Approximately 40% of patients in the U.S. with osteoarthritis have a medical condition known as High Blood Pressure (HBP)\textsuperscript{1}

**Are You One of Them?**

Consensi, is a fixed-dose combination drug therapy containing two prescription medications amlodipine besylate (for treating high blood pressure) and celecoxib (for managing the pain associated with osteoarthritis) in a single tablet taken once daily. Consensi should only be used:

- Exactly as prescribed by your doctor
- At the lowest dose possible for your treatment
- For the shortest time needed

The risk of getting an ulcer or bleeding increases with:

- past history of stomach ulcers, or stomach or intestinal bleeding with use of NSAIDs
- taking medicines called “corticosteroids”, “antiplatelet drugs”, “anticoagulants”, “selective serotonin reuptake inhibitors (SSRIs)”, or “serotonin norepinephrine reuptake inhibitors (SNRIs)”
- increasing doses of NSAIDs
- longer use of NSAIDs
- smoking
- drinking alcohol
- older age
- poor health
- advanced liver disease
- bleeding problems

You should not take other medicines that contain NSAIDs or salicylates during treatment with Consensi because of increased risk of stomach problems. Taking other medicines that contain NSAIDs or salicylates during treatment with Consensi will not provide increased relief of symptoms of osteoarthritis.

Consensi should only be used:

- exactly as prescribed
- at the lowest dose possible for your treatment
- for the shortest time needed

Who should not take CONSENSI?

Do not take Consensi:

- if you are allergic to amlodipine, celecoxib or any of the inactive ingredients in Consensi.
- if you have had an asthma attack, hives, or other allergic reaction with aspirin or any other NSAIDs.
- right before or after heart bypass surgery.
- if you have had an allergic reaction to sulfonamides.

Before taking Consensi, tell your healthcare provider about all your medical conditions, including if you:

- have heart problems.
- have liver or kidney problems.
- have asthma.
- are pregnant or plan to become pregnant. Talk to your healthcare provider if you are considering taking Consensi during pregnancy. Taking NSAIDs at about 20 weeks of pregnancy or later may harm your unborn baby. If you need to take NSAIDs for more than 2 days when you are between 20 and 30 weeks of pregnancy, your healthcare provider may need to monitor the amount of fluid in your womb around your baby. You should not take NSAIDs after about 30 weeks of pregnancy.
- are breastfeeding or plan to breastfeed. Consensi can pass into your breast milk. It is not known if Consensi will harm your baby. Talk with your healthcare provider about the best way to feed your baby if you take Consensi.

Please see additional Important Safety Information throughout. Please see accompanying full Prescribing Information with Boxed Warning and Medication Guide.
Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, or herbal supplements. Consensi and some other medicines can interact with each other and cause serious side effects. Do not start taking any new medicine without talking to your healthcare provider first.

What are the possible side effects of Consensi?

Consensi can cause serious side effects, including:

- liver problems, including liver failure
- worsening chest pain (angina) or heart attack, particularly in people with severe obstructive coronary artery disease
- heart failure
- swelling of your arms, legs, hands and feet (peripheral edema) is common with CONSENSI but can sometimes be serious.
- kidney problems, including kidney failure
- increased potassium levels (hyperkalemia)
- life-threatening allergic reactions
- life-threatening skin reactions
- low red blood cells (anemia)

Please see additional Important Safety Information throughout. Please see accompanying full Prescribing Information with Boxed Warning and Medication Guide.

Study results demonstrated that the combination of celecoxib and amlodipine provided similar blood pressure reduction to an equal dose of amlodipine.

There are no studies of the combination of celecoxib and amlodipine demonstrating reductions in the signs and symptoms of osteoarthritis, but one of the components, celecoxib, has demonstrated such effects. There are also no long-term studies to evaluate cardiovascular safety for the combination of celecoxib and amlodipine.


* Error bars – standard error of mean

See “What is the most important information I should know about Consensi?” for further detail regarding serious side effects.

Your healthcare provider will monitor your blood pressure and do blood tests to check you for side effects during treatment with Consensi.

Consensi may cause fertility problems in females that is reversible when treatment with Consensi is stopped. Talk to your healthcare provider if this is a concern for you.

