Brand Names

Celebrex, Elyxyb, VYSCOXA

Indication Specific Dosing

General Dosing Information
Celecoxib oral suspension (Vyscoxa) is not indicated for the management of acute pain or for the treatment of primary dysmenorrhea.
Initiate therapy at the lowest recommended dose in individuals weighing less than 50 kg, particularly in geriatric individuals.
The maximum single dose of celecoxib oral suspension (Vyscoxa) is 200 mg. Use a different product in individuals requiring single doses of celecoxib greater than 200 mg. Administering more than 200 mg of the suspension in a single dose may result in higher than intended plasma concentrations of celecoxib.
Use the lowest effective dosage for the shortest duration consistent with individual treatment goals.

For the treatment of osteoarthritis

Oral dosage (capsules and oral suspension, e.g., Vyscoxa)

Adults

200 mg PO once daily or 100 mg PO twice daily. Start celecoxib at half the lowest recommended dose in individuals who are poor CYP2C9 metabolizers.

For the relief of the signs and symptoms of rheumatoid arthritis

Oral dosage (capsules and oral suspension, e.g., Vyscoxa)

Adults

100 or 200 mg PO twice daily. Start celecoxib at half the lowest recommended dose in individuals who are poor CYP2C9 metabolizers.

For the relief of the signs and symptoms of juvenile rheumatoid arthritis (JRA)/juvenile idiopathic arthritis (JIA) including pauciarticular, polyarticular juvenile idiopathic arthritis

Oral dosage (capsules and oral suspension, e.g., Vyscoxa)

Children 2 to 12 years weighing 26 kg or more and Adolescents

100 mg PO twice daily. Consider alternative therapy in individuals who are known or suspected to be poor CYP2C9 metabolizers.

Children 2 to 12 years weighing 10 to 25 kg

50 mg PO twice daily. Consider alternative therapy in individuals who are known or suspected to be poor CYP2C9 metabolizers.

For the treatment of acute moderate pain or severe pain

Oral dosage (capsules)

Adults

400 mg PO once initially, followed by an additional 200 mg PO once on day 1 if needed, then 200 mg PO twice daily as needed. Start celecoxib at half the lowest recommended dose in individuals who are poor CYP2C9 metabolizers.

For the treatment of active ankylosing spondylitis

Oral dosage (capsules and oral suspension, e.g., Vyscoxa)

Adults

200 mg PO once daily or 100 mg PO twice daily. Consider increasing the dose to 200 mg PO twice daily if there is no response after 6 weeks. If there is no response after 6 weeks at the higher dose, consider alternate treatment as response is unlikely. Start celecoxib at half the lowest recommended dose in individuals who are poor CYP2C9 metabolizers.

For the acute treatment of migraine with or without aura

Oral dosage (oral solution, e.g., Elyxyb)

Adults

120 mg PO once daily for the fewest number of days per month as needed. Max: 120 mg/day (60 mg/day in individuals who are known or suspected CYP2C9 poor metabolizers). The safety and efficacy of a second dose in a 24-hour period have not been established. Guidelines classify celecoxib oral solution as having established efficacy for the treatment of acute migraine.

For the treatment of dysmenorrhea

Oral dosage (capsules)

Adults

400 mg PO once, then 200 mg PO every 12 hours as needed. The FDA-approved dosage is 400 mg PO once initially, followed by an additional 200 mg PO once on Day 1 if needed, then 200 mg PO twice daily as needed. Start celecoxib at half the lowest recommended dose in individuals who are poor CYP2C9 metabolizers.

Adolescents†

400 mg PO once, then 200 mg PO every 12 hours as needed.

For the treatment of acute gout† or acute gouty arthritis†

Oral dosage (capsules)

Adults

800 mg PO once followed by 400 mg PO 12 hours later on day 1, then 400 mg PO twice daily for 7 days.

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. Celecoxib is also contraindicated in individuals with a history of sulfonamide hypersensitivity.

cardiovascular disease, coronary artery bypass graft surgery (CABG), serious cardiovascular events

Celecoxib is contraindicated in the setting of coronary artery bypass graft surgery (CABG). An increased incidence of myocardial infarction and stroke was found in clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10 to 14 days after CABG surgery. NSAIDs may increase the risk of serious cardiovascular events, which can be fatal. Guidelines recommend against NSAID use in individuals presenting with and hospitalized for ST-elevation myocardial infarction (STEMI) due to increased risk of mortality and cardiovascular (CV) complications associated with their use. Avoid NSAID use in individuals with a recent myocardial infarction unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If an NSAID is used in individuals with a recent myocardial infarction, monitor for signs of cardiac ischemia. Observational data from a national registry demonstrated that individuals treated with NSAIDs in the post-MI period were at increased risk of reinfarction, CV-related death, and all-cause mortality beginning the first week of treatment. An increased relative risk of death in NSAID users continued during the follow-up period of 4 years. Data demonstrate that individuals treated with NSAIDs were more likely to die in the first year after a myocardial infarction compared to those not treated with NSAIDs. The relative increase in serious CV thrombotic events over baseline conferred by NSAID use appears to be similar in those with and without known CV disease or risk factors for CV disease; however, individuals with known cardiovascular disease or risk factors had a higher absolute incidence of excess serious CV thrombotic events, due to their increased baseline rate. Some observational studies found that this increased risk of serious CV thrombotic events began as early as the first weeks of treatment with an NSAID; the increase in CV thrombotic risk has been observed most consistently at higher doses. Current evidence is insufficient to determine if the risk of an event is higher or lower for any particular NSAID compared to other NSAIDs. There is no consistent evidence that concomitant use of aspirin mitigates the increased risk for CV thrombotic events. To minimize the potential risk for an adverse CV event in NSAID-treated individuals, use the lowest effective dose for the shortest duration possible; remain alert for the development of such events, throughout the entire treatment course, even in the absence of previous CV symptoms. NSAIDs may worsen pre-existing hypertension, which may contribute to the increased incidence of CV events. Monitor blood pressure during NSAID treatment initiation and throughout therapy. Avoid NSAID use in individuals with severe heart failure, unless the benefits of treatment are expected to outweigh the risks. Monitor for signs of worsening heart failure if an NSAID is used in individuals with severe heart failure. Monitor renal function in individuals with heart failure during use of an NSAID. Data demonstrate an increased risk for myocardial

infarction, hospitalization for heart failure, and death with NSAID use in individuals with heart failure.

General Information

When NSAIDs are used in individuals with systemic onset juvenile rheumatoid arthritis (JRA), monitor for signs and symptoms of abnormal clotting or bleeding and the development of abnormal coagulation tests. Disseminated intravascular coagulation and mild prolongation of activated partial thromboplastin time (APTT) have been reported with celecoxib use in individuals with systemic onset JRA.

bleeding disorder, ethanol ingestion, GI bleeding, peptic ulcer disease, serious gastrointestinal events, tobacco smoking

Individuals with a prior history of GI bleeding and/or peptic ulcer disease who use NSAIDs had a more than 10-fold increased risk of developing a GI bleed compared to individuals without these risk factors. Individuals with advanced hepatic disease or bleeding disorder are also at increased risk for GI bleeding. Other risk factors for GI bleeding in individuals receiving NSAIDs include longer duration of NSAID therapy, concomitant use of oral corticosteroids, aspirin, anticoagulants, or selective serotonin reuptake inhibitors (SSRIs), tobacco smoking, ethanol ingestion, older age, and poor general health status. Serious gastrointestinal events, including bleeding, inflammation, perforation, and ulceration, can occur at any time and without warning symptoms in individuals receiving NSAIDs. To minimize the risk of an adverse GI event in NSAID-treated individuals, use the lowest effective NSAID dose for the shortest possible duration. Avoid concurrent administration of other NSAIDs; in the setting of concomitant use of low-dose aspirin for cardiac prophylaxis, monitor more closely for evidence of GI bleeding. Avoid NSAID use in individuals at higher risk for GI adverse events unless benefits are expected to outweigh the increased bleeding risk, and consider alternate therapies other than NSAIDs for those individuals and individuals with active GI bleeding. Monitor individuals for signs and symptoms of GI bleeding and ulceration during NSAID therapy.

hypovolemia, renal disease

Celecoxib is not recommended for use in individuals with severe renal insufficiency. Avoid NSAID use in individuals with advanced renal disease, unless the benefits are expected to outweigh the risks of worsening renal function. If an NSAID is used in individuals with advanced renal disease, monitor for signs and symptoms of worsening renal function. Correct volume status in individuals with dehydration or hypovolemia prior to starting an NSAID. Monitor renal function in individuals with renal impairment, dehydration, or hypovolemia during use of an NSAID. NSAID use in individuals with renal

impairment, dehydration, or hypovolemia in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion may precipitate renal decompensation. The renal effects of NSAIDs may hasten the progression of renal dysfunction in individuals with pre-existing renal disease.

aspirin exacerbated respiratory disease, asthma

Celecoxib is contraindicated in individuals with aspirin exacerbated respiratory disease, which may include chronic rhinosinusitis complicated by nasal polyps, severe and potentially fatal acute bronchospasm, and/or intolerance to aspirin and other NSAIDs. When an NSAID is used in individuals with pre-existing asthma without known aspirin sensitivity, monitor for changes in the signs and symptoms of asthma.

hepatic disease

Avoid the use of celecoxib in individuals with severe hepatic impairment or hepatic failure (Child-Pugh class C). A celecoxib dosage adjustment is recommended in individuals with moderate hepatic impairment (Child-Pugh Class B). Monitor renal function in individuals with hepatic impairment during use of an NSAID. NSAID use in individuals with hepatic failure in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion may precipitate renal decompensation. Advanced hepatic disease is also a risk factor for GI bleeding in individuals who use NSAIDs.

CYP2C9 poor metabolizer

A celecoxib dosage adjustment is recommended in an individual who is a known or suspected CYP2C9 poor metabolizer based on genotype or previous history or experience with other CYP2C9 substrates. Consider alternative therapy in individuals with juvenile rheumatoid arthritis (JRA) identified as CYP2C9 poor metabolizers. Celecoxib plasma concentrations may be elevated in these individuals.

geriatric

Geriatric adults, compared to younger individuals, are at greater risk for NSAID-associated serious cardiovascular, gastrointestinal, and/or renal adverse reactions. If the anticipated benefit for the older adult outweighs these potential risks, start dosing at the low end of the dosing range, and monitor for adverse effects. According to the Beers Criteria, NSAIDs are considered potentially inappropriate medications (PIMs) in geriatric adults. There is an increased risk of GI bleeding and peptic ulcer disease in high-risk groups including those older than 75 years, or those taking systemic corticosteroids, anticoagulants, or antiplatelet medications. The risk of GI ulcers, gross bleeding, or perforation is cumulative with continued use. Avoid the chronic use of NSAIDs in high-

risk individuals, including those with a history of gastric or duodenal ulcers, unless other alternatives are not effective, and the individual can take a gastroprotective agent. The use of a gastroprotective agent, like a proton pump inhibitor or misoprostol, reduces but does not eliminate GI risks. NSAIDs may also increase blood pressure and induce kidney injury. Avoid use of NSAIDs in geriatric adults with the following conditions due to the potential for symptom exacerbation or adverse effects: symptomatic heart failure (fluid retention, symptom exacerbation) or chronic kidney disease Stage 4 or higher (CrCl less than 30 mL/minute) (acute kidney injury, further decline of renal function). Use with caution in individuals with asymptomatic heart failure.

pregnancy

Avoid the use of NSAIDs, such as celecoxib, during pregnancy starting at 30 weeks gestation due to the risk of premature closure of the fetal ductus arteriosus. When use is necessary between 20 and 30 weeks gestation, limit use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if treatment exceeds 48 hours. Discontinue the NSAID if oligohydramnios develops, and follow up according to clinical practice. Use of NSAIDs around 20 weeks gestation and later may also cause fetal renal dysfunction, leading to oligohydramnios, and in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation. Complications of prolonged oligohydramnios may include limb contractures and delayed lung maturation. In some cases, invasive neonatal procedures such as exchange transfusion or dialysis have been required. Observational data regarding other potential embryo-fetal risks of NSAID use during the first or second trimesters are inconclusive. In animal reproduction studies, an increase in embryonic death, diaphragmatic hernias, and fetal malformations were observed when celecoxib was given during the period of organogenesis at daily doses resulting in 2 to 6 times the human exposure. Animal studies indicate that prostaglandins play an important role in endometrial blood flow, embryo implantation, and fetal kidney development. Inhibiting prostaglandin synthesis has been associated with increased pre- and post-implantation loss and impaired kidney development in animals at NSAID doses relevant to clinical use. The effects of celecoxib on labor and obstetric delivery are unknown. In animal studies, NSAIDs inhibit prostaglandin synthesis, delay parturition, and increase the incidence of still birth. Celecoxib produced no evidence of delayed labor or parturition in animal studies at oral doses up to 100 mg/kg in rats (approximately 7-fold human exposure as measured by the AUC at 200 mg twice daily).

people who may become pregnant, reproductive risk

Counsel people who may become pregnant about the reproductive risk associated with celecoxib. NSAIDs may delay or prevent prostaglandin-mediated rupture of ovarian follicles, which has been associated with reversible infertility. Small studies have also shown a reversible delay in ovulation. Consider the withdrawal of NSAIDs in those who have difficulties conceiving or who are undergoing infertility evaluation.

breast-feeding

Use celecoxib with caution during breast-feeding. Limited data from 3 published reports that included a total of 12 breast-feeding individuals showed low concentrations of celecoxib in human milk. The calculated average daily infant dose was 10 to 40 mcg/kg/day, less than 1% of the weight-based therapeutic dose for a 2-year-old child. A report of 2 breastfed children who were 17 and 22 months old did not show any adverse events. Consider the developmental and health benefits of breast-feeding along with the patient's clinical need for celecoxib and any potential adverse effects on the breastfed child from celecoxib or the patient's underlying condition. Alternative analgesic and anti-inflammatory drugs considered to be usually compatible with breast-feeding include acetaminophen, ibuprofen, indomethacin, and piroxicam.

Pregnancy And Lactation

Avoid the use of NSAIDs, such as celecoxib, during pregnancy starting at 30 weeks gestation due to the risk of premature closure of the fetal ductus arteriosus. When use is necessary between 20 and 30 weeks gestation, limit use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if treatment exceeds 48 hours. Discontinue the NSAID if oligohydramnios develops, and follow up according to clinical practice. Use of NSAIDs around 20 weeks gestation and later may also cause fetal renal dysfunction, leading to oligohydramnios, and in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation. Complications of prolonged oligohydramnios may include limb contractures and delayed lung maturation. In some cases, invasive neonatal procedures such as exchange transfusion or dialysis have been required. Observational data regarding other potential embryo-fetal risks of NSAID use during the first or second trimesters are inconclusive. In animal reproduction studies, an increase in embryonic death, diaphragmatic hernias, and fetal malformations were observed when celecoxib was given during the period of organogenesis at daily doses resulting in 2 to 6 times the human exposure. Animal studies indicate that prostaglandins play an

important role in endometrial blood flow, embryo implantation, and fetal kidney development. Inhibiting prostaglandin synthesis has been associated with increased pre- and post-implantation loss and impaired kidney development in animals at NSAID doses relevant to clinical use. The effects of celecoxib on labor and obstetric delivery are unknown. In animal studies, NSAIDs inhibit prostaglandin synthesis, delay parturition, and increase the incidence of still birth. Celecoxib produced no evidence of delayed labor or parturition in animal studies at oral doses up to 100 mg/kg in rats (approximately 7-fold human exposure as measured by the AUC at 200 mg twice daily).

Interactions

Acebutolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Acetaminophen; Aspirin, ASA; Caffeine: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection.
Acetaminophen; Aspirin: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection.
Acetaminophen; Aspirin; diphenhydrAMINE: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection.
Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) Concomitant use of dihydrocodeine with celecoxib may increase dihydrocodeine plasma concentrations, but decrease the plasma concentration of the active metabolite, dihydromorphine, resulting in reduced efficacy or symptoms of opioid withdrawal. If coadministration is necessary,

monitor patients closely at frequent intervals and consider a dosage increase of dihydrocodeine until stable drug effects are achieved. Discontinuation of celecoxib could decrease dihydrocodeine plasma concentrations and increase dihydromorphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If celecoxib is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Dihydrocodeine is primarily metabolized by CYP2D6 to dihydromorphine, and by CYP3A4. Celecoxib is an inhibitor of CYP2D6.
Acetaminophen; Chlorpheniramine: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Acetaminophen; Chlorpheniramine; Dextromethorphan: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Acetaminophen; Chlorpheniramine; Phenylephrine : (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Acetaminophen; Codeine: (Moderate) Concomitant use of codeine with celecoxib may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6.
Acetaminophen; HYDROcodone: (Moderate) Concomitant use of hydrocodone with celecoxib may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of celecoxib could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If celecoxib is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Celecoxib is an inhibitor of CYP2D6.
Acetaminophen; Ibuprofen: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Acyclovir: (Moderate) Monitor patients for signs of worsening renal function during coadministration of acyclovir and nonsteroidal antiinflammatory drugs. Coadministration may increase the risk for drug-induced nephrotoxicity.
Adagrasib: (Moderate) Monitor for celecoxib-related adverse effects and consider a celecoxib dosage reduction as appropriate based on response if concomitant use with adagrasib is necessary. Concomitant use may increase celecoxib exposure. Celecoxib is a CYP2C9 substrate and adagrasib is a moderate CYP2C9 inhibitor. Concomitant use with another moderate CYP2C9 inhibitor increased celecoxib overall exposure by 2-fold.
Adefovir: (Moderate) Chronic coadministration of adefovir with nephrotoxic drugs, such as nonsteroidal antiinflammatory drugs may increase the risk of developing nephrotoxicity even in patients who have normal renal function. The use of adefovir with NSAIDs may be done cautiously. As stated in the current adefovir prescribing information, 'Ibuprofen (800 mg PO three times daily), when given concomitantly with adefovir dipivoxil, increased the adefovir Cmax by 33% and AUC by 23%, as well as urinary recovery. The increase appears to be due to higher oral bioavailability, not a reduction in renal clearance of adefovir.' In an in vitro investigation, the antiviral effect of adefovir was unaltered and the renal proximal tubule accumulation of adefovir was inhibited by the presence of a NSAID. Adefovir is efficiently transported by the human renal organic anion transporter 1, and the presence of this transporter appears to mediate the accumulation of the drug in renal proximal tubules. The in vitro study suggests that the use of a NSAID with adefovir may potentially reduce the nephrotoxic potential of adefovir. Of course, NSAIDs are associated with nephrotoxicity of their own;

therefore, further data on the interaction between NSAIDs and adefovir in humans are needed.
Albuterol; Budesonide: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Aldesleukin, IL-2: (Major) Aldesleukin, IL-2 may cause nephrotoxicity. Concurrent administration of drugs possessing nephrotoxic effects, such as nonsteroidal antiinflammatory agents (NSAIDs), with Aldesleukin, IL-2 may increase the risk of kidney dysfunction. In addition, reduced kidney function secondary to Aldesleukin, IL-2 treatment may delay elimination of concomitant medications and increase the risk of adverse events from those drugs.
Alendronate: (Minor) Monitor for gastrointestinal adverse events during concurrent use of alendronate and nonsteroidal antiinflammatory drugs. Both medications have been associated with gastrointestinal irritation although data suggest concomitant use introduces little additional risk for adverse effects for most patients.
Alendronate; Cholecalciferol: (Minor) Monitor for gastrointestinal adverse events during concurrent use of alendronate and nonsteroidal antiinflammatory drugs. Both medications have been associated with gastrointestinal irritation although data suggest concomitant use introduces little additional risk for adverse effects for most patients.
Aliskiren: (Moderate) NSAIDs may attenuate the antihypertensive effects of aliskiren by inhibiting the synthesis of vasodilatory prostaglandins. In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function who are being treated with NSAIDs, the coadministration of aliskiren may result in a further deterioration of renal function, including acute renal failure. These effects are usually reversible. Therefore, blood pressure and renal function should be monitored closely when an NSAID is administered to a patient taking aliskiren.
Aliskiren; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics. (Moderate) NSAIDs may attenuate the antihypertensive effects of aliskiren by inhibiting the synthesis of vasodilatory prostaglandins. In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function who are being treated with NSAIDs, the coadministration of aliskiren may result in a further deterioration of renal function, including acute renal failure. These effects are usually reversible. Therefore, blood pressure and renal function should be monitored closely when an NSAID is

