causes long-term growth inhibition, but height and weight should be monitored periodically throughout therapy. In a 10-week pediatric trial, sertraline-treated patients lost approximately 1 kg,

while those treated with placebo gained roughly 1 kg. There was a bigger difference between sertraline and placebo in the proportion of outliers for clinically important weight loss in children than in adolescents. Approximately 7% of children (ages 6 to 11 years) and 2% of adolescents (ages 12 to 17 years) had a weight loss more than 7% of body weight compared to 0% and 1%, respectively, of placebo-treated patients. In the patients who continued into a 24-week open-label extension, a mean weight loss of approximately 0.5 kg was recorded during the first 8 weeks of treatment for patients newly exposed to sertraline. However, for those who received a total of 34 weeks of sertraline (n = 68), weight gain was similar to the expected using data from age-adjusted peers. The mechanism of growth inhibition in children may be due to the suppression of growth hormone secretion, which is known to occur in adults taking SSRIs.

withdrawal

Avoid abrupt discontinuation of sertraline when possible. Gradual tapering during discontinuation is recommended to decrease or prevent the occurrence of potential withdrawal symptoms. The most common discontinuation symptoms include nausea, sweating, dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia, such as electric shock sensations), tremor, anxiety, confusion, headache, lethargy, emotional lability, insomnia, tinnitus, and seizures. Discontinuation symptoms usually begin 1 to 3 days after abrupt discontinuation of the SSRI and remit within 1 to 2 weeks. Discontinuation symptoms are most likely to occur after abruptly stopping SSRIs with a short half-life. Some dosage forms (i.e., sertraline capsules) do not have strengths available for tapering and the patient may need to switch to a different sertraline product to allow for tapering of the dose.

laboratory test interference

Sertraline has been reported to cause laboratory test interference. False-positive urine Immunoassay screening tests for benzodiazepines have been reported in patients taking sertraline. False-positive results may occur for several days following discontinuation of sertraline. Caution should be exercised when interpreting positive urine drug screens for these medications, and confirmation by alternative tests such as gas chromatography/mass spectrometry should be considered.

Description

Sertraline is an oral selective serotonin reuptake inhibitor (SSRI) indicated for major depressive disorder, obsessive-compulsive disorder (OCD), panic disorder, post-traumatic stress disorder, social anxiety disorder, and premenstrual dysphoric disorder in adults. Off-label uses of sertraline in adults include generalized anxiety disorder, hot

flashes, and premature ejaculation. Sertraline has also been examined for the treatment of non-emergent behavioral and psychological symptoms in dementia (BPSD), particularly in individuals who may also have underlying depression. Sertraline is also indicated for treating OCD in pediatric patients 6 years and older. Limited data suggest efficacy in children for depression and childhood anxiety disorders including generalized anxiety disorder, social phobia, and separation anxiety disorder. Sertraline has a lower potential for drug interactions involving CYP2D6 inhibition than other SSRIs such as fluoxetine or paroxetine. Product labels for all antidepressants contain a boxed warning related to an increased risk of suicidality in children, adolescents, and young adults during the initial stages of therapy when treating depression or other conditions; therefore, the necessity of pharmacologic therapy versus the potential risks should be carefully considered in these populations.

Mechanism Of Action

The precise antidepressant effect of SSRIs is not fully understood, but involves selective serotonin reuptake blockade at the neuronal membrane, which enhances the actions of serotonin (5-HT). Initially, SSRIs increase availability of serotonin in the somatodendritic area through serotonin reuptake blockade at the serotonin transport pump. During long-term administration of SSRIs, serotonin autoreceptors are down-regulated and desensitized, allowing the neuron to increase serotonin release in the axon terminal synapses and increase its neuronal impulses. Because of the delay in therapeutic response to SSRIs, it is theorized that the change in the balance of serotonin receptors over time is an important mechanism of effect. The therapeutic action of SSRIs in treating anxiety disorders is thought to occur from potent central serotonin reuptake blockade, although the exact mechanism is unknown. SSRIs have less sedative, anticholinergic, and cardiovascular effects than do tricyclic antidepressants due to dramatically decreased binding to histaminergic, muscarinic, and alpha-adrenergic receptors.

Pharmacokinetics

Sertraline is administered orally. In young adults, steady-state concentrations are achieved after about 1 week. Sertraline appears to be highly protein-bound (98%), but it does not compete with warfarin or propranolol for binding sites, possibly because its presumed binding site is alpha1-acid glycoprotein and not albumin. Sertraline undergoes extensive first pass metabolism. In vitro data suggest sertraline is a substrate of many hepatic CYP450 enzymes. One study noted that multiple enzymes catalyzed sertraline N-demethylation, with CYP2B6 contributing the greatest extent, and lesser contributions from CYP2C19, CYP2C9, CYP3A4, and CYP2D6. The primary metabolite of

N-demethylation is N-desmethylsertraline, which is substantially less active than sertraline. Both sertraline and N-desmethylsertraline undergo oxidative deamination and subsequent reduction, hydroxylation, and glucuronide conjugation. For deamination, data support a role for CYP3A4 and CYP2C19. The average elimination half-life of sertraline is approximately 26 hours. N-desmethylsertraline has an elimination half-life of 62 to 104 hours. Unchanged sertraline is not detected in the urine; however, 12% to 14% of unchanged sertraline is recovered in feces.