The most common side effects of Consensi include:

- swelling of the arms, legs, hands, and feet
- joint swelling
- dizziness
- stomach pain
- diarrhea
- heartburn
- headache
- frequent urination
- hot or warm feeling in your face (flushing)
- gas
- tiredness
- extreme sleepiness

Get emergency help right away if you get any of the following symptoms:

- shortness of breath or trouble breathing
- chest pain
- weakness in one part or side of your body
- slurred speech
- swelling of the face or throat
1. Treats two medical conditions high blood pressure and pain associated with osteoarthritis with one tablet taken once daily

2. Fewer tablets per day may make it easier to remember to take your medication

3. Copay savings card available that may allow you to pay as little as $0 for Consensi

Patients:
Present this page along with a valid prescription for Consensi to receive savings per 30 tablet supply. See Terms and Conditions.

Pharmacists:
For Insured Patients: Process a Coordination of Benefits (COB/split bill) claim using the patients prescription insurance for the Primary claim. Submit a Secondary claim to Simple Save Rx using BIN: 017290/PCN: 55101202. For Insured Not Covered/Cash Patients: Submit a Primary claim to Simple Save Rx using BIN: 017290/PCN:55101202. For issues submitting claims under this offer please contact the Simple Save Rx Pharmacy Help Desk at 1-844-SAVE4RX (844-728-3479).

Terms and Conditions:
This offer cannot be combined with any other rebate or coupon, free trial, or similar offer for the specified prescription. Not valid for prescriptions reimbursed in whole or in part by Medicaid, Medicare, VA, DOD, TriCare, or other federal or state programs (including state prescription drug programs.) Offer good only in the United States at participating retail pharmacies. Offer not valid where otherwise prohibited by law, for example by applicable state law prohibiting co-pay cards. Burke Therapeutics reserves the right to rescind, revoke, or amend the offer without notice. The selling, purchasing, trading, or counterfeiting of this offer is prohibited by law. This card is not insurance and is not intended to be a substitute for insurance. Participating patients and pharmacists understand and agree to comply with all Terms and Conditions of this offer. Patients must be 18 or older.

Stop taking Consensi and call your healthcare provider right away if you get any of the following symptoms:
- nausea
- more tired or weaker than usual
- diarrhea
- itching
- indigestion or stomach pain
- flu-like symptoms
- vomit blood
- there is blood in your bowel movement or it is black and sticky like tar
- unusual weight gain
- your skin or eyes look yellow
- skin rash or blisters with fever
- swelling of the arms, legs, hands and feet

These are not all the possible side effects of Consensi.

Please see: Full Prescribing Information, including BOXED WARNING, and Medication Guide.
Call your doctor for medical advice about side effects.
You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Burke Therapeutics, LLC at 1-888-275-1264.

Please see additional Important Safety Information throughout. Please see accompanying full Prescribing Information with Boxed Warning and Medication Guide.
What is the most important information I should know about CONSENSI?

Consensi contains celecoxib, a nonsteroidal anti-inflammatory drug (NSAID), and amlodipine, a calcium channel blocker (CCB). NSAIDs can cause serious side effects, including:

- **Increased risk of a heart attack or stroke that can lead to death.** This risk may happen early in treatment and may increase with duration of use.
- **Do not take CONSENSI right before or after a heart surgery called a “coronary artery bypass graft” (CABG).**
- **Avoid taking CONSENSI after a recent heart attack, unless your healthcare provider tells you to.** You may have an increased risk of another heart attack if you take NSAIDs after a recent heart attack.
- **NSAID medications, like celecoxib, cause an increase risk of bleeding, ulcers, and tears (perforation) of the esophagus, stomach, and intestines, at any time during treatment, which can occur without warning and may cause death.** Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events.

Do not take Consensi right before or after a heart surgery called a “coronary artery bypass graft” (CABG).

Avoid taking Consensi after a recent heart attack, unless your healthcare provider tells you to. You may have an increased risk of another heart attack if you take NSAIDs after a recent heart attack.

- **Increased risk of bleeding, ulcers, and tears (perforation) of the esophagus (tube leading from the mouth to the stomach), stomach, and intestines:**
  - anytime during use
  - without warning symptoms
  - that may cause death

The risk of getting an ulcer or bleeding increases with:

- past history of stomach ulcers, or stomach or intestinal bleeding with use of NSAIDs
- taking medicines called “corticosteroids”, “antiplatelet drugs”, “anticoagulants”, “selective serotonin reuptake inhibitors (SSRIs)”, or “serotonin norepinephrine reuptake inhibitors (SNRIs)”
- increasing doses of NSAIDs
- longer use of NSAIDs
- smoking
- drinking alcohol
- older age
- poor health
- advanced liver disease
- bleeding problems

You should not take other medicines that contain NSAIDs or salicylates during treatment with Consensi because of increased risk of stomach problems. Taking other medicines that contain NSAIDs or salicylates during treatment with Consensi will not provide increased relief of symptoms of osteoarthritis.