administered to a patient taking aliskiren.
Alpelisib: (Moderate) Monitor for decreased efficacy of celecoxib during coadministration of alpelisib as plasma concentrations of celecoxib may be decreased. Celecoxib is a sensitive CYP2C9 substrate; in vitro data suggest alpelisib is a CYP2C9 inducer.
Alpha-blockers: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Alteplase: (Moderate) NSAIDs can cause GI bleeding, inhibit platelet aggregation, prolong bleeding time; these pharmacodynamic effects may be increased when administered to patients receiving thrombolytic agents. Patients receiving these drugs concurrently should be monitored closely for bleeding.
Amikacin: (Moderate) It is possible that additive nephrotoxicity may occur in patients who receive nonsteroidal antiinflammatory drugs (NSAIDs) concurrently with other nephrotoxic agents, such as amikacin.
aMILoride: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may reduce the natriuretic effect of diuretics in some patients. NSAIDS have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain. Patients taking diuretics and NSAIDS concurrently are at higher risk of developing renal insufficiency. If an NSAID and a diuretic are used concurrently, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic efficacy.
aMILoride; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the

natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics. (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may reduce the natriuretic effect of diuretics in some patients. NSAIDS have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain. Patients taking diuretics and NSAIDS concurrently are at higher risk of developing renal insufficiency. If an NSAID and a diuretic are used concurrently, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic efficacy.
Aminolevulinic Acid: (Moderate) Agents that inhibit prostaglandin synthesis such as nonsteroidal antiinflammatory drugs (NSAIDs), could decrease the efficacy of photosensitizing agents used in photodynamic therapy. Avoidance of NSAIDs before and during photodynamic therapy may be advisable.
Amiodarone: (Moderate) Monitor for celecoxib-related adverse effects and consider a celecoxib dosage reduction as appropriate based on response if concomitant use with amiodarone is necessary. Concomitant use may increase celecoxib exposure. Celecoxib is a CYP2C9 substrate and amiodarone is a moderate CYP2C9 inhibitor. Concomitant use with another moderate CYP2C9 inhibitor increased celecoxib overall exposure by 2-fold.
Amitriptyline: (Moderate) Monitor for an increase in amitriptyline-related adverse reactions if coadministration with celecoxib is necessary; a dose reduction of amitriptyline may be necessary. Concurrent use may increase the plasma concentrations of amitriptyline. Amitriptyline is a CYP2D6 substrate and celecoxib is a CYP2D6 inhibitor.
amLODIPine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
amLODIPine; Atorvastatin: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of

antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. amLODIPine; Benazepril: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. amLODIPine; Celecoxib: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by

peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. amLODIPine; Olmesartan: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. amLODIPine; Valsartan: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. (Moderate) Monitor blood pressure and renal function periodically during concomitant

angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
amLODIPine; Valsartan; hydroCHLOROthiazide, HCTZ: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Amobarbital: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Amoxapine: (Moderate) A dosage adjustment may be warranted for amoxapine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of amoxapine. Celecoxib is a CYP2D6 inhibitor, and amoxapine is a

CYP2D6 substrate.
Amphotericin B lipid complex (ABLC): (Moderate) Concurrent use of amphotericin B and other nephrotoxic medications, including nonsteroidal antiinflammatory drugs (NSAIDs), may enhance the potential for drug-induced renal toxicity. Monitor renal function carefully during concurrent therapy. Amphotericin B dosage reduction may be necessary if renal impairment occurs.
Amphotericin B liposomal (LAmB): (Moderate) Concurrent use of amphotericin B and other nephrotoxic medications, including nonsteroidal antiinflammatory drugs (NSAIDs), may enhance the potential for drug-induced renal toxicity. Monitor renal function carefully during concurrent therapy. Amphotericin B dosage reduction may be necessary if renal impairment occurs.
Amphotericin B: (Moderate) Concurrent use of amphotericin B and other nephrotoxic medications, including nonsteroidal antiinflammatory drugs (NSAIDs), may enhance the potential for drug-induced renal toxicity. Monitor renal function carefully during concurrent therapy. Amphotericin B dosage reduction may be necessary if renal impairment occurs.
Anagrelide: (Moderate) Monitor for signs and symptoms of bleeding during concomitant platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of bleeding.
Angiotensin II receptor antagonists: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Angiotensin-converting enzyme inhibitors: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Antithrombin III: (Moderate) An additive risk of bleeding may be seen in patients receiving anticoagulants in combination with other agents known to increase the risk of bleeding such as nonsteroidal anti-inflammatory drugs (NSAIDs). Monitor clinical and laboratory response closely during concurrent use.
Apalutamide: (Moderate) Monitor for decreased efficacy of celecoxib if coadministration with apalutamide is necessary; a celecoxib dosage adjustment may be necessary. Celecoxib is a CYP2C9 substrate and apalutamide is a weak CYP2C9 inducer.

Coadministration may decrease plasma concentrations of celecoxib.
Apixaban: (Major) An additive risk of bleeding may be seen in patients receiving anticoagulants in combination with other agents known to increase the risk of bleeding such as nonsteroidal antiinflammatory drugs (NSAIDs). Monitor clinical and laboratory response closely during concurrent use.
Aprepitant, Fosaprepitant: (Minor) Use caution if celecoxib and aprepitant are used concurrently and monitor for a possible decrease in the efficacy of celecoxib. After administration, fosaprepitant is rapidly converted to aprepitant and shares the same drug interactions. Celecoxib is a CYP2C9 substrate and aprepitant is a CYP2C9 inducer. Administration of a CYP2C9 substrate, tolbutamide, on days 1, 4, 8, and 15 with a 3-day regimen of oral aprepitant (125 mg/80 mg/80 mg) decreased the tolbutamide AUC by 23% on day 4, 28% on day 8, and 15% on day 15. The AUC of tolbutamide was decreased by 8% on day 2, 16% on day 4, 15% on day 8, and 10% on day 15 when given prior to oral administration of aprepitant 40 mg on day 1, and on days 2, 4, 8, and 15. The effects of aprepitant on tolbutamide were not considered significant. When a 3-day regimen of aprepitant (125 mg/80 mg/80 mg) given to healthy patients on stabilized chronic warfarin therapy (another CYP2C9 substrate), a 34% decrease in S-warfarin trough concentrations was noted, accompanied by a 14% decrease in the INR at five days after completion of aprepitant.
Argatroban: (Moderate) An additive risk of bleeding may be seen in patients receiving anticoagulants in combination with other agents known to increase the risk of bleeding such as nonsteroidal anti-inflammatory drugs (NSAIDs). Monitor clinical and laboratory response closely during concurrent use.
ARIPiprazole: (Moderate) Monitor for aripiprazole-related adverse reactions during concomitant use of celecoxib. Patients receiving both a CYP3A inhibitor plus celecoxib 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. Aripiprazole is a CYP2D6 and CYP3A substrate; celecoxib is a weak CYP2D6 inhibitor.
Arsenic Trioxide: (Minor) Some antineoplastic agents cause thrombocytopenia, and patients with thrombocytopenia are at increased risk of bleeding complications. Celecoxib does not generally affect platelet counts, prothrombin time, or partial thromboplastin time, and does not inhibit platelet aggregation at indicated dosages. It is unclear if celecoxib is associated with less risk than other NSAIDs due to its lack of platelet inhibitory effects; bleeding events have occurred with celecoxib.
Asciminib: (Moderate) Monitor for celecoxib-related adverse effects and consider a celecoxib dosage reduction as appropriate based on response if concomitant use with asciminib 200 mg twice daily is necessary. Concomitant use may increase celecoxib exposure. Celecoxib is a CYP2C9 substrate and asciminib 200 mg twice daily is a

moderate CYP2C9 inhibitor. Concomitant use with another moderate CYP2C9 inhibitor increased celecoxib overall exposure by 2-fold.
Aspirin, ASA: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection.
Aspirin, ASA; Butalbital; Caffeine: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection. (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Aspirin, ASA; Caffeine: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection.
Aspirin, ASA; Caffeine; Orphenadrine: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection.
Aspirin, ASA; Carisoprodol; Codeine: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to

325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection. (Moderate) Concomitant use of codeine with celecoxib may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6.
Aspirin, ASA; Citric Acid; Sodium Bicarbonate: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection.
Aspirin, ASA; Dipyridamole: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection. (Moderate) Monitor for signs and symptoms of bleeding during concomitant platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of bleeding.
Aspirin, ASA; Omeprazole: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection.

Aspirin, ASA; oxyCODONE: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection.
Atenolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Atenolol; Chlorthalidone: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics. (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Auranofin: (Moderate) Due to the inhibition of renal prostaglandins by NSAIDs, concurrent use with other nephrotoxic agents, such as gold compounds, may lead to additive nephrotoxicity. Monitor renal function carefully during concurrent therapy.
azaTHIOprine: (Moderate) NSAIDs should be used with caution in patients receiving immunosuppressives as they may mask fever, pain, swelling and other signs and symptoms of an infection.
Azelastine; Fluticasone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Azilsartan: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Azilsartan; Chlorthalidone: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs

may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Bacitracin: (Major) Avoid concurrent use of bacitracin with nonsteroidal antiinflammatory drugs. Coadministration may increase the risk for drug-induced nephrotoxicity.
Balsalazide: (Moderate) Monitor patients for signs of worsening renal function during coadministration of balsalazide and celecoxib. Coadministration may increase the risk for drug-induced nephrotoxicity. Balsalazide is converted to mesalamine in the gastrointestinal tract; nephrotoxicity has been observed during mesalamine treatment.
Barbiturates: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Beclomethasone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Benazepril: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Benazepril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may

precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Benzgalantamine: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Major) Concurrent use of phenyl salicylate and celecoxib is generally not recommended due to the increased risks of bleeding and nephrotoxicity. Concurrent use of phenyl salicylate and NSAIDs does not produce greater therapeutic effect compared to the use of NSAIDs alone.
Beta-blockers: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Betamethasone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Betaxolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Bictegravir; Emtricitabine; Tenofovir Alafenamide: (Moderate) Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) and tenofovir alafenamide may result in additive nephrotoxicity. Monitor for renal toxicity if concomitant use is required. (Moderate) Monitor for nonsteroidal antiinflammatory drug (NSAID) or emtricitabine-related adverse events during concomitant use. Concomitant use may increase NSAID or emtricitabine concentrations. Coadministration of drugs that reduce renal function or compete for active tubular secretion, such as NSAIDs and emtricitabine, may increase the risk of adverse reactions.
Bismuth Subcitrate Potassium; metroNIDAZOLE; Tetracycline: (Minor) Since celecoxib is metabolized by cytochrome P450 2C9, concurrent administration with metronidazole, which can inhibit this enzyme, may result in increased levels of celecoxib. The clinical significance of this interaction has not been established.
Bismuth Subsalicylate: (Major) Avoid concomitant use of celecoxib with salicylates, such as bismuth subsalicylate, due to an increased risk of gastrointestinal toxicity, with little

or no increase in efficacy.
Bismuth Subsalicylate; metroNIDAZOLE; Tetracycline: (Major) Avoid concomitant use of celecoxib with salicylates, such as bismuth subsalicylate, due to an increased risk of gastrointestinal toxicity, with little or no increase in efficacy. (Minor) Since celecoxib is metabolized by cytochrome P450 2C9, concurrent administration with metronidazole, which can inhibit this enzyme, may result in increased levels of celecoxib. The clinical significance of this interaction has not been established.
Bisoprolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Bisoprolol; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics. (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Bivalirudin: (Moderate) An additive risk of bleeding may be seen in patients receiving anticoagulants in combination with other agents known to increase the risk of bleeding such as nonsteroidal anti-inflammatory drugs (NSAIDs). Monitor clinical and laboratory response closely during concurrent use.
Bosentan: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and bosentan. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and bosentan is a moderate CYP2C9 inducer.
Brexpiprazole: (Moderate) Monitor patients closely for brexpiprazole-related adverse reactions and consider a dosage reduction of brexpiprazole if coadministration with celecoxib is necessary. Celecoxib may enhance the systemic exposure and toxicity of brexpiprazole. In vitro studies indicate that celecoxib is an inhibitor of CYP2D6. Brexpiprazole is a CYP2D6 substrate.
Brimonidine; Timolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Budesonide: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Budesonide; Formoterol: (Moderate) Monitor for gastrointestinal toxicity during

concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Budesonide; Glycopyrrolate; Formoterol: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Bumetanide: (Moderate) If a nonsteroidal anti-inflammatory drug (NSAID) and a diuretic are used concurrently, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic efficacy. Patients taking diuretics and NSAIDs concurrently are at higher risk of developing renal insufficiency. NSAIDs may reduce the natriuretic effect of diuretics in some patients. NSAIDs have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain.
BUPivacaine; Meloxicam: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Busulfan: (Major) Due to the thrombocytopenic effects of busulfan, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, ASA, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Butalbital; Acetaminophen: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Butalbital; Acetaminophen; Caffeine: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Butalbital; Acetaminophen; Caffeine; Codeine: (Moderate) Concomitant use of codeine with celecoxib may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6. (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Butalbital; Aspirin; Caffeine; Codeine: (Major) Concomitant use of analgesic doses of aspirin and celecoxib is generally not recommended due to the increased risk of bleeding. Concurrent use of analgesic doses of aspirin with NSAIDs does not produce a greater therapeutic effect compared to the use of NSAIDs alone. Celecoxib (200 to 400 mg/day) did not interfere with the cardioprotective antiplatelet effect of aspirin (100 to 325 mg) in 2 studies in healthy volunteers and in patients with osteoarthritis and established heart disease. Celecoxib is not a substitute for low dose aspirin for cardiovascular protection. (Moderate) Concomitant use of codeine with celecoxib may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6. (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Calcium Phosphate, Supersaturated: (Moderate) Concomitant use of medicines with potential to alter renal perfusion or function such as nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk of acute phosphate nephropathy in patients taking sodium phosphate monobasic monohydrate; sodium phosphate dibasic anhydrous.
Calcium-channel blockers: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood

pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Candesartan: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Candesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Capreomycin: (Major) Because capreomycin is primarily eliminated by the kidney, coadministration with other potentially nephrotoxic drugs, including nonsteroidal antiinflammatory drugs (NSAIDs), may increase serum concentrations of either drug. Theoretically, the chronic coadministration of these drugs may increase the risk of developing nephrotoxicity, even in patients who have normal renal function. Monitor patients for changes in renal function if these drugs are coadministered.
Captopril: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result

in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Captopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Carmustine, BCNU: (Major) Due to the thrombocytopenic effects of carmustine, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, ASA, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding. These additive effects may not occur for at least 6 weeks after the administration of carmustine due to the delayed myelosuppressive effects of carmustine.
Carteolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Carvedilol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Cefotaxime: (Minor) Cefotaxime's product label states that cephalosporins may potentiate the adverse renal effects of nephrotoxic agents, such as aminoglycosides, nonsteroidal antiinflammatory drugs (NSAIDs), and loop diuretics. Carefully monitor renal function, especially during prolonged therapy or use of high aminoglycoside doses. The majority of reported cases involve the combination of aminoglycosides and cephalothin or cephaloridine, which are associated with dose-related nephrotoxicity as singular agents. Limited but conflicting data with other cephalosporins have been noted.
Celecoxib; Tramadol: (Moderate) Monitor for reduced efficacy of tramadol, signs of opioid withdrawal, seizures, or serotonin syndrome if coadministration with celecoxib is necessary. If celecoxib is discontinued, consider a dose reduction of tramadol and frequently monitor for signs of respiratory depression and sedation. Tramadol is a

CYP2D6 substrate and celecoxib 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.
Chlorambucil: (Major) Due to the thrombocytopenic effects of chlorambucil, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, ASA, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
chlordiazePOXIDE; Amitriptyline: (Moderate) Monitor for an increase in amitriptyline-related adverse reactions if coadministration with celecoxib is necessary; a dose reduction of amitriptyline may be necessary. Concurrent use may increase the plasma concentrations of amitriptyline. Amitriptyline is a CYP2D6 substrate and celecoxib is a CYP2D6 inhibitor.
Chlorothiazide: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Chlorpheniramine: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Chlorpheniramine; Codeine: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate. (Moderate) Concomitant use of codeine with celecoxib may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug

effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6.
Chlorpheniramine; Dextromethorphan: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Chlorpheniramine; HYDROcodone: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate. (Moderate) Concomitant use of hydrocodone with celecoxib may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of celecoxib could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If celecoxib is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Celecoxib is an inhibitor of CYP2D6.
Chlorpheniramine; Ibuprofen; Pseudoephedrine: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers. (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of

chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Chlorpheniramine; Phenylephrine: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Chlorpheniramine; Pseudoephedrine: (Moderate) A dosage adjustment may be warranted for chlorpheniramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of chlorpheniramine. Celecoxib is a CYP2D6 inhibitor, and chlorpheniramine is a CYP2D6 substrate.
Chlorthalidone: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Choline Salicylate; Magnesium Salicylate: (Major) Avoid concomitant use of celecoxib with salicylates, such as magnesium salicylate, due to an increased risk of gastrointestinal toxicity, with little or no increase in efficacy. (Major) Concurrent use of choline salicylate and celecoxib is generally not recommended due to the increased risks of bleeding and nephrotoxicity. Concurrent use of choline salicylate and NSAIDs does not produce greater therapeutic effect compared to the use of NSAIDs alone.
Cholinesterase inhibitors: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
Ciclesonide: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Cidofovir: (Contraindicated) The concomitant administration of cidofovir and nonsteroidal antiinflammatory drugs (NSAIDs) is contraindicated due to the potential for increased nephrotoxicity. NSAIDs should be discontinued 7 days prior to beginning cidofovir.
Cilostazol: (Moderate) Monitor for signs and symptoms of bleeding during concomitant

platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of bleeding.
Cimetidine: (Minor) Since celecoxib is metabolized by cytochrome P450 2C9, concurrent administration with cimetidine, which can inhibit this enzyme, may result in increased levels of celecoxib. The clinical significance of this interaction has not been established.
Ciprofloxacin: (Moderate) Use quinolones and nonsteroidal anti-inflammatory drugs (NSAIDs) concomitantly with caution due to potential increased risk of CNS stimulation and convulsive seizures. NSAIDs in combination with very high doses of quinolones have been shown to provoke convulsions in preclinical studies and postmarketing.
Citalopram: (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.
Citric Acid; Potassium Citrate; Sodium Citrate: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
Cladribine: (Major) Due to the thrombocytopenic effects of cladribine, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Clevidipine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Clofarabine: (Major) Due to the thrombocytopenic effects of clofarabine, an additive risk of bleeding may be seen in patients receiving concomitant NSAIDs. In addition, large

doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
clomiPRAMINE: (Moderate) A dosage adjustment may be warranted for clomipramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of clomipramine. Celecoxib is a CYP2D6 inhibitor, and clomipramine is a CYP2D6 substrate.
Clopidogrel: (Moderate) Monitor for signs and symptoms of bleeding during concomitant platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of bleeding.
cloZAPine: (Moderate) A dosage adjustment may be warranted for clozapine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of clozapine. Celecoxib is a CYP2D6 inhibitor, and clozapine is a CYP2D6 substrate.
Codeine: (Moderate) Concomitant use of codeine with celecoxib may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6.
Codeine; Dexbrompheniramine: (Moderate) Concomitant use of codeine with celecoxib may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6.
Codeine; guaiFENesin: (Moderate) Concomitant use of codeine with celecoxib may

increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6.
Codeine; guaiFENesin; Pseudoephedrine: (Moderate) Concomitant use of codeine with celecoxib may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6.
Codeine; Phenylephrine; Promethazine: (Moderate) Concomitant use of codeine with celecoxib may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6.
Codeine; Promethazine: (Moderate) Concomitant use of codeine with celecoxib may increase codeine plasma concentrations, but decrease the plasma concentration of the

active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of celecoxib 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 celecoxib 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. Celecoxib is an inhibitor of CYP2D6.
Colistimethate, Colistin, Polymyxin E: (Major) The administration of colistimethate sodium may increase the risk of developing nephrotoxicity, even in patients who have normal renal function. Nonsteroidal antiinflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when used concurrently. Monitor patients for changes in renal function if these drugs are coadministered. Since colistimethate sodium is eliminated by the kidney, coadministration with other potentially nephrotoxic drugs, including nonsteroidal antiinflammatory drugs (NSAIDs), may theoretically increase serum concentrations of either drug.
Colistin: (Major) The administration of colistimethate sodium may increase the risk of developing nephrotoxicity, even in patients who have normal renal function. Nonsteroidal antiinflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when used concurrently. Monitor patients for changes in renal function if these drugs are coadministered. Since colistimethate sodium is eliminated by the kidney, coadministration with other potentially nephrotoxic drugs, including nonsteroidal antiinflammatory drugs (NSAIDs), may theoretically increase serum concentrations of either drug.
Corticosteroids: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Cortisone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
cycloSPORINE: (Moderate) Serum creatinine,potassium concentrations, and cyclosporine concentrations should be closely monitored when systemic cyclosporine is given with nonsteroidal antiinflammatory drugs (NSAIDs). Renal dysfunction associated with cyclosporine may be potentiated by concurrent usage of NSAIDs. The effects of NSAIDs on the production of renal prostaglandins may cause changes in the elimination of cyclosporine. Potentiation of renal dysfunction may especially occur in a dehydrated patient. Patients should be monitored for signs and symptoms of cyclosporine toxicity

and infection, as NSAIDs may mask fever, pain, or swelling.
Cytarabine, ARA-C: (Major) The main toxic effect of cytarabine, ARA-C is bone marrow suppression with leukopenia, thrombocytopenia and anemia. Due to the thrombocytopenic effects of cytarabine, an additive risk of bleeding may be seen in patients receiving concomitant NSAIDs. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding. Dipyridamole can block membrane transport of cytarabine in tumor cells, therefore decreasing its antineoplastic activity.
Dabigatran: (Major) Educate patients about the signs of increased bleeding and the need to report these signs to a healthcare provider immediately if coadministration of dabigatran and a nonsteroidal antiinflammatory drug (NSAID) is necessary. Dabigatran can cause significant and, sometimes, fatal bleeding. This risk may be increased by concurrent use of chronic NSAID therapy.
Dabrafenib: (Major) The concomitant use of dabrafenib and celecoxib may lead to decreased celecoxib concentrations and loss of efficacy. Use of an alternative agent is recommended. If concomitant use of these agents is unavoidable, monitor patients for loss of celecoxib efficacy; a celecoxib dose adjustment may be necessary. Dabrafenib is a weak CYP2C9 inducer and celecoxib is a sensitive CYP2C9 substrate. Concomitant use of dabrafenib with a single dose of another sensitive CYP2C9 substrate decreased the AUC value of the sensitive CYP2C9 substrate by 37%.
Dacarbazine, DTIC: (Major) Leukopenia and thrombocytopenia are common toxicities of dacarbazine, DTIC. Due to the thrombocytopenic effects of dacarbazine, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, ASA, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Dalteparin: (Moderate) An additive risk of bleeding may be seen in patients receiving anticoagulants in combination with other agents known to increase the risk of bleeding such as nonsteroidal antiinflammatory drugs (NSAIDs). Monitor clinical and laboratory response closely during concurrent use.
Darifenacin: (Moderate) Monitor patients closely for darifenacin-related adverse reactions and consider a dosage reduction of darifenacin if coadministration with celecoxib is necessary. Celecoxib may enhance the systemic exposure and toxicity of darifenacin. In vitro studies indicate that celecoxib is an inhibitor of CYP2D6. Darifenacin is a CYP2D6 substrate.
Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Moderate) Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) and tenofovir alafenamide may result in additive nephrotoxicity. Monitor for renal toxicity if concomitant use is required. (Moderate) Monitor for nonsteroidal antiinflammatory drug (NSAID) or emtricitabine-related adverse events during concomitant use. Concomitant use may

increase NSAID or emtricitabine concentrations. Coadministration of drugs that reduce renal function or compete for active tubular secretion, such as NSAIDs and emtricitabine, may increase the risk of adverse reactions.
Dasatinib: (Major) Due to the thrombocytopenic and possible platelet inhibiting effects of dasatinib, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors (including aspirin), strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding. Caution should be exercised if patients are required to take medications that inhibit platelet function or anticoagulants concomitantly with dasatinib.
Deferasirox: (Moderate) Because gastric ulceration and GI bleeding have been reported in patients taking deferasirox, use caution when coadministering with other drugs known to increase the risk of peptic ulcers or gastric hemorrhage including NSAIDs. In addition, coadministration of deferasirox with other potentially nephrotoxic drugs, including NSAIDs, may increase the acute renal failure. Monitor serum creatinine and/or creatinine clearance in patients who are receiving deferasirox and nephrotoxic drugs concomitantly.
Deflazacort: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Delafloxacin: (Moderate) Use quinolones and nonsteroidal anti-inflammatory drugs (NSAIDs) concomitantly with caution due to potential increased risk of CNS stimulation and convulsive seizures. NSAIDs in combination with very high doses of quinolones have been shown to provoke convulsions in preclinical studies and postmarketing.
Desipramine: (Moderate) A dosage adjustment may be warranted for desipramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of desipramine. Celecoxib is a CYP2D6 inhibitor, and desipramine is a CYP2D6 substrate.
Desmopressin: (Major) Additive hyponatremic effects may be seen in patients treated with desmopressin and drugs associated with hyponatremia including NSAIDs. Use combination with caution, and monitor patients for signs and symptoms of hyponatremia. A woman who took both desmopressin and ibuprofen was found in a comatose state. As her serum sodium concentration was 121 mmol/L, and her plasma osmolality was low in the presence of a high-normal urine osmolality and normal sodium excretion, she was treated with fluid restriction. Her serum sodium concentration was 124 mmol/L within a day and was 135 mmol/L by the second day. The woman had previously received desmopressin without the development of clinical symptoms of hyponatremia.
Desvenlafaxine: (Moderate) Platelet aggregation may be impaired by desvenlafaxine due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication

(e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be monitored for signs and symptoms of bleeding while taking desvenlafaxine with NSAIDs.
dexAMETHasone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Diclofenac: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Diclofenac; miSOPROStol: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Diflunisal: (Major) Avoid concomitant use of diflunisal with any other NSAID, including COX-2 inhibitors, due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Digoxin: (Moderate) Monitor digoxin concentrations before and during concomitant use of celecoxib and reduce the digoxin dose if necessary. Elevated digoxin concentrations and prolonged digoxin half-life have been observed when celecoxib has been coadministered with digoxin.
dilTIAZem: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
diphenhydrAMINE; Ibuprofen: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
diphenhydrAMINE; Naproxen: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.

Dipyridamole: (Moderate) Monitor for signs and symptoms of bleeding during concomitant platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of bleeding.
DOCEtaxel: (Major) Due to the thrombocytopenic effects of docetaxel, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors (including aspirin), strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Dolasetron: (Moderate) Monitor patients closely for dolasetron-related adverse reactions and consider a dosage reduction of dolasetron if coadministration with celecoxib is necessary. Celecoxib may enhance the systemic exposure and toxicity of dolasetron. In vitro studies indicate that celecoxib is an inhibitor of CYP2D6. Dolasetron is a CYP2D6 substrate.
Donepezil: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
Donepezil; Memantine: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
Doravirine; lamiVUDine; Tenofovir disoproxil fumarate: (Moderate) Avoid administering tenofovir, PMPA concurrently with or recently after a nephrotoxic agent, such as high-dose or multiple nonsteroidal antiinflammatory drugs (NSAIDs). Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after high-dose or multiple NSAIDs were initiated in patients who appeared stable on tenofovir. Consider alternatives to NSAIDs in patients at risk for renal dysfunction. If these drugs must be coadministered, carefully monitor the estimated creatinine creatinine, serum phosphorus, urine glucose, and urine protein prior to, and periodically during, treatment.
Dorzolamide; Timolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive

effect of beta-blockers may be diminished by NSAIDs.
Doxazosin: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Doxepin: (Moderate) Monitor for an increase in doxepin-related adverse reactions if concomitant use of celecoxib is necessary. Concomitant use may increase doxepin exposure; doxepin is primarily metabolized by CYP2C19 and CYP2D6 and celecoxib is a CYP2D6 inhibitor.
DOXOrubicin Liposomal: (Major) Avoid coadministration of celecoxib and doxorubicin due to increased systemic exposure of doxorubicin resulting in increased treatment-related adverse reactions. Celecoxib is a CYP2D6 inhibitor, and doxorubicin is a CYP2D6 substrate. Clinically significant interactions have been reported when doxorubicin was coadministered with inhibitors of CYP2D6, resulting in increased concentration and clinical effect of doxorubicin.
DOXOrubicin: (Major) Avoid coadministration of celecoxib and doxorubicin due to increased systemic exposure of doxorubicin resulting in increased treatment-related adverse reactions. Celecoxib is a CYP2D6 inhibitor, and doxorubicin is a CYP2D6 substrate. Clinically significant interactions have been reported when doxorubicin was coadministered with inhibitors of CYP2D6, resulting in increased concentration and clinical effect of doxorubicin.
Drospirenone: (Minor) Drospirenone has antimineralocorticoid effects; the progestin may increase serum potassium. Other drugs that may have additive effects on serum potassium with drospirenone include chronic treatment with NSAIDs, and monitoring of serum potassium in the 1st month of concurrent therapy is recommended.
Drospirenone; Estetrol: (Minor) Drospirenone has antimineralocorticoid effects; the progestin may increase serum potassium. Other drugs that may have additive effects on serum potassium with drospirenone include chronic treatment with NSAIDs, and monitoring of serum potassium in the 1st month of concurrent therapy is recommended.

Drospirenone; Estradiol: (Minor) Drospirenone has antimineralocorticoid effects; the progestin may increase serum potassium. Other drugs that may have additive effects on serum potassium with drospirenone include chronic treatment with NSAIDs, and monitoring of serum potassium in the 1st month of concurrent therapy is recommended.
Drospirenone; Ethinyl Estradiol: (Minor) Drospirenone has antimineralocorticoid effects; the progestin may increase serum potassium. Other drugs that may have additive effects on serum potassium with drospirenone include chronic treatment with NSAIDs, and monitoring of serum potassium in the 1st month of concurrent therapy is recommended.
Drospirenone; Ethinyl Estradiol; Levomefolate: (Minor) Drospirenone has antimineralocorticoid effects; the progestin may increase serum potassium. Other drugs that may have additive effects on serum potassium with drospirenone include chronic treatment with NSAIDs, and monitoring of serum potassium in the 1st month of concurrent therapy is recommended.
DULoxetine: (Moderate) Monitor for signs and symptoms of bleeding during concomitant duloxetine 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.
Edoxaban: (Major) An additive risk of bleeding may be seen in patients receiving anticoagulants in combination with other agents known to increase the risk of bleeding such as nonsteroidal antiinflammatory drugs (NSAIDs). Monitor clinical and laboratory response closely during concurrent use.
Efavirenz: (Minor) Efavirenz inhibits CYP2C9 and CYP2C19 in the range of observed efavirenz plasma concentrations. Efavirenz may inhibit the metabolism of the celecoxib since it is a substrate for CYP2C9.
Efavirenz; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) Avoid administering tenofovir, PMPA concurrently with or recently after a nephrotoxic agent, such as high-dose or multiple nonsteroidal antiinflammatory drugs (NSAIDs). Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after high-dose or multiple NSAIDs were initiated in patients who appeared stable on tenofovir. Consider alternatives to NSAIDs in patients at risk for renal dysfunction. If these drugs must be coadministered, carefully monitor the estimated creatinine creatinine, serum phosphorus, urine glucose, and urine protein prior to, and periodically during, treatment. (Moderate) Monitor for nonsteroidal antiinflammatory drug (NSAID) or emtricitabine-related adverse events during concomitant use. Concomitant use may increase NSAID or emtricitabine concentrations. Coadministration of drugs that reduce renal function or compete for active tubular secretion, such as

NSAIDs and emtricitabine, may increase the risk of adverse reactions. (Minor) Efavirenz inhibits CYP2C9 and CYP2C19 in the range of observed efavirenz plasma concentrations. Efavirenz may inhibit the metabolism of the celecoxib since it is a substrate for CYP2C9.
Efavirenz; lamiVUDine; Tenofovir Disoproxil Fumarate: (Moderate) Avoid administering tenofovir, PMPA concurrently with or recently after a nephrotoxic agent, such as high-dose or multiple nonsteroidal antiinflammatory drugs (NSAIDs). Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after high-dose or multiple NSAIDs were initiated in patients who appeared stable on tenofovir. Consider alternatives to NSAIDs in patients at risk for renal dysfunction. If these drugs must be coadministered, carefully monitor the estimated creatinine creatinine, serum phosphorus, urine glucose, and urine protein prior to, and periodically during, treatment. (Minor) Efavirenz inhibits CYP2C9 and CYP2C19 in the range of observed efavirenz plasma concentrations. Efavirenz may inhibit the metabolism of the celecoxib since it is a substrate for CYP2C9.
Elexacaftor; tezacaftor; ivacaftor: (Minor) Increased monitoring is recommended if ivacaftor is administered concurrently with CYP2C9 substrates, such as celecoxib. In vitro studies showed ivacaftor to be a weak inhibitor of CYP2C9. Co-administration may lead to increased exposure to CYP2C9 substrates; however, the clinical impact of this has not yet been determined.
Eliglustat: (Moderate) In extensive CYP2D6 metabolizers (EM) with mild hepatic impairment, coadministration of celecoxib and eliglustat requires dosage reduction of eliglustat to 84 mg PO once daily. Celecoxib is a weak CYP2D6 inhibitor; eliglustat is a CYP3A and CYP2D6 substrate. Coadministration with CYP2D6 inhibitors, such as celecoxib, may increase eliglustat exposure and the risk of serious adverse events (e.g., QT prolongation and cardiac arrhythmias).
Eltrombopag: (Moderate) Eltrombopag is a UDP-glucuronyltransferase inhibitor. NSAIDs are a substrate of UDP-glucuronyltransferases. The significance or effect of this interaction is not known; however, elevated concentrations of the NSAID are possible. Monitor patients for adverse reactions if eltrombopag is administered with an NSAID.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Alafenamide: (Moderate) Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) and tenofovir alafenamide may result in additive nephrotoxicity. Monitor for renal toxicity if concomitant use is required. (Moderate) Monitor for nonsteroidal antiinflammatory drug (NSAID) or emtricitabine-related adverse events during concomitant use. Concomitant use may increase NSAID or emtricitabine concentrations. Coadministration of drugs that reduce renal function or compete for active tubular secretion, such as NSAIDs and emtricitabine, may increase the risk of adverse reactions. (Moderate) The plasma concentrations of celecoxib may be decreased when administered concurrently with elvitegravir. Patients may experience a decreased analgesic effect when these drugs are coadministered. Elvitegravir is a CYP2C9 inducer, while celecoxib is a CYP2C9 substrate.

Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) Avoid administering tenofovir, PMPA concurrently with or recently after a nephrotoxic agent, such as high-dose or multiple nonsteroidal antiinflammatory drugs (NSAIDs). Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after high-dose or multiple NSAIDs were initiated in patients who appeared stable on tenofovir. Consider alternatives to NSAIDs in patients at risk for renal dysfunction. If these drugs must be coadministered, carefully monitor the estimated creatinine creatinine, serum phosphorus, urine glucose, and urine protein prior to, and periodically during, treatment. (Moderate) Monitor for nonsteroidal antiinflammatory drug (NSAID) or emtricitabine-related adverse events during concomitant use. Concomitant use may increase NSAID or emtricitabine concentrations. Coadministration of drugs that reduce renal function or compete for active tubular secretion, such as NSAIDs and emtricitabine, may increase the risk of adverse reactions. (Moderate) The plasma concentrations of celecoxib may be decreased when administered concurrently with elvitegravir. Patients may experience a decreased analgesic effect when these drugs are coadministered. Elvitegravir is a CYP2C9 inducer, while celecoxib is a CYP2C9 substrate.
Emtricitabine: (Moderate) Monitor for nonsteroidal antiinflammatory drug (NSAID) or emtricitabine-related adverse events during concomitant use. Concomitant use may increase NSAID or emtricitabine concentrations. Coadministration of drugs that reduce renal function or compete for active tubular secretion, such as NSAIDs and emtricitabine, may increase the risk of adverse reactions.
Emtricitabine; Rilpivirine; Tenofovir alafenamide: (Moderate) Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) and tenofovir alafenamide may result in additive nephrotoxicity. Monitor for renal toxicity if concomitant use is required. (Moderate) Monitor for nonsteroidal antiinflammatory drug (NSAID) or emtricitabine-related adverse events during concomitant use. Concomitant use may increase NSAID or emtricitabine concentrations. Coadministration of drugs that reduce renal function or compete for active tubular secretion, such as NSAIDs and emtricitabine, may increase the risk of adverse reactions.
Emtricitabine; Rilpivirine; Tenofovir Disoproxil Fumarate: (Moderate) Avoid administering tenofovir, PMPA concurrently with or recently after a nephrotoxic agent, such as high-dose or multiple nonsteroidal antiinflammatory drugs (NSAIDs). Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after high-dose or multiple NSAIDs were initiated in patients who appeared stable on tenofovir. Consider alternatives to NSAIDs in patients at risk for renal dysfunction. If these drugs must be coadministered, carefully monitor the estimated creatinine creatinine, serum phosphorus, urine glucose, and urine protein prior to, and periodically during, treatment. (Moderate) Monitor for nonsteroidal antiinflammatory drug (NSAID) or emtricitabine-related adverse events during concomitant use.