Affected cytochrome P450 (CYP450) isoenzymes and drug transporters: CYP2D6
Because sertraline is metabolized by various CYP450 enzymes, inhibition of one enzyme by another drug is not likely to significantly affect sertraline concentrations. Sertraline inhibits CYP2D6 in vivo; it may be necessary to reduce the dosage of concomitantly administered drugs metabolized by CYP2D6. Sertraline appears to have little effect, if any, on the metabolic capacity of other CYP450 hepatic isoenzymes. Sertraline and N-desmethylsertraline have a high in vitro affinity for P-glycoprotein; the clinical significance of this finding is unknown.

Route-Specific Pharmacokinetics

- **Oral Route**

After oral administration of sertraline for 14 days in adults, the mean peak plasma concentration (Cmax) occurs between 4.5 to 8.4 hours. The single dose bioavailability of the tablets is approximately equal to an equivalent dose of oral solution. Administration with food causes a small increase in Cmax and exposure (AUC). Steady-state concentrations are achieved after 1 week of once daily dosing.

- **Hepatic Impairment**

In adult patients with chronic mild liver impairment (n = 10; eight patients with Child-Pugh scores of 5 to 6, and two with Child-Pugh scores of 7 to 8), sertraline clearance was reduced, resulting in about 3-fold greater exposure compared to those with no hepatic impairment. The exposure to desmethylsertraline was about 2-fold greater. There were no significant differences in plasma protein binding between the groups. The effects of moderate and severe hepatic impairment on the pharmacokinetics of sertraline have not been studied.

- **Renal Impairment**

Sertraline exposure does not appear to be affected by renal impairment. Pharmacokinetic data indicate that renal elimination of sertraline is comparable between healthy volunteers and adult patients with mild to severe renal impairment, including those on dialysis.

- **Pediatrics**

Relative to adults, pediatric patients 6 to 17 years of age showed about 22% lower AUC and Cmax values when plasma concentrations were adjusted for weight. Half-life was similar to adults.

- **Geriatric**

In a small group of 16 geriatric patients (8 males and 8 females), clearance of sertraline was approximately 40% less than in young adults. Steady-state was achieved after 2 to 3 weeks in the older patients. The same study showed decreased clearance of desmethylsertraline in older males, but not in older females.

Administration

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

Oral Administration

May administer without regard to meals in the morning or evening.

Oral Solid Formulations

Oral tablets (e.g., Zoloft)
Tablets may be scored for breakage along the scored line to allow for dosage as prescribed.

Oral capsules (e.g., Zercapli)
Do not initiate sertraline treatment with the capsule formulation, as the only available dose strengths are 150 mg and 200 mg. Patients currently taking sertraline tablets at a dose of 100 mg or 125 mg for at least 1 week may transition to the capsule formulation.
Have patient swallow capsules whole; do not cut, chew, or crush capsules.

Oral Liquid Formulations

Oral solution:
Must be diluted before use.
Use the supplied calibrated dropper to measure the correct dose. The supplied calibrated dropper has 25 mg and 50 mg graduation marks only.
Mix the measured dose with 4 ounces (120 mL) of water, ginger ale, lemon-lime soda, lemonade, or orange juice ONLY.
After mixing, a slight haze may appear; this is normal.
Have the patient consume the dose immediately after mixing; do not prepare in advance.
The dropper contains dry natural rubber; use with caution in patients with latex sensitivity.

Maximum Dosage Limits

- **Adults**
  200 mg/day PO.
- **Geriatric**
  200 mg/day PO; however, lower dosages may be effective/better tolerated.
- **Adolescents**
  200 mg/day PO.
- **Children**
  6 to 12 years: 200 mg/day PO.
  1 to 5 years: Safety and efficacy have not been established.
- **Infants**
  Not indicated.
- **Neonates**
  Not indicated.

Dosage Forms

- Sertraline Hydrochloride 100mg Oral tablet
- Sertraline Hydrochloride 150mg Oral capsule
- Sertraline Hydrochloride 200mg Oral capsule
- Sertraline Hydrochloride 20mg/1mL Oral solution
- Sertraline Hydrochloride 25mg Oral tablet
- Sertraline Hydrochloride 50mg Oral tablet
- Sertraline Hydrochloride Bulk powder
- Zoloft 100mg Tablet
- Zoloft 100mg Tablet
- Zoloft 20mg/mL Solution
- Zoloft 25mg Tablet
- Zoloft 50mg Tablet
- Zoloft 50mg Tablet

Dosage Adjustment Guidelines

Hepatic Impairment

Oral tablets or oral solution:
In mild hepatic impairment (Child Pugh A, score 5 or 6): The initial dose and therapeutic range dosing is 50% of the normal daily dosage.
For moderate to severe hepatic impairment (Child Pugh B or C, scores 7 to 15): Use is not recommended.
Oral Capsules:
Sertraline capsules are not recommended in patients with mild, moderate, or severe hepatic impairment because dosage adjustments are not possible with the capsule strengths available.

Renal Impairment

No dosage adjustments are needed.

Intermittent hemodialysis
No dosage adjustments are needed. Sertraline is unlikely to be significantly removed by hemodialysis given its large volume of distribution.