Consensi should only be used:

- exactly as prescribed
- at the lowest dose possible for your treatment
- for the shortest time needed

Who should not take CONSENSI?

Do not take Consensi:

- if you are allergic to amlodipine, celecoxib or any of the inactive ingredients in Consensi.
- if you have had an asthma attack, hives, or other allergic reaction with aspirin or any other NSAIDs.
- right before or after heart bypass surgery.
- if you have had an allergic reaction to sulfonamides.

Before taking Consensi, tell your healthcare provider about all your medical conditions, including if you:

- have heart problems.
- have liver or kidney problems.
- have asthma.

Please see additional Important Safety Information throughout. Please see accompanying full Prescribing Information with Boxed Warning and Medication Guide.
• are pregnant or plan to become pregnant. Talk to your healthcare provider if you are considering taking Consensi during pregnancy. Taking NSAIDs at about 20 weeks of pregnancy or later may harm your unborn baby. If you need to take NSAIDs for more than 2 days when you are between 20 and 30 weeks of pregnancy, your healthcare provider may need to monitor the amount of fluid in your womb around your baby. You should not take NSAIDs after about 30 weeks of pregnancy.

• are breastfeeding or plan to breastfeed. Consensi can pass into your breast milk. It is not known if Consensi will harm your baby. Talk with your healthcare provider about the best way to feed your baby if you take Consensi.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, or herbal supplements. Consensi and some other medicines can interact with each other and cause serious side effects. Do not start taking any new medicine without talking to your healthcare provider first.

What are the possible side effects of Consensi?

Consensi can cause serious side effects, including:

• liver problems, including liver failure
• worsening chest pain (angina) or heart attack, particularly in people with severe obstructive coronary artery disease
• heart failure
• swelling of your arms, legs, hands and feet (peripheral edema) is common with CONSENSI but can sometimes be serious.
• kidney problems, including kidney failure
• increased potassium levels (hyperkalemia)
• life-threatening allergic reactions
• life-threatening skin reactions
• low red blood cells (anemia)

See “What is the most important information I should know about Consensi?” for further detail regarding serious side effects.

Your healthcare provider will monitor your blood pressure and do blood tests to check you for side effects during treatment with Consensi.

Consensi may cause fertility problems in females that is reversible when treatment with Consensi is stopped. Talk to your healthcare provider if this is a concern for you.

The most common side effects of Consensi include:

• swelling of the arms, legs, hands, and feet
• joint swelling
• dizziness
• stomach pain
• diarrhea
• heartburn
• headache
• frequent urination
• hot or warm feeling in your face (flushing)
• gas
• tiredness
• extreme sleepiness

Get emergency help right away if you get any of the following symptoms:

• shortness of breath or trouble breathing
• chest pain
• weakness in one part or side of your body
• slurred speech
• swelling of the face or throat

Stop taking Consensi and call your healthcare provider right away if you get any of the following symptoms:

• nausea
• more tired or weaker than usual
• diarrhea
• itching
• indigestion or stomach pain
• flu-like symptoms
• vomit blood
• there is blood in your bowel movement or it is black and sticky like tar
• unusual weight gain
• your skin or eyes look yellow
• skin rash or blisters with fever
• swelling of the arms, legs, hands and feet

These are not all the possible side effects of Consensi.

Please see Full Prescribing Information, including BOXED WARNING, and Medication Guide.

Call your doctor for medical advice about side effects.

You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Burke Therapeutics, LLC at 1-888-275-1264.
WARNINGS AND PRECAUTIONS

1 INDICATIONS AND USAGE

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

See full prescribing information for complete boxed warning.

- Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular (CV) thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in the treatment and may increase with duration of use. (5.1)
- CONSENSI is contraindicated in the setting of coronary artery bypass graft (CABG) surgery. (4, 5.1)
- NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events. (5.2)

2 DOSAGE AND ADMINISTRATION

CONSENSI is a combination of amlodipine besylate, a calcium channel blocker, and celecoxib, a nonsteroidal anti-inflammatory drug (NSAID), indicated for patients for whom treatment with amlodipine for hypertension and celecoxib for osteoarthritis are appropriate. Lowering blood pressure reduces the risk of fatal and nonfatal CV events, primarily strokes and myocardial infarctions. (1.1)

Limitations of Use

CONSENSI is only available in a celecoxib strength of 200 mg and is only to be taken once daily. (1.1)

DOSEAGE AND ADMINISTRATION

Use the lowest effective dosage of celecoxib for the shortest duration consistent with individual treatment goals. If analgesic therapy is no longer indicated, discontinue CONSENSI and initiate patient on alternative antihypertensive therapy. (2.1, 2.2)

Start at (amlodipine/celecoxib) 5 mg/200 mg (2.5 mg/200 mg for small, elderly, or frail patients or patients with hepatic impairment) orally once daily. Titrates to 5 mg/200 mg or 10 mg/200 mg once daily as needed for blood pressure control. (2.1)

CONSENSI may be substituted for its individual components. (2.3)

DOSE FORMS AND STRENGTHS

Tablets (amlodipine/celecoxib): 2.5 mg/200 mg, 5 mg/200 mg, or 10 mg/200 mg (3)

CONTRAINDICATIONS

- Known hypersensitivity to amlodipine, celecoxib, or any inactive ingredients of CONSENSI (4)
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs (4)
- In the setting of CABG surgery (4)
- Demonstrated allergic-type reactions to sulfonamides (4)

WARNINGS AND PRECAUTIONS

- Hepatotoxicity and Patients with Hepatic Failure: Inform patients of warning signs and symptoms of hepatotoxicity. Discontinue if abnormal liver tests persist or worsen or if clinical signs of liver disease develop. (5.5)
- Hypertension: Patients taking some antihypertensive medications may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure. (5.4, 7)

7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS

9 DESCRIPTION

10 OVERDOSE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

13 NONCLINICAL TOXICOLOGY

14 CLINICAL STUDIES

15 HOW SUPPLIED/STORAGE AND HANDLING

16 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed
CONSENSI (amlodipine and celecoxib) tablets are white and biconvex, non-coated, non-scored, with the tablet strength debossed on one side, available in the following strengths: substitute CONSENSI containing the same component doses. Monitor blood pressure carefully.

2. DOSSAGE AND ADMINISTRATION

2.1 Recommended Dosage

Use the lowest effective dosage of celecoxib for the shortest duration consistent with individual patient treatment goals. In clinical studies, the use of CELEBREX 200 mg once daily was effective for osteoarthritis and rheumatoid arthritis.

Start CONSENSI in adults at amlodipine/celecoxib 2.5 mg/200 mg once daily or 5 mg/200 mg twice daily. Alternatively, start CONSENSI at 2.5 mg/200 mg once daily, increase the dosage to 5 mg/200 mg at regular intervals (e.g., 50 mg over 2 days and/or 25 mg every other day) until the desired blood pressure is achieved. Adjust celecoxib component dosage according to blood pressure goals. In general, wait 7 to 14 days between titration steps. More rapid titration is cautiously monitored, close the therapy.

The maximum dose is 10 mg/200 mg once daily.

2.2 Discontinuation

If analgesic therapy is no longer indicated, discontinue CONSENSI and initiate patient on alternate analgesic therapy, such as amiodopine monotherapy. If CONSENSI is stopped and replaced with the equivalent dose of amiodopine, monitor blood pressure carefully.

2.3 Replacement Therapy

For patients requiring a change in celecoxib or amiodopine from separate capsules and tablets, respectively, substitute CONSENSI containing the same component doses. Monitor blood pressure carefully.

3 DOSAGE FORMS AND STRENGTHS

CONSIDI (amlodipine/celecoxib) are white and biconvex, non-coated, non-scored, with the tablet strength debossed on one side, available in the following strengths:

Amiodopine

Celecoxib

Shape

2.5 mg/200 mg

2 mg/200 mg

25 mg/200 mg

10 mg/200 mg

Elongated oval

Round

Capsule

4 CONTRAINDICATIONS

CONSIDI is contraindicated in the following patients:

• Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to amlodipine, celecoxib, or any of the inactive ingredients in CONSENSI (see Warnings and Precautions (5.9, 5.10)).

• History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Several aminopyrine trials have been conducted in these patients (see Warnings and Precautions (5.9, 5.10)).

• In the setting of coronary artery bypass graft (CABG) surgery (see Warnings and Precautions (5.1)).