Concomitant use may increase NSAID or emtricitabine concentrations. Coadministration of drugs that reduce renal function or compete for active tubular secretion, such as NSAIDs and emtricitabine, may increase the risk of adverse reactions.
Emtricitabine; Tenofovir alafenamide: (Moderate) Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) and tenofovir alafenamide may result in additive nephrotoxicity. Monitor for renal toxicity if concomitant use is required. (Moderate) Monitor for nonsteroidal antiinflammatory drug (NSAID) or emtricitabine-related adverse events during concomitant use. Concomitant use may increase NSAID or emtricitabine concentrations. Coadministration of drugs that reduce renal function or compete for active tubular secretion, such as NSAIDs and emtricitabine, may increase the risk of adverse reactions.
Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) Avoid administering tenofovir, PMPA concurrently with or recently after a nephrotoxic agent, such as high-dose or multiple nonsteroidal antiinflammatory drugs (NSAIDs). Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after high-dose or multiple NSAIDs were initiated in patients who appeared stable on tenofovir. Consider alternatives to NSAIDs in patients at risk for renal dysfunction. If these drugs must be coadministered, carefully monitor the estimated creatinine creatinine, serum phosphorus, urine glucose, and urine protein prior to, and periodically during, treatment. (Moderate) Monitor for nonsteroidal antiinflammatory drug (NSAID) or emtricitabine-related adverse events during concomitant use. Concomitant use may increase NSAID or emtricitabine concentrations. Coadministration of drugs that reduce renal function or compete for active tubular secretion, such as NSAIDs and emtricitabine, may increase the risk of adverse reactions.
Enalapril, Enalaprilat: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Enalapril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic

use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Enoxaparin: (Major) Whenever possible, discontinue agents which may enhance the risk of hemorrhage, including nonsteroidal antiinflammatory drugs, before initiation of enoxaparin therapy. If coadministration is essential, conduct close clinical and laboratory monitoring.
Entecavir: (Moderate) The manufacturer of entecavir recommends monitoring for adverse effects when coadministered with NSAIDs. Entecavir is primarily eliminated by the kidneys; NSAIDs can affect renal function. Concurrent administration may increase the serum concentrations of entecavir and adverse events.
Enzalutamide: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and enzalutamide. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and enzalutamide is a moderate CYP2C9 inducer.
Eplerenone: (Major) Monitor serum potassium and serum creatinine concentrations within 3 to 7 days of initiating coadministration of eplerenone and nonsteroidal antiinflammatory drugs (NSAIDs), and monitor blood pressure. The concomitant use of other potassium-sparing antihypertensives with NSAIDs has been shown to reduce the antihypertensive effect in some patients and result in severe hyperkalemia in patients with impaired renal function. Patients who develop hyperkalemia may continue eplerenone with proper dose adjustment; eplerenone dose reduction decreases potassium concentrations.
Epoprostenol: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.
Eptifibatide: (Moderate) Monitor for signs and symptoms of bleeding during concomitant platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of bleeding.
Erlotinib: (Moderate) Monitor for symptoms of gastrointestinal (GI) perforation (e.g., severe abdominal pain, fever, nausea, and vomiting) if coadministration of erlotinib with nonsteroidal antiinflammatory drugs (NSAIDs) is necessary. Permanently discontinue erlotinib in patients who develop GI perforation. The pooled incidence of GI perforation clinical trials of erlotinib ranged from 0.1% to 0.4%, including fatal cases. Patients receiving concomitant NSAIDs may be at increased risk of perforation.
Escitalopram: (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.
Esmolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Ethacrynic Acid: (Moderate) If a nonsteroidal anti-inflammatory drug (NSAID) and a diuretic are used concurrently, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic efficacy. Patients taking diuretics and NSAIDs concurrently are at higher risk of developing renal insufficiency. NSAIDs may reduce the natriuretic effect of diuretics in some patients. NSAIDs have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain.
Ethanol: (Major) Advise patients to avoid alcohol and alcohol-containing products while taking NSAIDs. Concomitant ingestion of alcohol with NSAIDs increases the risk of developing gastric irritation and GI mucosal bleeding. Alcohol is a mucosal irritant and NSAIDs decrease platelet aggregation. Routine ingestion of alcohol and NSAIDs can cause significant GI bleeding, which may or may not be overt. Even occasional concomitant use of NSAIDs and alcohol should be avoided. Chronic alcohol ingestion is often associated with hypoprothrombinemia and this condition increases the risk of bleeding.
Ethiodized Oil: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when given to patients receiving a contrast agents. When possible, withhold NSAID therapy during administration of a contrast agent.
Etodolac: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Felodipine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related

decreases in renal function and an increased risk of stroke and coronary artery disease.
Fenofibric Acid: (Minor) At therapeutic concentrations, fenofibric acid is a mild-to-moderate inhibitor of CYP2C9. Concomitant use of fenofibric acid with CYP2C9 substrates, such as celecoxib, has not been formally studied. Fenofibric acid may theoretically increase plasma concentrations of CYP2C9 substrates and could lead to toxicity for drugs that have a narrow therapeutic range. Monitor the therapeutic effect of celecoxib during coadministration with fenofibric acid.
Fenoprofen: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Flecainide: (Moderate) Monitor for an increase in flecainide-related adverse reactions, including QT prolongation, if coadministration with celecoxib is necessary. Flecainide is a CYP2D6 substrate and celecoxib is a weak CYP2D6 inhibitor. Plasma concentrations of flecainide may increase, especially in extensive CYP2D6 metabolizers.
Floxuridine: (Major) Due to the thrombocytopenic effects of floxuridine, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Fluconazole: (Moderate) Monitor for celecoxib-related adverse effects and consider a celecoxib dosage reduction as appropriate based on response if concomitant use with fluconazole is necessary. Concomitant use may increase celecoxib exposure. Celecoxib is a CYP2C9 substrate and fluconazole is a moderate CYP2C9 inhibitor. Concomitant use increased celecoxib overall exposure by 2-fold.
Fludrocortisone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Flunisolide: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
FLUoxetine: (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.
fluPHENAZine: (Moderate) A dosage adjustment may be warranted for fluphenazine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of fluphenazine. Celecoxib is a CYP2D6 inhibitor, and fluphenazine is a CYP2D6 substrate.

Flurbiprofen: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Fluticasone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Fluticasone; Salmeterol: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Fluticasone; Umeclidinium; Vilanterol: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Fluticasone; Vilanterol: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
fluvoxaMINE: (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.
Fondaparinux: (Moderate) An additive risk of bleeding may be seen in patients receiving anticoagulants in combination with other agents known to increase the risk of bleeding such as nonsteroidal antiinflammatory drugs (NSAIDs). Monitor clinical and laboratory response closely during concurrent use.
Formoterol; Mometasone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Foscarnet: (Minor) The risk of renal toxicity may be increased if foscarnet is used in conjuction with other nephrotoxic agents, such as nonsteroidal antiinflammatory drugs (NSAIDs). Monitor renal function carefully during concurrent therapy.
Fosinopril: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Fosinopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor

and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Fosphenytoin: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and phenytoin. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and phenytoin is a moderate CYP2C9 inducer.
Furosemide: (Moderate) If a nonsteroidal anti-inflammatory drug (NSAID) and a diuretic are used concurrently, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic efficacy. Patients taking diuretics and NSAIDs concurrently are at higher risk of developing renal insufficiency. NSAIDs may reduce the natriuretic effect of diuretics in some patients. NSAIDs have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain.
Galantamine: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
Ganciclovir: (Minor) Concurrent use of nephrotoxic agents, such as NSAIDs, with ganciclovir should be done cautiously to avoid additive nephrotoxicity. Monitor renal function carefully if concomitant therapy is required.
Garlic, Allium sativum: (Minor) Garlic, Allium sativum may produce clinically-significant antiplatelet effects; until more data are available, garlic should be used cautiously in patients receiving drugs with a known potential risk for bleeding such as nonsteroidal antiinflammatory drugs (NSAIDs).
Gemifloxacin: (Moderate) Use quinolones and nonsteroidal anti-inflammatory drugs

(NSAIDs) concomitantly with caution due to potential increased risk of CNS stimulation and convulsive seizures. NSAIDs in combination with very high doses of quinolones have been shown to provoke convulsions in preclinical studies and postmarketing.
Gentamicin: (Moderate) It is possible that additive nephrotoxicity may occur in patients who receive nonsteroidal anti-inflammatory drugs (NSAIDs) concurrently with other nephrotoxic agents, such as gentamicin.
Gepotidacin: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
Ginger, Zingiber officinale: (Minor) Patients receiving regular therapy with nonsteroidal antiinflammatory drugs (NSAIDs) should use ginger with caution, due to a theoretical risk of bleeding resulting from additive pharmacology related to the COX enzymes. However, clinical documentation of interactions is lacking. Several pungent constituents of ginger (Zingiber officinale) are reported to inhibit arachidonic acid (AA) induced platelet activation in human whole blood. The constituent (8)-paradol is the most potent inhibitor of COX-1 and exhibits the greatest anti-platelet activity versus other gingerol analogues. The mechanism of ginger-associated platelet inhibition may be related to decreased COX-1/Thomboxane synthase enzymatic activity.
Ginkgo, Ginkgo biloba: (Moderate) Monitor for signs or symptoms of bleeding with coadministration of ginkgo biloba and NSAIDs as an increased bleeding risk may occur. Although data are mixed, ginkgo biloba is reported to inhibit platelet aggregation and several case reports describe bleeding complications with ginkgo biloba, with or without concomitant drug therapy.
Glimepiride: (Moderate) NSAIDs may enhance hypoglycemia in diabetic patients via inhibition of prostaglandin synthesis, which indirectly increases insulin secretion. If NSAIDs are administered or discontinued in patients receiving oral antidiabetic agents, patients should be monitored for hypoglycemia or loss of blood glucose control. No clinically significant interaction between sulindac at daily doses of 400 mg and oral hypoglycemic agents has been observed. Sulindac, its sulfide metabolite, and sulfonylureas are highly bound to protein. Sulindac could displace the sulfonylureas, altering hypoglycemic activity. Careful patient monitoring is recommended to ensure that no change in their diabetes medicine dosage is required. A sulfonylurea dose adjustment may be needed, especially if sulindac doses greater than 400 mg daily are used or if the drug combination is used in patients with renal impairment or other metabolic defects that might increase sulindac blood concentrations.

glipiZIDE: (Moderate) NSAIDs may enhance hypoglycemia in diabetic patients via inhibition of prostaglandin synthesis, which indirectly increases insulin secretion. If NSAIDs are administered or discontinued in patients receiving oral antidiabetic agents, patients should be monitored for hypoglycemia or loss of blood glucose control. No clinically significant interaction between sulindac at daily doses of 400 mg and oral hypoglycemic agents has been observed. Sulindac, its sulfide metabolite, and sulfonylureas are highly bound to protein. Sulindac could displace the sulfonylureas, altering hypoglycemic activity. Careful patient monitoring is recommended to ensure that no change in their diabetes medicine dosage is required. A sulfonylurea dose adjustment may be needed, especially if sulindac doses greater than 400 mg daily are used or if the drug combination is used in patients with renal impairment or other metabolic defects that might increase sulindac blood concentrations.
glipiZIDE; metFORMIN: (Moderate) NSAIDs may enhance hypoglycemia in diabetic patients via inhibition of prostaglandin synthesis, which indirectly increases insulin secretion. If NSAIDs are administered or discontinued in patients receiving oral antidiabetic agents, patients should be monitored for hypoglycemia or loss of blood glucose control. No clinically significant interaction between sulindac at daily doses of 400 mg and oral hypoglycemic agents has been observed. Sulindac, its sulfide metabolite, and sulfonylureas are highly bound to protein. Sulindac could displace the sulfonylureas, altering hypoglycemic activity. Careful patient monitoring is recommended to ensure that no change in their diabetes medicine dosage is required. A sulfonylurea dose adjustment may be needed, especially if sulindac doses greater than 400 mg daily are used or if the drug combination is used in patients with renal impairment or other metabolic defects that might increase sulindac blood concentrations.
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antidiabetic agents, patients should be monitored for hypoglycemia or loss of blood glucose control. No clinically significant interaction between sulindac at daily doses of 400 mg and oral hypoglycemic agents has been observed. Sulindac, its sulfide metabolite, and sulfonylureas are highly bound to protein. Sulindac could displace the sulfonylureas, altering hypoglycemic activity. Careful patient monitoring is recommended to ensure that no change in their diabetes medicine dosage is required. A sulfonylurea dose adjustment may be needed, especially if sulindac doses greater than 400 mg daily are used or if the drug combination is used in patients with renal impairment or other metabolic defects that might increase sulindac blood concentrations.
Gold: (Moderate) Due to the inhibition of renal prostaglandins by NSAIDs, concurrent use with other nephrotoxic agents, such as gold compounds, may lead to additive nephrotoxicity. Monitor renal function carefully during concurrent therapy.
Grapefruit juice: (Major) Advise patients to avoid grapefruit and grapefruit juice during celecoxib treatment due to the risk of increased celecoxib exposure and adverse reactions. Celecoxib is a CYP2C9 substrate and grapefruit juice is a CYP2C9 inhibitor.
guanFACINE: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.
Haloperidol: (Moderate) A dosage adjustment may be warranted for haloperidol if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of haloperidol. Celecoxib is a CYP2D6 inhibitor, and haloperidol is a CYP2D6 substrate.
Heparin: (Moderate) An additive risk of bleeding may be seen in patients receiving anticoagulants in combination with other agents known to increase the risk of bleeding such as nonsteroidal antiinflammatory drugs (NSAIDs). Monitor clinical and laboratory response closely during concurrent use.
Homatropine; HYDROcodone: (Moderate) Concomitant use of hydrocodone with celecoxib may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of celecoxib could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If celecoxib is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Celecoxib is an inhibitor of CYP2D6.
Hyaluronidase, Recombinant; Immune Globulin: (Moderate) Immune Globulin (IG) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Patients predisposed to acute renal failure include

patients receiving known nephrotoxic drugs like nonsteroidal anti-inflammatory drugs (NSAIDs) and salicylates. Coadminister IG products at the minimum concentration available and the minimum rate of infusion practicable. Also, closely monitor renal function.
hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
hydroCHLOROthiazide, HCTZ; Moexipril: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
HYDROcodone: (Moderate) Concomitant use of hydrocodone with celecoxib may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of celecoxib could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If celecoxib is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Celecoxib is an inhibitor of CYP2D6.
HYDROcodone; Ibuprofen: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers. (Moderate) Concomitant use of hydrocodone

with celecoxib may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of celecoxib could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If celecoxib is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Celecoxib is an inhibitor of CYP2D6.
Hydrocortisone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate; Sodium Biphosphate: (Major) Concurrent use of phenyl salicylate and celecoxib is generally not recommended due to the increased risks of bleeding and nephrotoxicity. Concurrent use of phenyl salicylate and NSAIDs does not produce greater therapeutic effect compared to the use of NSAIDs alone.
Ibandronate: (Moderate) Monitor renal function and for gastrointestinal adverse events during concurrent use of intravenous or oral ibandronate, respectively, and nonsteroidal antiinflammatory drugs. Acute renal failure has been observed with intravenous ibandronate and concomitant use of other nephrotoxic agents may increase this risk. Additionally, the oral formulations of both medications have been associated with gastrointestinal irritation although data suggest concomitant use introduces little additional risk for adverse effects for most patients.
Ibritumomab Tiuxetan: (Major) During and after therapy, avoid the concomitant use of Yttrium (Y)-90 ibrutumomab tiuxetan with drugs that interfere with platelet function such as nonsteroidal antiinflammatory drugs (NSAIDs); the risk of bleeding may be increased. If coadministration with NSAIDs is necessary, monitor platelet counts more frequently for evidence of thrombocytopenia. (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
Ibuprofen lysine: (Major) Because ibuprofen lysine exerts similar pharmacologic characteristics to other systemic NSAIDs, including COX-2 inhibitors, additive pharmacodynamic effects, including a potential increase for additive adverse GI effects, may be seen if ibuprofen lysine is used with other NSAIDs. In general, concurrent use of ibuprofen lysine and another NSAID should be avoided.
Ibuprofen: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI

perforation, or peptic ulcers.
Ibuprofen; Famotidine: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Ibuprofen; Pseudoephedrine: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Iloprost: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Imipramine: (Moderate) A dosage adjustment may be warranted for imipramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of imipramine. Celecoxib is a CYP2D6 inhibitor, and imipramine is a CYP2D6 substrate.
Immune Globulin IV, IVIG, IGIV: (Moderate) Immune Globulin (IG) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Patients predisposed to acute renal failure include patients receiving known nephrotoxic drugs like nonsteroidal anti-inflammatory drugs (NSAIDs) and salicylates. Coadminister IG products at the minimum concentration available and the minimum rate of infusion practicable. Also, closely monitor renal function.
Indapamide: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may reduce the natriuretic effect of diuretics in some patients. NSAIDS have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain. Patients taking diuretics and NSAIDS concurrently are at higher risk of developing renal insufficiency. If an NSAID and a diuretic are used concurrently, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic efficacy.
Indomethacin: (Major) Avoid concomitant use of celecoxib with any other NSAID due to

the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Inotersen: (Moderate) Use caution with concomitant use of inotersen and nonsteroidal antiinflammatory drugs (NSAIDs) due to the risk of glomerulonephritis and nephrotoxicity as well as the potential risk of bleeding from thrombocytopenia. Consider discontinuation of NSAIDs in a patient taking inotersen with a platelet count of less than 50,000 per microliter.
Iodine; Potassium Iodide, KI: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
Iodixanol: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when given to patients receiving a contrast agents. When possible, withhold NSAID therapy during administration of a contrast agent.
Iohexol: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when given to patients receiving a contrast agents. When possible, withhold NSAID therapy during administration of a contrast agent.
Iomeprol: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when given to patients receiving a contrast agents. When possible, withhold NSAID therapy during administration of a contrast agent.
Ionic Contrast Media: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when given to patients receiving a contrast agents. When possible, withhold NSAID therapy during administration of a contrast agent.
Iopamidol: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when given to patients receiving a contrast agents. When possible, withhold NSAID therapy during administration of a contrast agent.
Iopromide: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when given to patients receiving a contrast agents. When possible, withhold NSAID therapy during administration of a contrast agent.
Ioversol: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when given to patients receiving a contrast agents. When possible, withhold NSAID therapy during administration of a contrast agent.
Irbesartan: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Irbesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers

may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Isosulfan Blue: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when given to patients receiving a contrast agents. When possible, withhold NSAID therapy during administration of a contrast agent.
Isradipine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Ivacaftor: (Minor) Increased monitoring is recommended if ivacaftor is administered concurrently with CYP2C9 substrates, such as celecoxib. In vitro studies showed ivacaftor to be a weak inhibitor of CYP2C9. Co-administration may lead to increased exposure to CYP2C9 substrates; however, the clinical impact of this has not yet been determined.
Ivosidenib: (Moderate) Monitor for loss of efficacy of celecoxib during coadministration of ivosidenib; a celecoxib dose adjustment may be necessary. Celecoxib is a sensitive substrate of CYP2C9; ivosidenib may induce CYP2C9 leading to decreased celecoxib concentrations.
Ketoprofen: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.

Ketorolac: (Contraindicated) Concomitant use of ketorolac with another NSAID is contraindicated. Increased adverse gastrointestinal effects are possible if ketorolac is used with other systemic nonsteroidal antiinflammatory drugs (NSAIDs), including COX-2 inhibitors.
Labetalol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
lamiVUDine; Tenofovir Disoproxil Fumarate: (Moderate) Avoid administering tenofovir, PMPA concurrently with or recently after a nephrotoxic agent, such as high-dose or multiple nonsteroidal antiinflammatory drugs (NSAIDs). Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after high-dose or multiple NSAIDs were initiated in patients who appeared stable on tenofovir. Consider alternatives to NSAIDs in patients at risk for renal dysfunction. If these drugs must be coadministered, carefully monitor the estimated creatinine creatinine, serum phosphorus, urine glucose, and urine protein prior to, and periodically during, treatment.
Landiolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Leflunomide: (Moderate) In vitro studies indicate that the M1 metabolite of leflunomide inhibits cytochrome P450 2C9, the enzyme responsible for the metabolism of many NSAIDs. Leflunomide altered protein binding and thus, increased the free fraction of ibuprofen by 13% to 50%. The clinical significance of the interactions with NSAIDs is unknown. There was extensive concomitant use of NSAIDs in phase III clinical studies of leflunomide in the treatment of rheumatoid arthritis, and no clinical differential effects were observed. However, because some NSAIDs have been reported to cause hepatotoxic effects, some caution may be warranted in their use with leflunomide.
Levamlodipine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related

decreases in renal function and an increased risk of stroke and coronary artery disease.
Levobunolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
levoFLOXacin: (Moderate) Use quinolones and nonsteroidal anti-inflammatory drugs (NSAIDs) concomitantly with caution due to potential increased risk of CNS stimulation and convulsive seizures. NSAIDs in combination with very high doses of quinolones have been shown to provoke convulsions in preclinical studies and postmarketing.
Levomilnacipran: (Moderate) Platelet aggregation may be impaired by SNRIs such as levomilnacipran due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Monitor for signs and symptoms of bleeding in patients taking levomilnacipran and NSAIDs.
Lisinopril: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Lisinopril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Lithium: (Moderate) Monitor serum lithium concentrations during concomitant nonsteroidal anti-inflammatory (NSAID) use; reduce the lithium dose based on serum lithium concentrations and clinical response. NSAIDs decrease renal blood flow, resulting in decreased renal clearance and increased serum lithium concentrations.
Lofexidine: (Moderate) A dosage adjustment may be warranted for lofexidine if

coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of lofexidine. Celecoxib is a CYP2D6 inhibitor, and lofexidine is a CYP2D6 substrate.
Lomustine, CCNU: (Major) Due to the bone marrow suppressive and thrombocytopenic effects of lomustine, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, ASA, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Lopinavir; Ritonavir: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and ritonavir. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and ritonavir is a moderate CYP2C9 inducer.
Losartan: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Losartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Lumacaftor; Ivacaftor: (Minor) Although the clinical significance of this interaction is unknown, concurrent use of celecoxib and lumacaftor; ivacaftor may alter celecoxib exposure; caution and close monitoring are advised if these drugs are used together. Celecoxib is a substrate of CYP2C9; in vitro data suggest that lumacaftor; ivacaftor may induce and/or inhibit CYP2C9. The net effect of lumacaftor; ivacaftor on CYP2C9-mediated metabolism is not clear, but CYP2C9 substrate exposure may be affected. (Minor) Increased monitoring is recommended if ivacaftor is administered concurrently with CYP2C9 substrates, such as celecoxib. In vitro studies showed ivacaftor to be a

weak inhibitor of CYP2C9. Co-administration may lead to increased exposure to CYP2C9 substrates; however, the clinical impact of this has not yet been determined.
Lumacaftor; Ivacaftor: (Minor) Although the clinical significance of this interaction is unknown, concurrent use of celecoxib and lumacaftor; ivacaftor may alter celecoxib exposure; caution and close monitoring are advised if these drugs are used together. Celecoxib is a substrate of CYP2C9; in vitro data suggest that lumacaftor; ivacaftor may induce and/or inhibit CYP2C9. The net effect of lumacaftor; ivacaftor on CYP2C9-mediated metabolism is not clear, but CYP2C9 substrate exposure may be affected.
Macimorelin: (Major) Avoid use of macimorelin with drugs that directly affect pituitary growth hormone secretion, such as nonsteroidal antiinflammatory drugs (NSAIDs). Healthcare providers are advised to discontinue NSAID therapy and observe a sufficient washout period before administering macimorelin. Use of these medications together may impact the accuracy of the macimorelin growth hormone test.
Magnesium Salicylate: (Major) Avoid concomitant use of celecoxib with salicylates, such as magnesium salicylate, due to an increased risk of gastrointestinal toxicity, with little or no increase in efficacy.
Magnesium Sulfate; Potassium Sulfate; Sodium Sulfate: (Moderate) Use caution when prescribing sulfate salt bowel preparation in patients taking concomitant medications that may affect renal function such as nonsteroidal anti-inflammatory drugs (NSAIDs).
Mannitol: (Major) Avoid use of mannitol and nonsteroidal anti-inflammatory drugs (NSAIDs), if possible. If use together is necessary, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic efficacy. Concomitant administration of nephrotoxic drugs, such as NSAIDs, increases the risk of renal failure after administration of mannitol. NSAIDs may reduce the natriuretic effect of diuretics in some patients. NSAIDS have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain.
Maprotiline: (Moderate) A dosage adjustment may be warranted for maprotiline if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of maprotiline. Celecoxib is a CYP2D6 inhibitor, and maprotiline is a CYP2D6 substrate.
Mavacamten: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and mavacamten. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and mavacamten is a moderate CYP2C9 inducer.
Mecamylamine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs,

to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Meclizine: (Moderate) A dosage adjustment may be warranted for meclizine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of meclizine. Celecoxib is a CYP2D6 inhibitor, and meclizine is a CYP2D6 substrate.
Meclofenamate Sodium: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Mefenamic Acid: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Meloxicam: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Meloxicam; Rizatriptan: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Mesalamine, 5-ASA: (Minor) The concurrent use of mesalamine with known nephrotoxic agents such as nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk of nephrotoxicity.
Methadone: (Moderate) Consider a reduced dose of methadone with frequent monitoring for respiratory depression and sedation if concurrent use of celecoxib is necessary. If celecoxib is discontinued, consider increasing the methadone dose until stable drug effects are achieved and monitor for evidence of opioid withdrawal. Methadone is a CYP2D6 substrate, and coadministration with CYP2D6 inhibitors like celecoxib can increase methadone exposure resulting in increased or prolonged opioid effects including fatal respiratory depression, particularly when an inhibitor is added to a stable dose of methadone. If celecoxib is discontinued, methadone plasma concentrations will decrease resulting in reduced efficacy of the opioid and potential withdrawal syndrome in a patient who has developed physical dependence to methadone.

Methamphetamine: (Moderate) A dosage adjustment may be warranted for methamphetamine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of methamphetamine. Celecoxib is a CYP2D6 inhibitor, and methamphetamine is a CYP2D6 substrate.
Methohexital: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Methotrexate: (Major) Do not administer nonsteroidal anti-inflammatory drugs (NSAIDs) before or concomitantly with high doses of methotrexate, such as used in the treatment of osteosarcoma. Concomitant administration of some NSAIDs with high dose methotrexate therapy has been reported to elevate and prolong serum methotrexate concentrations, resulting in deaths from severe hematologic and gastrointestinal toxicity. Use caution when NSAIDs are administered concomitantly with lower doses of methotrexate as they have been reported to reduce the tubular secretion of methotrexate in an animal model and may enhance its toxicity. Despite potential interactions, patients with rheumatoid arthritis (RA) are often receiving concurrent treatment with NSAIDs without apparent problems. However, these doses are lower than those used in psoriasis or malignancy; higher methotrexate doses may lead to unexpected toxicity in combination with NSAIDs. NSAIDs may be continued in patients with RA receiving treatment with methotrexate, although the possibility of increased toxicity has not been fully explored.
Methyldopa: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
methylPREDNISolone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Metoclopramide: (Moderate) A dosage adjustment may be warranted for

metoclopramide if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of metoclopramide. Celecoxib is a CYP2D6 inhibitor, and metoclopramide is a CYP2D6 substrate.
metOLazone: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Metoprolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Metoprolol; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics. (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
metroNIDAZOLE: (Minor) Since celecoxib is metabolized by cytochrome P450 2C9, concurrent administration with metronidazole, which can inhibit this enzyme, may result in increased levels of celecoxib. The clinical significance of this interaction has not been established.
Mexiletine: (Moderate) A dosage adjustment may be warranted for mexiletine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of mexiletine. Celecoxib is a CYP2D6 inhibitor, and mexiletine is a CYP2D6 substrate.
miFEPRIStone: (Moderate) Mifepristone significantly increased exposure of drugs metabolized by CYP2C8/2C9 in interaction studies. Therefore, when mifepristone is used chronically, as in the treatment of Cushing's syndrome, use caution with coadministered CYP2C8/2C9 substrates, including the NSAIDs. Use the lowest doses of the substrate and patients should be monitored closely for adverse reactions.
Milnacipran: (Moderate) Platelet aggregation may be impaired by milnacipran due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in

patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Monitor for signs and symptoms of bleeding in patients taking milnacipran and NSAIDs.
mitoXANTRONE: (Major) Due to the thrombocytopenic effects of mitoxantrone, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Moexipril: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Mometasone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Moxifloxacin: (Moderate) Use quinolones and nonsteroidal anti-inflammatory drugs (NSAIDs) concomitantly with caution due to potential increased risk of CNS stimulation and convulsive seizures. NSAIDs in combination with very high doses of quinolones have been shown to provoke convulsions in preclinical studies and postmarketing.
Nabumetone: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Nadolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Naproxen: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Naproxen; Esomeprazole: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Naproxen; Pseudoephedrine: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Nebivolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Nelarabine: (Major) Due to the thrombocytopenic effects of nelarabine, an additive risk

of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Neomycin: (Minor) It is possible that additive nephrotoxicity may occur in patients who receive NSAIDs concurrently with other nephrotoxic agents, such as aminoglycosides.
Neostigmine: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
Neostigmine; Glycopyrrolate: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
NiCARdipine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
NIFEdipine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs,

to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. niMODipine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. Nirmatrelvir; Ritonavir: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and ritonavir. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and ritonavir is a moderate CYP2C9 inducer. Nisoldipine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term

NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Nitisinone: (Major) A dosage adjustment of celecoxib may be necessary when administered with nitisinone as concurrent use may result in increased celecoxib exposure. Celecoxib is a sensitive CYP2C9 substrate; nitisinone is a moderate CYP2C9 inhibitor. Concurrent use of celecoxib with another moderate CYP2C9 inhibitor increased celecoxib exposure by 2-fold. FDA-approved labeling for nitisinone recommends reducing the dose of sensitive CYP2C9 substrates by 50% with subsequent dosage adjustments to maintain therapeutic drug concentrations.
Non-Ionic Contrast Media: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when given to patients receiving a contrast agents. When possible, withhold NSAID therapy during administration of a contrast agent.
Nortriptyline: (Moderate) A dosage adjustment may be warranted for nortriptyline if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of nortriptyline. Celecoxib is a CYP2D6 inhibitor, and nortriptyline is a sensitive CYP2D6 substrate.
Ofloxacin: (Moderate) Use quinolones and nonsteroidal anti-inflammatory drugs (NSAIDs) concomitantly with caution due to potential increased risk of CNS stimulation and convulsive seizures. NSAIDs in combination with very high doses of quinolones have been shown to provoke convulsions in preclinical studies and postmarketing.
OLANZapine; FLUoxetine: (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.
Olmesartan: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Olmesartan; amLODIPine; hydroCHLOROthiazide, HCTZ: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-

dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.

Olmesartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.

Olopatadine; Mometasone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.

Olsalazine: (Moderate) Monitor patients for signs of worsening renal function during coadministration of olsalazine and celecoxib. Coadministration may increase the risk for

drug-induced nephrotoxicity. Olsalazine is converted to mesalamine in the gastrointestinal tract; nephrotoxicity has been observed during mesalamine treatment.
Omacetaxine: (Major) Avoid the concomitant use of omacetaxine and nonsteroidal antiinflammatory drugs (NSAIDs) when the platelet count is less than 50,000 cells/microliter due to an increased risk of bleeding.
Oritavancin: (Moderate) Celecoxib is metabolized by CYP2C9; oritavancin is a weak CYP2C9 inhibitor. Coadministration may result in elevated celecoxib plasma concentrations. If these drugs are administered concurrently, monitor patients for signs of celecoxib toxicity, such as dizziness, stomach upset, or nausea.
Oxaprozin: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
PACLitaxel: (Major) Due to the thrombocytopenic effects of paclitaxel, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Pamidronate: (Moderate) Monitor renal function during concomitant pamidronate and nonsteroidal antiinflammatory drug use due to risk for additive nephrotoxicity.
PARoxetine: (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.
Pentamidine: (Major) Avoid concurrent or sequential use of pentamidine with celecoxib. Coadministration may increase the risk for drug-induced nephrotoxicity. Closely monitor renal function if coadministration is unavoidable. Celecoxib may enhance the exposure and toxicity of pentamidine. Celecoxib is a CYP2D6 inhibitor, and pentamidine is a CYP2D6 substrate.
PENTobarbital: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Pentosan: (Moderate) An additive risk of bleeding may be seen in patients receiving anticoagulants in combination with other agents known to increase the risk of bleeding such as nonsteroidal antiinflammatory drugs (NSAIDs). Monitor clinical and laboratory response closely during concurrent use.
Pentostatin: (Major) Due to the thrombocytopenic effects of pentostatin, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs,

platelet inhibitors, including aspirin, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Perindopril: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Perindopril; amLODIPine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Perphenazine: (Moderate) A dosage adjustment may be warranted for perphenazine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of perphenazine. Celecoxib is a CYP2D6 inhibitor, and perphenazine is a CYP2D6 substrate.
Perphenazine; Amitriptyline: (Moderate) A dosage adjustment may be warranted for perphenazine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of perphenazine. Celecoxib is a CYP2D6 inhibitor, and perphenazine is a CYP2D6 substrate. (Moderate) Monitor for an increase in amitriptyline-related adverse reactions if coadministration with celecoxib is necessary; a dose reduction of amitriptyline may be necessary. Concurrent use may increase the

plasma concentrations of amitriptyline. Amitriptyline is a CYP2D6 substrate and celecoxib is a CYP2D6 inhibitor.
PHENobarbital: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
PHENobarbital; Hyoscyamine; Atropine; Scopolamine: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Phenoxybenzamine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Phentolamine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Phenytoin: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the

celecoxib dosage as appropriate based on response during concomitant use of celecoxib and phenytoin. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and phenytoin is a moderate CYP2C9 inducer.
Photosensitizing agents (topical): (Moderate) Agents that inhibit prostaglandin synthesis such as nonsteroidal antiinflammatory drugs (NSAIDs), could decrease the efficacy of photosensitizing agents used in photodynamic therapy. Avoidance of NSAIDs before and during photodynamic therapy may be advisable.
PHYSostigmine: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
Pimozide: (Moderate) A dosage adjustment may be warranted for pimozide if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of pimozide. Celecoxib is a CYP2D6 inhibitor, and pimozide is a CYP2D6 substrate.
Pindolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Pioglitazone; Glimepiride: (Moderate) NSAIDs may enhance hypoglycemia in diabetic patients via inhibition of prostaglandin synthesis, which indirectly increases insulin secretion. If NSAIDs are administered or discontinued in patients receiving oral antidiabetic agents, patients should be monitored for hypoglycemia or loss of blood glucose control. No clinically significant interaction between sulindac at daily doses of 400 mg and oral hypoglycemic agents has been observed. Sulindac, its sulfide metabolite, and sulfonylureas are highly bound to protein. Sulindac could displace the sulfonylureas, altering hypoglycemic activity. Careful patient monitoring is recommended to ensure that no change in their diabetes medicine dosage is required. A sulfonylurea dose adjustment may be needed, especially if sulindac doses greater than 400 mg daily are used or if the drug combination is used in patients with renal impairment or other metabolic defects that might increase sulindac blood concentrations.
Piroxicam: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Platelet Inhibitors: (Moderate) Monitor for signs and symptoms of bleeding during concomitant platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID)

use. Concomitant use increases the risk of bleeding.
Pneumococcal Vaccine, Polyvalent: (Moderate) Concomitant administration of antipyretics, such as nonsteroidal antiinflammatory drugs (NSAIDS), may decrease an individual's immunological response to the pneumococcal vaccine. A post-marketing study conducted in Poland using a non-US vaccination schedule (2, 3, 4, and 12 months of age) evaluated the impact of prophylactic oral acetaminophen on antibody responses to Prevnar 13. Data show that acetaminophen, given at the time of vaccination and then dosed at 6 to 8 hour intervals for 3 doses on a scheduled basis, reduced the antibody response to some serotypes after the third dose of Prevnar 13 when compared to the antibody responses of infants who only received antipyretics 'as needed' for treatment. However, reduced antibody responses were not observed after the fourth dose of Prevnar 13 with prophylactic acetaminophen.
Polyethylene Glycol; Electrolytes: (Moderate) Use caution when prescribing sulfate salt bowel preparation in patients taking concomitant medications that may affect renal function such as nonsteroidal anti-inflammatory drugs (NSAIDs).
Polyethylene Glycol; Electrolytes; Ascorbic Acid: (Moderate) Use caution when prescribing sulfate salt bowel preparation in patients taking concomitant medications that may affect renal function such as nonsteroidal anti-inflammatory drugs (NSAIDs).
Polymyxin B: (Major) The chronic coadministration of systemic polymyxins may increase the risk of developing nephrotoxicity, even in patients who have normal renal function. Nonsteroidal antiinflammatory drugs (NSAIDs) may increase the risk for nephrotoxicity when used concurrently. Monitor patients for changes in renal function if these drugs are coadministered. Since Polymyxin B is eliminated by the kidney, coadministration with other potentially nephrotoxic drugs, including nonsteroidal antiinflammatory drugs (NSAIDs), may theoretically increase serum concentrations of either drug.
Potassium Acetate: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
Potassium Bicarbonate: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
Potassium Chloride: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
Potassium Citrate: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
Potassium Citrate; Citric Acid: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.

Potassium Gluconate: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
Potassium Iodide, KI: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
Potassium: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
PRALAtrexate: (Major) Renal elimination accounts for approximately 34% of the overall clearance of pralatrexate. Concomitant administration of drugs that undergo substantial renal clearance, such as nonsteroidal antiinflammatory drugs (NSAIDs), may result in delayed clearance of pralatrexate.
Prasugrel: (Moderate) Monitor for signs and symptoms of bleeding during concomitant platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of bleeding.
Prazosin: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
prednisoLONE: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
predniSONE: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Primidone: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.