• In patients who have demonstrated allergic-type reactions to sulfafoxides (see Warnings and Precautions (5.11)).

5 WARNINGS AND PRECAUTIONS

5.1 Cardiovascular Thrombotic Events

Celecoxib

Clinical trials of several cyclo-oxygenase-2 (COX-2) selective and nonselective NSIDs of up to three years have shown an increased risk of serious cardiovascular (CV) thrombotic events, including myocardial infarction (MI) and stroke, which can be fatal. Based on available data, it is unclear that the risk for CV thrombotic events is similar for all NSIDs. The relative increase in serious CV thrombotic events over baseline conferred by NSID use appears to be similar in those with and without known CV disease or risk factors for CV disease. However, patients with known CV disease or risk factors had a higher absolute incidence of excess serious CV thrombotic events compared to placebo. It has been consistently found that this increased risk of serious CV thrombotic events began as early as the first weeks of treatment. The increase in CV thrombotic risk has been observed most consistently at higher doses.

In the APEX (Aspirin Platelet Inhibition and elves of CV events, either of which may contribute to the increased incidence of CV events. Patients with CV disease may be at a higher risk of CV events with nonselective COX inhibitors (e.g., ibuprofen, aspirin, ketoprofen) and may have an increased risk of CV events with CELEBREX when compared to placebo.

A randomized control trial entitled the Prospective Randomized Evaluation of Celecoxib Integrated Safety vs. Ibuprofen Or Naproxen (PRECISION) was conducted to assess the relative cardiovascular safety of celecoxib vs. ibuprofen, naproxen, and placebo in patients with known CV disease and/or risk factors. The results of this study indicate that the use of celecoxib is associated with a reduced risk of CV events compared to ibuprofen and naproxen.

In the heart Failure and Edema

The COX-2 inhibitor celecoxib has been shown to cause increased edema and fluid retention, and to increase the risk of heart failure in patients with fluid retention and edema.

5.2 Gastrointestinal Bleeding, Ulceration, and Perforation

• NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including perforation, bleeding, and ulceration, and in patients with previous CV symptoms, these serious adverse events may be more likely to occur, with the risk increasing with duration of use (see Warnings and Precautions (5.1)).

• CONSENSI is contraindicated in the setting of upper endoscopy with biopsy, endoscopy, or ulceration caused by NSAID use and/or GI bleeding are at greater risk for serious GI events (see Warnings and Precautions (5.2)).

5.3 Hepatotoxicity and Patients with Hepatic Failure

• Amlodipine is extensively metabolized by the liver and the plasma elimination half-life (t1/2) is 36 hours in healthy subjects.

5.4 Hypertension

• NSIDs, including celecoxib, can lead to the new onset of hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of CV events. Patients may be at a higher risk of CV events with nonselective COX inhibitors (e.g., ibuprofen, aspirin, ketoprofen) and may have an increased risk of CV events with CELEBREX when compared to placebo.

5.5 Hypotension

• Amlodipine is a calcium channel blocker that causes vasodilation and may decrease blood pressure. Celecoxib may also cause a decrease in blood pressure. Avoid the use of celecoxib in patients with severe hypovolemia or shock.

5.6 Increased Angina or Myocardial Infarction

• Amlodipine and the adverse cardiovascular effects associated with COX-2 inhibition, resulting in an increased risk of myopathy and rhabdomyolysis.

5.7 Heart Failure and Edema

• Amlodipine is a calcium channel blocker that causes vasodilation and may decrease blood pressure. Celecoxib may also cause a decrease in blood pressure. Avoid the use of celecoxib in patients with severe hypovolemia or shock.

5.8 Renal Toxicity and Hyperkalemia

• Amlodipine is a calcium channel blocker that causes vasodilation and may decrease blood pressure. Celecoxib may also cause a decrease in blood pressure. Avoid the use of celecoxib in patients with severe hypovolemia or shock.

5.9 Impaired Hepatic Function

• Celecoxib is extensively metabolized by the liver and the plasma elimination half-life (t1/2) is 36 hours in healthy subjects.

5.10 Impaired Renal Function

• Celecoxib is extensively metabolized by the liver and the plasma elimination half-life (t1/2) is 36 hours in healthy subjects.

5.11 Allergic Reactions

• Celecoxib may cause anaphylactic reactions and serious skin reactions. Inform patients of the warning signs and symptoms of anaphylaxis. Discontinue CONSENSI immediately, and perform a clinical evaluation of the patient.