Probenecid: (Major) Probenecid can decrease the renal clearance of nonsteroidal antiinflammatory agents (NSAIDs). Reduction of the NSAID dose may be necessary when it is used together with probenecid.
Probenecid; Colchicine: (Major) Probenecid can decrease the renal clearance of nonsteroidal antiinflammatory agents (NSAIDs). Reduction of the NSAID dose may be necessary when it is used together with probenecid.
Procarbazine: (Major) Due to the thrombocytopenic effects of procarbazine, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Propafenone: (Moderate) Monitor for increased propafenone toxicity if coadministered with celecoxib; concurrent use may increase propafenone exposure and therefore increase the risk of proarrhythmias. Avoid simultaneous use of propafenone and celecoxib with a CYP3A4 inhibitor. Propafenone is a CYP3A4 and CYP2D6 substrate and celecoxib is a weak CYP2D6 inhibitor.
Propranolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Protriptyline: (Moderate) A dosage adjustment may be warranted for protriptyline if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of protriptyline. Celecoxib is a CYP2D6 inhibitor, and protriptyline is a CYP2D6 substrate.
pyRIDostigmine: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
Quinapril: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Quinapril; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor

and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Quinolones: (Moderate) Use quinolones and nonsteroidal anti-inflammatory drugs (NSAIDs) concomitantly with caution due to potential increased risk of CNS stimulation and convulsive seizures. NSAIDs in combination with very high doses of quinolones have been shown to provoke convulsions in preclinical studies and postmarketing.
Ramipril: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Reteplase, r-PA: (Moderate) NSAIDs can cause GI bleeding, inhibit platelet aggregation, prolong bleeding time; these pharmacodynamic effects may be increased when administered to patients receiving thrombolytic agents. Patients receiving these drugs concurrently should be monitored closely for bleeding.
rifAMPin: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and rifampin. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and rifampin is a moderate CYP2C9 inducer.
Rifapentine: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and rifapentine. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and rifapentine is a moderate CYP2C9 inducer.
Risedronate: (Minor) Monitor for gastrointestinal adverse events during concurrent use of risedronate and nonsteroidal antiinflammatory drugs. Both medications have been associated with gastrointestinal irritation although data suggest concomitant use introduces little additional risk for adverse effects for most patients.
Ritonavir: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the

celecoxib dosage as appropriate based on response during concomitant use of celecoxib and ritonavir. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and ritonavir is a moderate CYP2C9 inducer.
Rivaroxaban: (Major) An additive risk of bleeding may be seen in patients receiving anticoagulants in combination with other agents known to increase the risk of bleeding such as nonsteroidal antiinflammatory drugs (NSAIDs). Monitor clinical and laboratory response closely during concurrent use.
Rivastigmine: (Moderate) NSAIDs may cause additive pharmacodynamic GI effects with cholinesterase inhibitors, leading to gastrointestinal intolerance. Patients receiving concurrent NSAIDs should be monitored closely for symptoms of active or occult gastrointestinal bleeding. While NSAIDs appear to suppress microglial activity, which in turn may slow inflammatory neurodegenerative processes important for the progression of Alzheimer's disease (AD), there are no clinical data at this time to suggest that NSAIDs alone or as combined therapy with AD agents result in synergistic effects in AD.
Rucaparib: (Moderate) Monitor for an increase in celecoxib-related adverse reactions if coadministration with rucaparib is necessary. Celecoxib is a CYP2C9 substrate and rucaparib is a weak CYP2C9 inhibitor.
Sacubitril; Valsartan: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Salsalate: (Major) Concurrent use of salsalate and celecoxib is generally not recommended due to the increased risks of bleeding and nephrotoxicity. Concurrent use of salsalate and NSAIDs does not produce greater therapeutic effect compared to the use of NSAIDs alone.
Secobarbital: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and barbiturates. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and barbiturates is a moderate CYP2C9 inducer.
Selective serotonin reuptake inhibitors: (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.
Sertraline: (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.
Sodium Phosphate Monobasic Monohydrate; Sodium Phosphate Dibasic Anhydrous: (Moderate) Concomitant use of medicines with potential to alter renal perfusion or function such as nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk of acute phosphate nephropathy in patients taking sodium phosphate monobasic monohydrate; sodium phosphate dibasic anhydrous.
Sodium picosulfate; Magnesium oxide; Anhydrous citric acid: (Moderate) Use caution when prescribing sodium picosulfate; magnesium oxide; anhydrous citric acid in patients taking concomitant medications that may affect renal function such as nonsteroidal anti-inflammatory drugs (NSAIDs).
Sodium Sulfate; Magnesium Sulfate; Potassium Chloride: (Moderate) Monitor serum potassium concentrations closely if potassium supplements and nonsteroidal anti-inflammatory drugs (NSAIDs) are used together. Concomitant use may increase the risk of hyperkalemia.
Sotalol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Sparsentan: (Moderate) Monitor for worsening renal function during concomitant use of sparsentan and nonsteroidal antiinflammatory drugs (NSAIDs), including selective cyclooxygenase (COX-2) inhibitors. Concomitant use increases the risk for nephrotoxicity, especially in patients with additional risk factors such as hypovolemia and chronic renal impairment.
Spironolactone: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant spironolactone and nonsteroidal antiinflammatory drug (NSAID) use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Spironolactone; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may

blunt the cardiovascular effects of diuretics. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant spironolactone and nonsteroidal antiinflammatory drug (NSAID) use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
St. John's Wort, Hypericum perforatum: (Moderate) Monitor for a decrease in celecoxib efficacy and increase the celecoxib dosage as appropriate based on response during concomitant use of celecoxib and St. John's wort. Concomitant use may decrease celecoxib exposure. Celecoxib is a CYP2C9 substrate and St. John's wort is a moderate CYP2C9 inducer.
Streptomycin: (Moderate) It is possible that additive nephrotoxicity may occur in patients who receive nonsteroidal anti-inflammatory drugs (NSAIDs) concurrently with other nephrotoxic agents, such as streptomycin.
Sulfamethoxazole; Trimethoprim, SMX-TMP, Cotrimoxazole: (Moderate) Monitor for celecoxib-related adverse effects and consider a celecoxib dosage reduction as appropriate based on response if concomitant use with sulfamethoxazole is necessary. Concomitant use may increase celecoxib exposure. Celecoxib is a CYP2C9 substrate and sulfamethoxazole is a moderate CYP2C9 inhibitor. Concomitant use with another moderate CYP2C9 inhibitor increased celecoxib overall exposure by 2-fold.
sulfaSALAzine: (Moderate) Monitor patients for signs of worsening renal function during coadministration of sulfasalazine and celecoxib. Coadministration may increase the risk for drug-induced nephrotoxicity.
Sulfonylureas: (Moderate) NSAIDs may enhance hypoglycemia in diabetic patients via inhibition of prostaglandin synthesis, which indirectly increases insulin secretion. If NSAIDs are administered or discontinued in patients receiving oral antidiabetic agents, patients should be monitored for hypoglycemia or loss of blood glucose control. No clinically significant interaction between sulindac at daily doses of 400 mg and oral hypoglycemic agents has been observed. Sulindac, its sulfide metabolite, and sulfonylureas are highly bound to protein. Sulindac could displace the sulfonylureas, altering hypoglycemic activity. Careful patient monitoring is recommended to ensure that no change in their diabetes medicine dosage is required. A sulfonylurea dose adjustment may be needed, especially if sulindac doses greater than 400 mg daily are used or if the drug combination is used in patients with renal impairment or other metabolic defects that might increase sulindac blood concentrations.
Sulindac: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Sulopenem Etzadroxil; Probenecid: (Major) Probenecid can decrease the renal clearance

of nonsteroidal antiinflammatory agents (NSAIDs). Reduction of the NSAID dose may be necessary when it is used together with probenecid.
SUMAtriptan; Naproxen: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Tacrolimus: (Moderate) Monitor patients for signs of worsening renal function during coadministration of tacrolimus and nonsteroidal antiinflammatory drugs. Coadministration may increase the risk for drug-induced nephrotoxicity.
Telavancin: (Minor) Concurrent or sequential use of telavancin with drugs that inhibit renal prostaglandins such as nonsteroidal antiinflammatory drugs (NSAIDS) may lead to additive nephrotoxicity. Closely monitor renal function and adjust telavancin doses based on calculated creatinine clearance.
Telmisartan: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Telmisartan; amLODIPine: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Telmisartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-

inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Temozolomide: (Major) Myelosuppression, primarily neutropenia and thrombocytopenia, is the dose-limiting toxicity of temozolomide. Due to the thrombocytopenic effects of temozolomide, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, ASA, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Tenecteplase: (Moderate) NSAIDs can cause GI bleeding, inhibit platelet aggregation, prolong bleeding time; these pharmacodynamic effects may be increased when administered to patients receiving thrombolytic agents. Patients receiving these drugs concurrently should be monitored closely for bleeding.
Tenofovir Alafenamide: (Moderate) Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) and tenofovir alafenamide may result in additive nephrotoxicity. Monitor for renal toxicity if concomitant use is required.
Tenofovir Disoproxil Fumarate: (Moderate) Avoid administering tenofovir, PMPA concurrently with or recently after a nephrotoxic agent, such as high-dose or multiple nonsteroidal antiinflammatory drugs (NSAIDs). Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after high-dose or multiple NSAIDs were initiated in patients who appeared stable on tenofovir. Consider alternatives to NSAIDs in patients at risk for renal dysfunction. If these drugs must be coadministered, carefully monitor the estimated creatinine creatinine, serum phosphorus, urine glucose, and urine protein prior to, and periodically during, treatment.
Terazosin: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect

is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Tezacaftor; Ivacaftor: (Minor) Increased monitoring is recommended if ivacaftor is administered concurrently with CYP2C9 substrates, such as celecoxib. In vitro studies showed ivacaftor to be a weak inhibitor of CYP2C9. Co-administration may lead to increased exposure to CYP2C9 substrates; however, the clinical impact of this has not yet been determined.
Thiazide diuretics: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Thioguanine, 6-TG: (Major) Due to the thrombocytopenic effects of thioguanine, an additive risk of bleeding may be seen in patients receiving concomitant anticoagulants, NSAIDs, platelet inhibitors, including aspirin, strontium-89 chloride, and thrombolytic agents. In addition, large doses of salicylates (>= 3-4 g/day) can cause hypoprothrombinemia, an additional risk factor for bleeding.
Thioridazine: (Contraindicated) Coadministration of celecoxib and thioridazine is contraindicated due to the potential for celecoxib to enhance the exposure and toxicity of thioridazine. Elevated thioridazine concentrations would be expected to augment the prolongation of the QTc interval associated with thioridazine and may increase the risk of serious cardiac arrhythmias, such as torsade de pointes. Celecoxib is a CYP2D6 inhibitor, and thioridazine is a CYP2D6 substrate.
Thrombolytic Agents: (Moderate) NSAIDs can cause GI bleeding, inhibit platelet aggregation, prolong bleeding time; these pharmacodynamic effects may be increased when administered to patients receiving thrombolytic agents. Patients receiving these drugs concurrently should be monitored closely for bleeding.
Ticagrelor: (Moderate) Monitor for signs and symptoms of bleeding during concomitant platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of bleeding.

Timolol: (Moderate) Monitor blood pressure during concomitant beta-blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of beta-blockers may be diminished by NSAIDs.
Tirofiban: (Moderate) Monitor for signs and symptoms of bleeding during concomitant platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of bleeding.
Tobacco: (Major) Advise patients to avoid smoking tobacco while taking nonsteroidal anti-inflammatory drugs (NSAIDs). Concomitant use of NSAIDs with tobacco smoking may enhance the risk of gastrointestinal side effects, including peptic ulcer and GI bleeding. Patients using tobacco and NSAIDs concurrently should be monitored closely for GI adverse reactions.
Tobramycin: (Moderate) It is possible that additive nephrotoxicity may occur in patients who receive nonsteroidal anti-inflammatory drugs (NSAIDs) concurrently with other nephrotoxic agents, such as tobramycin.
Tolmetin: (Major) Avoid concomitant use of celecoxib with any other NSAID due to the risk of additive serious NSAID toxicities including but not limited to GI bleeding, GI perforation, or peptic ulcers.
Tolterodine: (Moderate) Monitor patients closely for tolterodine-related adverse reactions and consider a dosage reduction of tolterodine if coadministration with celecoxib is necessary. Celecoxib may enhance the systemic exposure and toxicity of tolterodine. In vitro studies indicate that celecoxib is an inhibitor of CYP2D6. Tolterodine is a CYP2D6 substrate.
Torsemide: (Moderate) If celecoxib (an NSAID) and torsemide (a diuretic) are used concurrently, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic efficacy; side effects from celecoxib may also increase. The concomitant use of celecoxib, a sensitive substrate of CYP2C9, and torsemide, a CYP2C9 inhibitor, may result in increased plasma concentrations of celecoxib. Patients taking diuretics and NSAIDs concurrently are at higher risk of developing renal insufficiency. NSAIDs may reduce the natriuretic effect of diuretics in some patients. NSAIDs have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain.
traMADol: (Moderate) Monitor for reduced efficacy of tramadol, signs of opioid withdrawal, seizures, or serotonin syndrome if coadministration with celecoxib is necessary. If celecoxib is discontinued, consider a dose reduction of tramadol and frequently monitor for signs of respiratory depression and sedation. Tramadol is a CYP2D6 substrate and celecoxib 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 celecoxib is necessary. If celecoxib is discontinued, consider a dose reduction of tramadol and frequently monitor for signs of respiratory depression and sedation. Tramadol is a CYP2D6 substrate and celecoxib 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.
Trandolapril: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Trandolapril; Verapamil: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease. (Moderate) Monitor blood pressure and renal function periodically during concomitant

angiotensin-converting enzyme (ACE) inhibitor and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of ACE inhibitors may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of ACE inhibitors and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
traZODone: (Moderate) Platelet aggregation may be impaired by trazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking trazodone concurrently with medications that impair platelet function and to promptly report any bleeding events to the practitioner.
Treprostinil: (Moderate) NSAIDs may decrease the effect of antihypertensive agents through various mechanisms, including renal and peripheral vasoactive pathways.
Triamcinolone: (Moderate) Monitor for gastrointestinal toxicity during concurrent corticosteroid and nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of GI bleeding.
Triamterene: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors, may reduce the natriuretic effect of diuretics in some patients. NSAIDS have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain. Patients taking diuretics and NSAIDS concurrently are at higher risk of developing renal insufficiency. If celecoxib and a diuretic are used concurrently, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic efficacy.
Triamterene; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics. (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors, may reduce the natriuretic effect of diuretics in some patients. NSAIDS have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain. Patients taking diuretics and NSAIDS concurrently are at higher risk of developing renal insufficiency. If celecoxib and a diuretic are used concurrently, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic

efficacy.
Trimipramine: (Moderate) A dosage adjustment may be warranted for trimipramine if coadministered with celecoxib due to the potential for celecoxib to enhance the exposure and toxicity of trimipramine. Celecoxib is a CYP2D6 inhibitor, and trimipramine is a CYP2D6 substrate.
Urea: (Moderate) Nonsteroidal anti-inflammatory drugs (NSAIDs) may reduce the natriuretic effect of diuretics in some patients. NSAIDS have been associated with an inhibition of prostaglandin synthesis, which may result in reduced renal blood flow leading to renal insufficiency and increases in blood pressure that are often accompanied by peripheral edema and weight gain. Patients taking diuretics and NSAIDS concurrently are at higher risk of developing renal insufficiency. If an NSAID and a diuretic are used concurrently, carefully monitor the patient for signs and symptoms of decreased renal function and diuretic efficacy.
valACYclovir: (Moderate) Monitor patients for signs of worsening renal function during coadministration of valacyclovir and nonsteroidal antiinflammatory drugs. Coadministration may increase the risk for drug-induced nephrotoxicity.
valGANciclovir: (Minor) Concurrent use of nephrotoxic agents, such as NSAIDs, with valganciclovir should be done cautiously to avoid additive nephrotoxicity.
Valsartan: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible.
Valsartan; hydroCHLOROthiazide, HCTZ: (Moderate) Monitor blood pressure and renal function periodically during concomitant angiotensin II blocker and nonsteroidal anti-inflammatory drug (NSAID) use. The antihypertensive effect of angiotensin II blockers may be diminished by NSAIDs. In persons who are elderly, volume-depleted, or with compromised renal function, coadministration of angiotensin II blockers and NSAIDs may result in deterioration of renal function, including possible acute renal failure; these effects are usually reversible. (Moderate) Monitor blood pressure as well as for signs of worsening renal function and loss of diuretic efficacy, including antihypertensive effects, during concomitant nonsteroidal antiinflammatory drug (NSAID) and thiazide diuretic use. NSAIDs may cause a dose-dependent reduction in renal blood flow, which may precipitate overt renal decompensation, and concomitant diuretic use increases the risk of this reaction. NSAIDs have been shown to reduce the natriuretic effect of thiazide diuretics and are associated with fluid retention which may blunt the cardiovascular effects of diuretics.
Vancomycin: (Minor) It is possible that additive nephrotoxicity may occur in patients who receive NSAIDs concurrently with other nephrotoxic agents, including vancomycin.

Venlafaxine: (Moderate) Platelet aggregation may be impaired by venlafaxine due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Monitor patients for signs and symptoms of bleeding when coadministering venlafaxine with NSAIDs.
Verapamil: (Moderate) If nonsteroidal anti-inflammatory drugs (NSAIDs) and an antihypertensive drug are concurrently used, carefully monitor the patient for signs and symptoms of renal insufficiency and blood pressure control. Doses of antihypertensive medications may require adjustment in patients receiving concurrent NSAIDs. NSAIDs, to varying degrees, have been associated with an elevation in blood pressure. This effect is most significant in patients receiving concurrent antihypertensive agents and long-term NSAID therapy. NSAIDs cause a dose-dependent reduction in prostaglandin formation, which may result in a reduction in renal blood flow leading to renal insufficiency and an increase in blood pressure that are often accompanied by peripheral edema and weight gain. Patients who rely upon renal prostaglandins to maintain renal perfusion may have acute renal blood flow reduction with NSAID usage. Elderly patients may be at increased risk of adverse effects from combined long-term NSAID therapy and antihypertensive agents, especially diuretics, due to age-related decreases in renal function and an increased risk of stroke and coronary artery disease.
Verteporfin: (Moderate) Use caution if coadministration of verteporfin with nonsteroidal anti-inflammatory drugs is necessary due to the risk of decreased verteporfin efficacy. Oxaprozin may additionally worsen photosensitivity. Verteporfin is a light-activated drug. Once activated, local damage to neovascular endothelium results in a release of procoagulant and vasoactive factors resulting in platelet aggregation, fibrin clot formation, and vasoconstriction. Concomitant use of drugs that decrease platelet aggregation like nonsteroidal anti-inflammatory drugs could decrease the efficacy of verteporfin therapy.
Vilazodone: (Moderate) Platelet aggregation may be impaired by vilazodone due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Patients should be instructed to monitor for signs and symptoms of bleeding while taking vilazodone concurrently with NSAIDs and to promptly report any bleeding events to the practitioner.
Voclosporin: (Moderate) Concomitant use of voclosporin and nonsteroidal anti-inflammatory drugs (NSAIDs) may result in additive nephrotoxicity. Monitor for renal toxicity if concomitant use is required.
Vorapaxar: (Moderate) Monitor for signs and symptoms of bleeding during concomitant platelet inhibitor and chronic nonsteroidal antiinflammatory drug (NSAID) use. Concomitant use increases the risk of bleeding.

Voriconazole: (Major) Isoenzyme CYP2C9 is responsible for the metabolism of many nonsteroidal antiinflammatory drugs. Voriconazole is known to be an inhibitor of CYP2C9 and may lead to increased plasma levels of some NSAIDs, such as celecoxib. The clinican should consider introducing the NSAID at the lowest recommended dose in patients receiving voriconazole. Monitor for NSAID-related side effects, such as GI irritation, fluid retention or increased blood pressure, GI bleeding, or renal dysfunction and adjust the dose of the NSAID if needed.
Vortioxetine: (Moderate) Platelet aggregation may be impaired by vortioxetine due to platelet serotonin depletion, possibly increasing the risk of a bleeding complication (e.g., gastrointestinal bleeding, ecchymoses, epistaxis, hematomas, petechiae, hemorrhage) in patients receiving nonsteroidal antiinflammatory drugs (NSAIDs). Bleeding events related to drugs that inhibit serotonin reuptake have ranged from ecchymosis to life-threatening hemorrhages. Patients should be instructed to monitor for signs and symptoms of bleeding while taking vortioxetine concurrently with medications which impair platelet function and to promptly report any bleeding events to the practitioner.
Warfarin: (Moderate) Monitor patients for signs or symptoms of bleeding during concurrent use of warfarin and nonsteroidal antiinflammatory drugs (NSAIDs). To minimize the potential for GI bleeding, use the lowest effective NSAID dose for the shortest possible duration. If signs or symptoms of bleeding occur, promptly evaluate and treat. Systemic hematological effects may also occur with the use of topical NSAIDs. NSAIDs inhibit platelet aggregation and may prolong bleeding time in some patients.
Zafirlukast: (Minor) Celecoxib is a substrate of the cytochrome P450 2C9 isoenzyme. Coadministration of celecoxib with drugs that are known to inhibit CYP2C9 such as zafirlukast should be done with caution.
Zoledronic Acid: (Moderate) Monitor renal function during concomitant zoledronic acid and nonsteroidal antiinflammatory drug use due to risk for additive nephrotoxicity.