5.12 Increased Bleeding

• Celecoxib, including celecoxib, cause serious GI adverse events including inflammation, bleeding, ulceration, and perforation of the esophagus, stomach, small intestine, or large intestine, which may be fatal. Discontinue CONSENSI and perform a clinical evaluation of the patient.

5.13 Cardiovascular Thrombotic Events

• NSIDs cause an increased risk of serious gastrointestinal (GI) adverse events including perforation, bleeding, and ulceration, and in patients with previous CV symptoms, these serious adverse events may be more likely to occur, with the risk increasing with duration of use (see Warnings and Precautions (5.1)).

• CONSENSI is contraindicated in the setting of upper endoscopy with biopsy, endoscopy, or ulceration caused by NSAID use and/or GI bleeding are at greater risk for serious GI events (see Warnings and Precautions (5.2)).
Correct volume status in dehydrated or hypovolemic patients prior to initiating celecoxib. Monitor renal function throughout treatment and reevaluate prior to repeat dosing. Monitor patients for signs of worsening renal function. If celecoxib is used in patients with advanced renal disease, monitor patients for signs of worsening renal function.

5.4 Anaphylactic Reactions

Celecoxib has been associated with anaphylactic reactions in patients with and without known hypersensitivity to celecoxib and in patients with aspirin sensitive asthma. Celecoxib is a sulfonamide and both NSIs and sulfonamides may cause type II allergic reactions including anaphylaxis, angioedema and urticaria. These reactions may be seen in patients with preexisting asthma (without known aspirin sensitivity), monitor patients for changes in the signs and symptoms of asthma as well as suspected symptoms of hypotension.

5.5 Serious Skin Reactions

Serious skin reactions have occurred following treatment with celecoxib, including erythema multiforme, toxic epidermal necrolysis (TEN), exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP). These serious events may occur without warning and can be fatal.

5.6 Use in Specific Populations

5.6.1 Pregnancy

Celecoxib is teratogenic in rats and rabbits at doses associated with human exposures (based on AUC) at least 10 times the human exposure at the usual recommended doses. Celecoxib is contraindicated in pregnancy due to the potential for fetal harm. Celecoxib is excreted in both human milk and rat milk. Celecoxib should be used during breastfeeding only if the potential benefit justifies the potential risk to the infant.

5.6.2 Nursing Mothers

Celecoxib is excreted in both human milk and rat milk. Celecoxib should be used during breastfeeding only if the potential benefit justifies the potential risk to the infant.

5.6.3 Labor and Delivery

Celecoxib is contraindicated in labor and delivery.

5.6.4 Neonates and Infants

5.6.4.2 Neonates and Infants

The incidence of clinically significant decreases in hemoglobin (>2 g/dL) was 8.9% in infants treated with celecoxib for ≥2 days. Among patients receiving placebo, 0.3% discontinued due to anemia. Monitor hematocrit in neonates if CONSENSI treatment extends beyond 48 hours.

5.6.5 Pediatric Use

5.6.5.4.4 Pediatric Use

The incidence of clinically significant decreases in hemoglobin (>2 g/dL) was 8.9% in infants treated with celecoxib for ≥2 days. Among patients receiving placebo, 0.3% discontinued due to anemia. Monitor hematocrit in neonates if CONSENSI treatment extends beyond 48 hours.

5.6.6 Adverse Reactions

CBX = Celecoxib 100 – 200 mg twice daily or 200 mg once daily; DCF = Diclofenac 75 mg twice daily; IBU = Ibuprofen 400 mg twice daily; N=387

5.6.6.2 Adverse Reactions

5.6.6.3 Withdrawals/Serious Adverse Events

Kaplan-Meier cumulative rates at 9 months for CONSENSI versus placebo in patients treated with celecoxib for at least 9 months (N≥120 patients.

6. ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates.

Celecoxib Clinical Trials

Approximately 500 patients in the pre-marketing controlled clinical trials, approximately 4,250 were patients with osteoarthritis, approximately 2,700 were patients with rheumatoid arthritis, and approximately 1,300 were patients in studies to determine the effects of celecoxib at doses of 200 mg or 400 mg once daily or more, including more than 400 treated at 600 mg (400 mg twice daily). Approximately 390 patients received celecoxib at doses of 300 mg once daily or more, approximately 320 of these have received it for 1 year or more and 124 of these have received it for 2 years or more. Pre-Marketing Controlled Clinical Trials

The table below lists all adverse events, regardless of causality, occurring in ≥2% of patients treated with celecoxib and selected adverse events occurring in ≥2% of patients treated with CONSENSI. For each adverse event, the table includes the Kaplan-Meier cumulative rates at 9 months for CONSENSI versus placebo in patients treated with celecoxib for at least 9 months (N≥120 patients).