Adverse Reaction

abdominal pain, anorexia, colitis, constipation, diarrhea, dysgeusia, dyspepsia, eructation, flatulence, gastritis, gastroesophageal reflux, GI bleeding, GI obstruction, GI perforation, hemorrhoids, ileus, melena, nausea, peptic ulcer, stomatitis, tenesmus, vomiting, xerostomia

NSAIDs can cause serious gastrointestinal (GI) adverse events including GI bleeding, inflammation, ulceration, and GI perforation of the esophagus, stomach, or small or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in individuals treated with NSAIDs. Only 1 in 5 individuals who develop a serious upper GI adverse event on NSAID therapy is symptomatic. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occurred

in approximately 1% of individuals treated for 3 to 6 months, and in about 2% to 4% of individuals treated for 1 year; however, short-term NSAID therapy is not without risk. Remain alert for signs and symptoms of GI bleeding during NSAID therapy. Consider monitoring complete blood count (CBC) periodically in individuals on long-term NSAID treatment. If a serious GI adverse event is suspected, promptly initiate evaluation and treatment, and discontinue the NSAID until a serious GI adverse event is ruled out. To minimize the potential risk for an adverse GI event in NSAID-treated individuals, use the lowest effective dose for the shortest duration possible. The most frequently reported reactions to celecoxib are GI adverse events and may be more frequent with higher doses. Among 4,146 subjects who received celecoxib 100 to 200 mg twice daily or 200 mg once daily in clinical trials, the most common GI-related adverse reactions were mild to moderate gastrointestinal complaints and included dyspepsia (8.8%), diarrhea (5.6%), abdominal pain (4.1%), nausea (3.5%), and flatulence (2.2%). Less common adverse GI reactions (0.1% to 1.9%) reported with celecoxib included anorexia, constipation, diverticulitis, eructation, gastritis, gastroenteritis, gastroesophageal reflux disease (GERD), hemorrhoids, hiatal hernia, melena, stomatitis, tenesmus, vomiting, and xerostomia. Rare (less than 0.1%) GI adverse effects reported with celecoxib therapy (regardless of causality) in premarketing trials included GI obstruction, GI perforation, GI bleeding, colitis with bleeding, and ileus. In subjects with familial adenomatous polyposis (FAP), the adverse reactions reported during clinical trials were largely similar to those seen in the arthritis trials. Among 2,285 subjects who received celecoxib 400 to 800 mg/day for up to 3 years for the prevention of adenomatous polyps, 10.5% had diarrhea, 6.8% had nausea, 4.7% had gastroesophageal reflux, and 3.2% had vomiting. GI adverse events reported with celecoxib in 5% or more of pediatric subjects 2 to 17 years in clinical trials for juvenile rheumatoid arthritis (JRA) included abdominal pain (4% to 8%), diarrhea (4% to 5%), vomiting (3% to 6%), and nausea (4% to 7%). In subjects who received celecoxib 400 mg twice daily, complicated and symptomatic ulcer rates were 0.78% at 9 months in the CLASS trial, and 2.19% for the subgroup on low-dose aspirin. Subjects 65 years and older had an incidence of 1.4% at 9 months; those on aspirin had an incidence of 3.06%. Celecoxib premarketing clinical trials demonstrate that the incidence of endoscopically observed GI ulceration is lower than that observed for nonselective NSAIDs. Endoscopic trials compared celecoxib (50 to 400 mg twice daily), comparator NSAIDs (naproxen 500 mg twice daily; ibuprofen 800 mg 3 times daily; and diclofenac 75 mg twice daily), and/or placebo over 3 to 6 months in over 4,500 rheumatoid arthritis and osteoarthritis subjects. A statistically lower incidence of endoscopically observed peptic ulcer ranging from 1.5% to 5.9% was reported for celecoxib relative to the 9.6% to 17.6% for the comparator NSAIDs. There was no statistical difference between diclofenac (2.9%) and celecoxib (1.8%). In contrast to the comparator NSAIDs, celecoxib did not alter platelet aggregation or bleeding time. During 2 randomized, double-blind, placebo-controlled trials, 3% of subjects who received

celecoxib oral solution experienced dysgeusia compared to 1% of subjects who received placebo.

dysphagia, esophageal stricture, esophageal ulceration, esophagitis, odynophagia, pyrosis (heartburn)

Among 4,146 subjects who took celecoxib 100 to 200 mg twice daily or 200 mg once daily in clinical trials, 0.1% to 1.9% had dysphagia or esophagitis. Rare (less than 0.1%) GI adverse effects occurring with celecoxib therapy (regardless of causality) in premarketing trials included esophageal perforation. NSAID-induced esophagitis is characterized by sudden onset odynophagia, pyrosis (heartburn), retrosternal pain, and dysphagia. Severe complications such as esophageal ulceration, esophageal stricture, bleeding, and perforation have been reported rarely. Risk factors for NSAID-induced esophageal effects include taking the medication without water and at night. Symptoms usually resolve within days to weeks after stopping the medication.

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

Elevated hepatic enzymes [alanine aminotransferase (ALT) or aspartate aminotransferase (AST)] of 3 or more times the upper limit of normal (ULN) have been reported in approximately 1% of NSAID-treated subjects in clinical trials. In addition, rare, sometimes fatal, cases of severe hepatic injury, including fulminant hepatitis, hepatic necrosis, and hepatic failure have been reported. Elevations of ALT or AST less than 3 times ULN may occur in up to 15% of individuals treated with NSAIDs. Among 4,146 subjects who received celecoxib 100 to 200 mg twice daily or 200 mg once daily in clinical trials, abnormal hepatic function, increased alkaline phosphatase, and elevated hepatic enzymes were reported in 0.1% to 1.9% of subjects. In controlled clinical trials of celecoxib, the incidence of borderline elevated hepatic enzymes (1.2 to less than 3 times the upper limit of normal) was 6% for celecoxib and 5% for placebo, and approximately 0.2% of subjects taking celecoxib and 0.3% of subjects taking placebo had notable elevations of ALT and AST (approximately 3 or more times the upper limit of normal). Pancreatitis and cholelithiasis occurred in less than 0.1% of subjects during clinical trials. Additionally, hepatic failure, hepatic necrosis, hepatitis, and jaundice have been reported with celecoxib in postmarketing. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), discontinue the NSAID immediately, and perform a clinical evaluation of the individual. Consider monitoring a chemistry profile periodically in individuals on long-term NSAID treatment.

agranulocytosis, anemia, aplastic anemia, disseminated intravascular coagulation, ecchymosis, epistaxis, intracranial bleeding, leukopenia,

pancytopenia, thrombocytopenia

Anemia has occurred in NSAID-treated individuals. This may be related to occult or gross blood loss, fluid retention, or an incompletely described effect on erythropoiesis. NSAIDs may increase the risk of bleeding events. If an individual treated with an NSAID has any signs or symptoms of anemia, monitor hemoglobin or hematocrit. Consider monitoring complete blood count (CBC) periodically in individuals on long-term NSAID treatment. In controlled clinical trials, the incidence of anemia was 0.6% with celecoxib and 0.4% with placebo. Among 4,146 subjects who received celecoxib 100 to 200 mg twice daily or 200 mg once daily in clinical trials, anemia, ecchymosis, epistaxis, and thrombocythemia occurred in 0.1% to 1.9% of subjects. Hemoglobin decreases more than 2 g/dL were reported in 0.5% of subjects receiving celecoxib 400 mg twice daily. Fatal intracranial bleeding has been reported rarely (less than 0.1%), but the causality to celecoxib has not been established. Conjunctival hemorrhage was noted in 0.1% to less than 1% of subjects who received celecoxib. Thrombocytopenia has been reported with celecoxib in less than 0.1% of subjects. Agranulocytosis, aplastic anemia, leukopenia, and pancytopenia have been reported with celecoxib during postmarketing. Celecoxib does not generally affect platelet counts, prothrombin time (PT), or partial thromboplastin time (PTT), and does not appear to inhibit platelet aggregation at indicated dosages. In premarketing studies of platelet dysfunction, celecoxib at single doses up to 800 mg and multiple doses of 600 mg twice daily for up to 7 days duration did not affect platelet aggregation and bleeding time. In some subjects with systemic onset juvenile rheumatoid arthritis (JRA), celecoxib was associated with mild prolongation of activated partial thromboplastin time (APTT) but not prothrombin time (PT). Disseminated intravascular coagulation has occurred with celecoxib use in individuals with systemic onset JRA.

anaphylactoid reactions, angioedema, bronchospasm, urticaria

Anaphylactoid reactions and angioedema have been observed in association with celecoxib in postmarketing. Anaphylactoid reactions occurred in individuals without known prior exposure to celecoxib. Among 4,146 subjects who received celecoxib 100 to 200 mg twice daily or 200 mg once daily in clinical trials, allergic reaction, face edema, urticaria, and/or bronchospasm were reported in 0.1% to 1.9% of subjects. Allergic reactions to celecoxib were reported in 33% of subjects tested who had previous cutaneous reactions to other NSAIDs. Celecoxib contains a sulfonamide side chain; however, celecoxib does not contain the aromatic amine or the N1-substituent that are present in sulfonamide antibiotics. These components of the chemical structures are thought to play essential roles in the pathogenesis of hypersensitivity reactions to sulfonamide antibiotics. Differences in chemical structure and subsequent metabolism

provide rationale that the incidence of cross-sensitivity between celecoxib and sulfonamide antibiotics may be low. A meta-analysis of 11,008 subjects from 14 trials demonstrated that the incidence of allergic reactions with celecoxib was not significantly different from placebo or active comparators (i.e., other NSAIDs). The subset of subjects with a history of sulfonamide hypersensitivity had a 3- to 6-fold higher incidence of dermatologic reactions, in general, than did the entire arthritis trial cohort. Although the incidence of dermatologic reactions occurred with greater frequency in subjects with sulfonamide hypersensitivity, the trend was consistent across all treatment groups (e.g., celecoxib, placebo, NSAIDs).

cystitis, dysuria, edema, hematuria, hyperkalemia, hypernatremia, hypokalemia, hyponatremia, increased urinary frequency, interstitial nephritis, nephrolithiasis, peripheral edema, proteinuria, renal failure, renal papillary necrosis, weight gain

Long-term use of NSAIDs has resulted in renal papillary necrosis and other renal injury. Albuminuria, cystitis, dysuria, hematuria, increased urinary frequency, increased BUN, increased creatinine, increased nonprotein nitrogen, and renal calculus (nephrolithiasis) have been reported with celecoxib in 0.1% to 1.9% of subjects, and acute renal failure occurred in less than 0.1% of subjects in clinical trials. Hematuria, increased blood uric acid, proteinuria, and abnormal urine analysis have been reported with celecoxib among abnormal laboratory tests in 3% to 11% of subjects in clinical trials. Additionally, interstitial nephritis has been reported with celecoxib in postmarketing. Generalized edema, weight gain, and facial edema were noted in 0.1% to 1.9% of subjects who received 100 to 200 mg twice daily or 200 mg once daily of celecoxib, and peripheral edema was observed in 2.1%. In the CLASS study, the Kaplan-Meier cumulative rates at 9 months of peripheral edema in subjects on celecoxib 400 mg twice daily were 4.5%. Hyperkalemia and increases in serum potassium concentration have been reported with the use of NSAIDs. In individuals with normal renal function, increases in potassium have been attributed to a hyporeninemic-hypoaldosteronism state. In the long-term polyp prevention studies, hyperkalemia and hypernatremia occurred in at least 0.1% but less than 1% of subjects. Hypokalemia occurred in 0.1% to 1.9% of subjects who received celecoxib 100 to 200 mg twice daily or 200 mg once daily. Hyponatremia has been reported during postmarketing experience. Consider monitoring a chemistry profile periodically in individuals on long-term NSAID treatment.

heart failure, hypertension

Celecoxib may cause new-onset hypertension or aggravate existing hypertension; monitor blood pressure carefully during therapy. Aggravated hypertension occurred in 0.1% to 1.9% of subjects, whereas congestive heart failure occurred in less than 0.1% of

subjects. The rate of hypertension from the CLASS trial in celecoxib-treated subjects was 2.4%. Among 2,285 subjects who took celecoxib 400 to 800 mg daily for up to 3 years for the prevention of adenomatous polyps, 12.5% had hypertension as compared with 9.8% of 1,303 placebo recipients. Both diclofenac 75 mg twice daily and celecoxib 200 mg once daily raised the systolic and diastolic blood pressures of Hispanic or African American subjects with normal renal function who received each drug in a randomized, crossover fashion after stabilization of their blood pressure with trandolapril, hydrochlorothiazide, and clonidine, if necessary. During the study, no antihypertensive drug dosage changes or additions were allowed. Although not a prespecified outcome measure, the mean increases in systolic pressure between the hours of 11 A.M. and 4 P.M. were 4.16 +/- 1.84 mmHg and 3.6 +/- 0.04 mmHg with celecoxib and diclofenac, respectively. The respective mean increases in diastolic pressure were 4.32 +/- 0.89 mmHg and 2 +/- 0.89 mmHg. The morning dose of each drug was given between the hours of 7 and 9. Receipt of celecoxib did not affect the mean systolic blood pressure over 24 hours (128 +/- 11 mmHg at baseline to 129 +/- 9 mmHg after 4 weeks of celecoxib). Conversely, the mean systolic blood pressure over 24 hours went from 130 +/- 14 mmHg at baseline to 134 +/- 15 mmHg after 4 weeks of diclofenac 75 mg twice daily. Similar results of each treatment on diastolic blood pressure were found. Thus, NSAID drug administration frequency and timing of blood pressure measurement are important considerations. In another study, the mean change from baseline in average 24-hour systolic and diastolic blood pressure was -0.1 +/- 0.6 to 1 mmHg after 6 weeks of celecoxib 200 mg once daily in adults (76% White subjects, 14% Black subjects) with stable hypertension (systolic less than 150 mmHg) and normal renal function. Blood pressure was measured every 20 minutes during 24-hour ambulatory monitoring, and no antihypertensive drug changes were allowed (all subjects took at least an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker). Similar findings were obtained when blood pressure was measured in a clinic between 7 and 11 in the morning. Of the 114 subjects, an increase in the systolic blood pressure of 0 to 10 mmHg occurred in 32%, an increase of 10 to 20 mmHg occurred in 14%, and an increase more than 20 mmHg occurred in 3%. Furthermore, of 68 subjects who had a baseline ambulatory systolic blood pressure less than 135 mmHg, 11 had a reading of 135 mmHg or higher at week 6. Monitoring of the individual's fluid status, serum creatinine, and blood urea nitrogen concentrations is recommended. Closely monitor blood pressure during celecoxib initiation and throughout the therapy course.

acute generalized exanthematous pustulosis (AGEP), alopecia, contact dermatitis, diaphoresis, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), erythema, erythema multiforme, exfoliative dermatitis, fixed drug eruption, maculopapular rash, photosensitivity, pruritus, rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, xerosis

Serious and potentially fatal skin reactions, including erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), and fixed drug eruption (FDE), which may present as a more severe variant known as generalized bullous fixed drug eruption (GBFDE) have occurred after treatment with celecoxib. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. These serious events may occur without warning. Inform individuals about the signs and symptoms of serious skin reactions and instruct them to discontinue use of the NSAID at the first appearance of skin rash or any other sign of hypersensitivity. In addition to an idiosyncratic reaction as the etiology for serious skin reactions, a hypersensitivity syndrome that consists of fever, rash, and internal organ involvement may occur. The exact mechanism of severe skin reactions to celecoxib, which has a sulfonamide component but not an aromatic amine component, is unknown but is likely different from the mechanism associated with sulfonamide antibiotics, which have an aromatic amine moiety. Rash was reported with celecoxib in 2.2% of subjects during clinical trials. Other dermatologic adverse events reported with celecoxib 0.1% to 1.9% of subjects include alopecia, dermatitis, photosensitivity reaction, pruritus, erythematous rash (erythema), maculopapular rash, contact dermatitis, skin disorder, xerosis, and diaphoresis.

angina, bradycardia, chest pain (unspecified), hypercholesterolemia, myocardial infarction, palpitations, phlebitis, pulmonary embolism, sinus tachycardia, stroke, syncope, thromboembolism, thrombosis, vasculitis, ventricular fibrillation

Celecoxib, like all nonsteroidal anti-inflammatory drugs (NSAIDs), may cause an increased risk of serious cardiovascular thromboembolism, myocardial infarction, and stroke, which can be fatal. Careful selection and use of the lowest effective dose for the shortest duration possible is recommended. Estimates of increased relative risk range from 10% to 50% or more, based on the drug and dose studied. The risk may increase with increased exposure, as measured in dose or duration. Significant cardiovascular risk has been observed within days to weeks of NSAID initiation. The relative increase in cardiovascular thrombotic events over baseline appears to be similar in subjects with or without cardiovascular disease or risk factors for cardiovascular disease; however,

subjects with known cardiovascular disease or risk factors may be at greater risk because of a higher baseline risk of events. Of 4,146 subjects who took celecoxib for arthritis, 0.1% to 1.9% had angina pectoris, chest pain (unspecified), coronary artery disorder, hypercholesterolemia, sinus tachycardia, palpitations, or myocardial infarction. Less than 0.1% had syncope, ventricular fibrillation, pulmonary embolism, stroke, peripheral gangrene, or thrombo-phlebitis. Unstable angina, cerebral infarction, aortic valve incompetence, coronary artery atherosclerosis, sinus bradycardia, deep vein thrombosis, and ventricular hypertrophy were noted in 0.1% or more to less than 1% of subjects who received celecoxib 400 to 800 mg daily for up to 3 years. Vasculitis and deep venous thrombosis have been noted during postmarketing experience. Increased cardiovascular events were noted in celecoxib recipients, compared with placebo, in two 3-year, randomized, double-blind, placebo-controlled, multicenter studies designed to investigate whether celecoxib could prevent colorectal adenomas in those with a history of colon polyps. In 1 study, a dose-related increase in the composite endpoint of cardiovascular death, myocardial infarction, or stroke was demonstrated; the composite endpoint was met by 1% (7 of 676 subjects) who received placebo, as compared to 2.6% (18 of 683) who received celecoxib 200 mg twice daily and 3.4% (23 of 669) who received celecoxib 400 mg twice daily. Similar numbers of subjects in each treatment arm had a history of cardiovascular events (13.7% to 14.8%), a history of hypertension (39.3% to 42.3%), a history of diabetes (9% to 9.8%), were current cigarette smokers (14.3% to 18%), or took an aspirin regimen (30.4% to 31.2%). In a similarly designed study, 1.9% (12 of 628 subjects) who received placebo and 2.4% (23 of 933) who received celecoxib 400 mg daily had myocardial infarction, stroke, congestive heart failure, or cardiovascular death. Findings from a meta-analysis of 31 large-scale, randomized controlled trials involving NSAID use in 116,429 subjects with more than 115,000 person years of follow-up confirm that all NSAIDs are associated with an increased risk of cardiovascular adverse effects. The safety profile of compared NSAIDs (celecoxib, diclofenac, etoricoxib, ibuprofen, lumiracoxib, naproxen, and rofecoxib) varied considerably depending on the outcome. The rate ratios for celecoxib compared to placebo were estimated as 1.35 (95% creditability interval, 0.71 to 2.72) for myocardial infarction, 1.12 (0.6 to 1.82) for stroke, 2.07 (0.98 to 4.55) for cardiovascular death, and 1.5 (0.96 to 2.54) for death from any cause; investigators prespecified a rate ratio threshold of 1.3, an increase in risk of at least 30%, as clinically relevant. In a non-placebo controlled safety study, similar cumulative rates of serious cardiovascular thromboembolic adverse events were demonstrated among approximately 8,000 osteoarthritis and rheumatoid arthritis subjects treated for 9 months with celecoxib 400 mg twice daily (1.2%), diclofenac 75 mg twice daily (1.4%), or ibuprofen 800 mg 3 times daily (1.1%); the incidence of such events in non-aspirin users at 9 months was less than 1% in each of the 3 treatment groups. While comprehensive data regarding relative cardiovascular safety of any particular NSAID compared to other NSAIDs is not available, celecoxib 100 mg twice daily was

shown to be non-inferior to ibuprofen 600 to 800 mg 3 times daily or naproxen 375 to 500 mg twice daily for the composite endpoint of cardiovascular death, nonfatal MI, and nonfatal stroke in osteoarthritis or rheumatoid arthritis adult subjects with or at high risk for cardiovascular disease. The intention-to-treat (ITT) analysis followed subjects for 30 months, with 8,072 subjects randomized to celecoxib, 8,040 randomized to ibuprofen, and 7,969 randomized to naproxen. ITT hazard ratios (95% CI) were 0.93 (0.76 to 1.13) for celecoxib vs. naproxen, 0.86 (0.7 to 1.04) for celecoxib vs. ibuprofen, and 1.08 (0.89 to 1.31) for ibuprofen vs. naproxen (p less than 0.001 for non-inferiority for all celecoxib comparisons). Celecoxib also met non-inferiority criteria in a modified ITT analysis of all subjects who received at least 1 dose of study medication and had 1 or more post-baseline visits followed until the earlier of treatment discontinuation plus 30 days, or 43 months. Average 24-hour systolic pressure decreased by 0.3 mmHg in subjects receiving celecoxib in a 4-month substudy of 444 subjects, while average 24-hour systolic pressures increased by 3.7 mmHg and 1.6 mmHg in subjects taking ibuprofen and naproxen, respectively. The relative cardiovascular risks associated with celecoxib doses greater than 200 mg daily are not known. There is no consistent evidence that concomitant use of aspirin mitigates the increased risk for cardiovascular thrombotic events. Inform subjects of the signs and symptoms of CV events, and advise them to seek medical help immediately if such signs or symptoms occur.

back pain, headache, medication overuse headache, migraine, withdrawal

In the post-oral surgery pain study, post-dental extraction alveolar osteitis (dry socket) was noted. Among 4,146 adults who received celecoxib, 2.8% had back pain, 15.8% had headache, and 0.1% to 1.9% had migraine. Headache was a commonly reported side effect in a clinical trial for juvenile rheumatoid arthritis in pediatric patients 2 to 17 years, occurring in 13% of subjects receiving celecoxib 3 mg/kg twice daily and 10% of subjects receiving 6 mg/kg twice daily. Overuse of drugs for treating acute headaches, including NSAIDs, may lead to medication overuse headache. Subjects may experience migraine-like daily headaches or a significant increase in migraine attack frequency. Discontinuation of the overused drug and treatment of withdrawal symptoms (e.g., transient worsening of headache) may be necessary. Advise individuals about the risks of medication overuse (e.g., use of celecoxib or any combination of therapy for at least 10 days/month) and encourage them to keep a written record of headache frequency and drug use.

aseptic meningitis

Aseptic meningitis has been reported during the postmarketing period of celecoxib. Ibuprofen has been the most common NSAID implicated in this adverse reaction;

however, cases have been reported with other NSAIDs. Aseptic meningitis from 1 NSAID does not preclude use of another NSAID; most individuals can be treated with another drug without incident. However, a subject with Sjogren's syndrome experienced aseptic meningitis after receipt of naproxen, ibuprofen, and rofecoxib at different times; aseptic meningitis developed about a week after each drug exposure, and the symptoms abated roughly 2 days after each drug cessation. The occurrence of aseptic meningitis is not related to NSAID chemical class or prostaglandin inhibition. A Type III or IV immunological hypersensitivity reaction is the proposed mechanism of action. Drug-induced aseptic meningitis usually occurs shortly after drug initiation but can occur after years of drug usage. Although NSAID-induced aseptic meningitis is primarily reported in subjects with systemic lupus erythematosus (SLE), healthy subjects and subjects with other disease states such as ankylosing spondylitis, connective tissue disease, osteoarthritis, and rheumatoid arthritis have developed NSAID-induced aseptic meningitis. Symptoms of aseptic meningitis include confusion, drowsiness, general feeling of illness, severe headache, nausea, nuchal rigidity, and photophobia. As aseptic meningitis is a diagnosis of exclusion, the suspected drug should be discontinued and not restarted unless a rechallenge is desired.

hearing loss, tinnitus

Tinnitus and hearing loss (deafness) occurred with celecoxib (0.1% to 1.9%) during premarketing clinical trials. Labyrinthitis was noted in at least 0.1% but less than 1% of subjects.

cyanosis, methemoglobinemia

Celecoxib is chemically designated as a benzene sulfonamide. Methemoglobinemia is known to be associated with sulfonamides and with benzene derivatives. A case report of methemoglobinemia due to celecoxib has been reported. A healthy man developed a severe headache and progressive confusion and agitation while taking celecoxib 100 mg twice daily for osteoarthritis; celecoxib had been started 1 month prior to the development of symptoms. Due to a serum methemoglobin fraction of 9% (reference range 0 to 0.2) on admission, the patient received methylene blue treatment. Within 5 minutes, his cyanosis significantly improved. Repeat administration of methylene blue was needed 4 hours later. The serum methemoglobin concentrations decreased to 0.7% and 0.4% after the first and second methylene blue treatments, respectively. Celecoxib was discontinued and the patient received methylene blue (100 mg PO 3 times daily), ascorbic acid (300 mg PO 3 times daily), and riboflavin (20 mg PO once daily) for 3 days. He was discharged and remained symptom-free. Although a rechallenge was not feasible, celecoxib as the cause of the event was thought probable via use of the Naranjo probability scale.

anosmia, ataxia, dizziness, hypertonia, hypoesthesia, muscle cramps, paresthesias, vertigo

In clinical trials, dizziness occurred in 2% of celecoxib adult recipients and in 1% of subjects with juvenile rheumatoid arthritis. Leg muscle cramps, hypertonia, hypoesthesia, paresthesias, and vertigo occurred in 0.1% to 1.9% of adults. Ataxia and suicide were noted in less than 0.1% of subjects; ageusia and anosmia were noted during postmarketing experience. Vitreous floaters were noted in at least 0.1% but less than 1% of subjects who received celecoxib.

anxiety, depression, drowsiness, insomnia

Among 4,146 celecoxib recipients in premarketing clinical trials, 2.3% had insomnia. Psychiatric events that occurred in 0.1% to 1.9% of subjects who received celecoxib 200 to 400 mg/day included anxiety, depression, nervousness, and drowsiness.

cough, dyspnea, infection, laryngitis, pharyngitis, rhinitis, sinusitis

Among 4,146 adult celecoxib recipients, 2.3% had pharyngitis, 2% had rhinitis, 5% had sinusitis, and 8.1% had upper respiratory infection. Laryngitis, cough, dyspnea, bronchitis, influenza-like symptoms, pain, peripheral pain, cellulitis, and pneumonia were noted in 0.1% to 1.9% of subjects. Sepsis and sudden death were noted in less than 0.1% of subjects. Among subjects with juvenile rheumatoid arthritis, cough occurred in 7% and nasopharyngitis occurred in 5% to 6%. Dyspnea was noted in 2.8% of 2,285 subjects who took celecoxib 400 to 800 mg daily for up to 3 years for the prevention of adenomatous polyps.

arthralgia, elevated creatine kinase, myalgia, synovitis, tendon rupture

Arthralgia, arthrosis, myalgia, synovitis, elevated creatine kinase, and tendinitis occurred in 0.1% to 1.9% of adults who received celecoxib. Among subjects with juvenile rheumatoid arthritis, 3% to 7% had arthralgia. In the long-term polyp prevention studies, epicondylitis and tendon rupture occurred in at least 0.1% but less than 1% of subjects.

fever, hot flashes

Hot flashes and fever were noted in 0.1% to 1.9% of adults who received celecoxib. Among subjects with juvenile rheumatoid arthritis, 8% to 9% had fever. Decreased blood testosterone and ovarian cyst were noted in at least 0.1% of subjects but less than 1% of subjects.

hyperglycemia, hypoglycemia

Hyperglycemia was noted in 0.1% to 1.9% of celecoxib recipients, whereas hypoglycemia was noted less than 0.1%.

infertility, ovarian cyst

Ovarian cyst was a reported reproductive and genitourinary adverse reaction in 0.1% to less than 1% of subjects taking celecoxib, at an incidence greater than placebo in the long-term polyp prevention studies, and were either not reported during the controlled arthritis premarketing trials or occurred with greater frequency in the long-term, placebo-controlled polyp prevention studies. Additionally, NSAIDs, such as celecoxib, may delay or prevent prostaglandin-mediated rupture of ovarian follicles, which has been associated with reversible infertility. Small studies of women treated with NSAIDs demonstrated a reversible delay in ovulation. Consider withdrawal of NSAIDs in women who have difficulties conceiving or who are undergoing infertility evaluation.

diagnostic test interference

The pharmacological activity of NSAIDs in reducing inflammation, and possibly fever, may result in diagnostic test interference by diminishing the utility of these diagnostic signs in detecting infection.

Description

Celecoxib is an oral nonsteroidal anti-inflammatory drug (NSAID), a selective cyclooxygenase-2 (COX-2) inhibitor, indicated for osteoarthritis, rheumatoid arthritis, juvenile rheumatoid arthritis (JRA), ankylosing spondylitis, primary dysmenorrhea, acute pain, and migraine with or without aura. All NSAIDs, including celecoxib, cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and GI perforation of the esophagus, stomach, small intestine, or large intestine and are associated with an increased risk of serious cardiovascular (CV) thromboembolism, including myocardial infarction or stroke. Use the lowest effective dose for the shortest possible duration; the increase in CV risk has been most consistently observed at higher doses. Celecoxib was FDA-approved in December 1998.

Mechanism Of Action

Celecoxib has analgesic, anti-inflammatory, and antipyretic properties. The mechanism of action of celecoxib is believed to be due to inhibition of prostaglandin synthesis,

primarily via inhibition of cyclooxygenase-2 (COX-2). Celecoxib is a potent inhibitor of prostaglandin synthesis in vitro. Celecoxib concentrations reached during therapy have produced in vivo effects. Prostaglandins sensitize afferent nerves and potentiate the action of bradykinin in inducing pain in animal models. Prostaglandins are mediators of inflammation. Since celecoxib is an inhibitor of prostaglandin synthesis, its mode of action may be due to a decrease of prostaglandins in peripheral tissues. The mechanism of action by which celecoxib exerts therapeutic effects for migraines is not fully understood but may involve inhibition of prostaglandin synthesis.

Pharmacokinetics

Celecoxib is administered orally. Celecoxib is widely distributed and highly bound to plasma proteins (approximately 97%), primarily to albumin, and to a lesser extent, alpha-1-acid glycoprotein. Celecoxib is not preferentially bound to red blood cells. The celecoxib apparent Vd at steady-state is approximately 400 L for capsules and oral suspension (Vyscoxa) and 288 L for the oral solution (Elyxyb). Celecoxib metabolism is primarily mediated via CYP2C9. Three inactive metabolites, a primary alcohol, the corresponding carboxylic acid, and its glucuronide conjugate, have been identified in human plasma. Celecoxib is eliminated predominantly by hepatic metabolism with less than 3% of unchanged drug recovered in the urine and feces. About 57% of the total dose was excreted in the feces and 27% recovered in the urine; the carboxylic acid metabolite is the primary metabolite in both urine and feces. The apparent plasma clearance is about 500 mL/minute. The mean effective half-life is 11.2 hours under fasted conditions. The low solubility of the drug prolongs the absorption process, making terminal half-life determinations variable.

Affected cytochrome P450 isoenzymes and drug transporters: CYP2C9, CYP2D6
Celecoxib is a CYP2C9 substrate. In vitro studies indicate that celecoxib is an inhibitor of CYP2D6.

Route-Specific Pharmacokinetics

- **Oral Route**

Capsules
The Tmax of celecoxib occurs approximately 3 hours after an oral capsule dose. Both Cmax and AUC are roughly dose-proportional up to 200 mg twice daily. At higher doses and under fasting conditions, there are less proportional increases in celecoxib Cmax and AUC, which is thought to be due to the low aqueous solubility of the drug. Absolute bioavailability studies have not been conducted. When celecoxib capsules are taken with a high-fat meal, Cmax is delayed for about 1 to 2 hours with an increase in AUC of 10% to 20%.

Solution (e.g., Elyxyb)
After administration of 120 to 240 mg once daily of oral solution, celecoxib exhibits a dose-proportional increase in exposure. Tmax was 1 hour (range 0.67 to 3 hours) after administration of 120 mg of oral solution under fasting condition in 24 healthy subjects. Tmax was delayed by 2 hours with an approximately 50% decrease in Cmax and no change in AUC when celecoxib oral solution was taken with a high-fat meal compared to fasting conditions.

Suspension (e.g., Vyscoxa)
Following a single dose administration of 200 mg oral suspension and 200 mg capsules under fasting conditions in 52 healthy subjects, the median Tmax of celecoxib was 1.5 hours (range 0.67 to 8 hours) and the overall AUC was equivalent to celecoxib capsules with a decrease in Cmax of 22%. Absolute bioavailability studies have not been conducted and the comparative bioavailability between celecoxib oral suspension and capsules at doses above 200 mg has not been determined. With multiple dosing of celecoxib, steady-state conditions are reached on or before day 5. When a single dose of 200 mg was taken with a high fat, high-calorie meal, the median Tmax was delayed by 1.5 hours. The extent and rate of absorption of celecoxib was significantly increased when a single dose of 200 mg was administered under fed conditions compared to the fasting state and showed an increase in the mean AUC and Cmax of celecoxib by 35% to 50% and 144%, respectively.

- **Hepatic Impairment**

In mild (Child-Pugh Class A) and moderate (Child-Pugh Class B) hepatic impairment, steady-state celecoxib AUC is increased about 40% and 180%, respectively, above that seen in healthy subjects. People with severe hepatic impairment have not been studied.

- **Renal Impairment**

Celecoxib AUC was approximately 40% lower in people with chronic renal insufficiency (GFR 35 to 60 mL/minute) than in subjects with normal renal function. No significant relationship was found between GFR and celecoxib clearance. People with severe renal insufficiency have not been studied.

- **Pediatrics**

The steady state pharmacokinetics of celecoxib administered as an investigational oral suspension were evaluated in 152 juvenile rheumatoid arthritis (JRA) individuals 2 to 17 years weighing 10 kg or more. The oral clearance (unadjusted for body weight) of celecoxib increases less than proportionally to increasing weight, with 10 kg and 25 kg subjects predicted to have 40% and 24% lower clearance, respectively, compared with a 70 kg adult with rheumatoid arthritis. Twice daily administration of 50 mg to JRA subjects weighing 12 to 25 kg and 100 mg to JRA subjects weighing more than 25 kg should

achieve plasma concentrations similar to those observed in a clinical trial that demonstrated the non-inferiority of celecoxib to naproxen 7.5 mg/kg twice daily.

- **Geriatric**

Elderly subjects (over 65 years) have a 40% higher celecoxib Cmax and a 50% higher AUC compared to young subjects. In elderly females, celecoxib Cmax and AUC are higher than those for elderly males, but these increases are predominantly due to lower body weight in elderly females.

- **Gender Differences**

In elderly females, celecoxib Cmax and AUC are higher than those for elderly males, but these increases are predominantly due to lower body weight in elderly females.

- **Ethnic Differences**

A meta-analysis of pharmacokinetics studies suggests an approximately 40% higher AUC of celecoxib in Blacks compared to Caucasians. The cause and clinical significance of this finding is unknown.

- **Other**

CYP2C9 Poor Metabolizers
CYP2C9 activity is reduced in individuals with genetic polymorphisms that lead to reduced enzyme activity, such as those homozygous for the CYP2C9*2 and CYP2C9*3 polymorphisms. Limited data in subjects with the homozygous CYP2C9*3/*3 genotype (n = 8) showed celecoxib systemic concentrations that were 3- to 7-fold higher compared to subjects with CYP2C9*1/*1 or *I/*3 genotypes. The pharmacokinetics of celecoxib have not been evaluated in subjects with other CYP2C9 polymorphisms, such as *2, *5, *6, *9 and *11.

Administration

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

Oral Administration

Oral Solid Formulations

Capsules
Doses up to 200 mg twice daily may be administered without regard to timing of meals. Administer higher doses with food to improve absorption.
For individuals who have difficulty swallowing capsules, the contents of a capsule may be emptied onto a level teaspoon of cool or room temperature applesauce and ingested immediately with water.

Storage: The sprinkled capsule contents on applesauce is stable for up to 6 hours when refrigerated at 2 to 8 degrees C (35 to 45 degrees F).

Oral Liquid Formulations

Oral Solution (e.g., Elyxyb)
Administer with or without food.

Oral Suspension (e.g., Vyscoxa)
Shake well prior to administration.
Must be administered on an empty stomach at least 2 hours before or 1 hour after food.
If individuals cannot tolerate on an empty stomach, discontinue use.
Storage: Discard 21 days after opening.

Maximum Dosage Limits

- **Adults**
  800 mg/day PO for capsules; 400 mg/day PO for oral suspension (Vyscoxa); 120 mg/day PO for oral solution (Elyxyb).
- **Geriatric**
  800 mg/day PO for capsules; 400 mg/day PO for oral suspension (Vyscoxa); 120 mg/day PO for oral solution (Elyxyb).
- **Adolescents**
  200 mg/day PO for capsules and oral suspension (Vyscoxa) for juvenile rheumatoid arthritis. Safety and efficacy have not been established for other indications or for oral solution (Elyxyb).
- **Children**
  2 to 12 years weighing 26 kg or more: 200 mg/day PO for capsules and oral suspension (Vyscoxa) for juvenile rheumatoid arthritis. Safety and efficacy have not been established for other indications or for oral solution (Elyxyb).
  2 to 12 years weighing 10 to 25 kg: 100 mg/day PO for capsules and oral suspension (Vyscoxa) for juvenile rheumatoid arthritis. Safety and efficacy have not been established for other indications or for oral solution (Elyxyb).
  2 to 12 years weighing less than 10 kg: Safety and efficacy have not been established.
  1 year: Safety and efficacy have not been established.
- **Infants**
  Safety and efficacy have not been established.
- **Neonates**
  Safety and efficacy have not been established.

Dosage Forms

- Celebrex 100mg Capsule
- Celebrex 100mg Capsule
- Celebrex 200mg Capsule
- Celebrex 200mg Capsule
- Celebrex 200mg Capsule
- Celebrex 200mg Capsule
- Celebrex 200mg Capsule
- Celebrex 400mg Capsule
- Celebrex 50mg Capsule
- Celecoxib 100mg Oral capsule
- Celecoxib 200mg Oral capsule
- Celecoxib 400mg Oral capsule
- Celecoxib 50mg Oral capsule
- Celecoxib Bulk powder
- Elyxyb 120mg/4.8mL Solution
- SEGLENTIS 56mg-44mg Tablet
- VYSCOXA 10mg/1mL Oral Suspension

Dosage Adjustment Guidelines

Hepatic Impairment

Reduce the daily dose of capsules and oral suspension (Vyscoxa) by approximately 50% in people with moderate hepatic impairment (Child-Pugh Class B). Do not exceed a daily dose of 60 mg of oral solution (Elyxyb) in people with moderate hepatic impairment (Child-Pugh Class B). Celecoxib is not recommended in people with severe hepatic impairment (Child-Pugh Class C).

Renal Impairment

No dosage adjustment is needed for people with mild or moderate renal impairment. Celecoxib is not recommended in people with severe renal impairment.