6.2 Gender

The following table lists all adverse events, regardless of causality, occurring in ≥2% of patients treated with celecoxib and selected adverse events occurring in ≥2% of patients treated with CONSENSI. For each adverse event, the table includes the Kaplan-Meier cumulative rates at 9 months for CONSENSI versus placebo in patients treated with celecoxib for at least 9 months (N≥120 patients).

6.3 Age

The following table lists all adverse events, regardless of causality, occurring in ≥2% of patients treated with celecoxib and selected adverse events occurring in ≥2% of patients treated with CONSENSI. For each adverse event, the table includes the Kaplan-Meier cumulative rates at 9 months for CONSENSI versus placebo in patients treated with celecoxib for at least 9 months (N≥120 patients).

6.4 Race

The following table lists all adverse events, regardless of causality, occurring in ≥2% of patients treated with celecoxib and selected adverse events occurring in ≥2% of patients treated with CONSENSI. For each adverse event, the table includes the Kaplan-Meier cumulative rates at 9 months for CONSENSI versus placebo in patients treated with celecoxib for at least 9 months (N≥120 patients).

6.5 Administration"

The following table lists all adverse events, regardless of causality, occurring in ≥2% of patients treated with celecoxib and selected adverse events occurring in ≥2% of patients treated with CONSENSI. For each adverse event, the table includes the Kaplan-Meier cumulative rates at 9 months for CONSENSI versus placebo in patients treated with celecoxib for at least 9 months (N≥120 patients).

6.6 Concomitant Use of Celecoxib with Other Drugs

The following table lists all adverse events, regardless of causality, occurring in ≥2% of patients treated with celecoxib and selected adverse events occurring in ≥2% of patients treated with CONSENSI. For each adverse event, the table includes the Kaplan-Meier cumulative rates at 9 months for CONSENSI versus placebo in patients treated with celecoxib for at least 9 months (N≥120 patients).

6.7 Other"
Juvenile Rheumatoid Arthritis Study

In a 12-week, double-blind, active-controlled study, 242 juvenile rheumatoid arthritis patients 2 years to 17 years of age were treated with celecoxib or naproxen; 77 juvenile rheumatoid arthritis patients were treated with celecoxib 3 mg/kg twice daily, 82 patients were treated with celecoxib 6 mg/kg twice daily, and 83 patients were treated with naproxen 7.5 mg/kg twice daily. The most commonly occurring (≥3%) adverse events in celecoxib-treated patients were headache, fever (pyrexia), upper abdominal pain, cough, nasopharyngitis, abdominal pain, nausea, arthralgia, diarrhea and vomiting. The most commonly occurring (≥5%) adverse events for naproxen-treated patients were headache, nausea, vomiting, fever, upper abdominal pain, diarrhea, cough, abdominal pain, and dizziness. Compared with naproxen, celecoxib at doses of 3 and 6 mg/kg twice daily had no observable deleterious effect on growth and development during the course of the 12-week double-blind study. There was no substantial difference in the number of clinical exacerbations of utsitis or systemic features of juvenile rheumatoid arthritis among treatment groups.

In a 12-week, open-label extension of the double-blind study described above, 202 juvenile rheumatoid arthritis patients were treated with celecoxib 6 mg/kg twice daily. The incidence of adverse events was similar to that observed during the double-blind study; no unexpected adverse events of clinical importance emerged.

Adverse Events Occurring in ≥5% of Juvenile Rheumatoid Arthritis Patients in Any Treatment Group, by System Organ Class (% of patients with events)

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Preferred Term</th>
<th>Celecoxib 3 mg/kg N=77</th>
<th>Celecoxib 6 mg/kg N=82</th>
<th>Naproxen 7.5 mg/kg N=83</th>
<th>All Doses Twice Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Event</td>
<td>64</td>
<td>70</td>
<td>72</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye Disorders</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>26</td>
<td>24</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain NOS</td>
<td>4</td>
<td>7</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain upper</td>
<td>8</td>
<td>6</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting NOS</td>
<td>3</td>
<td>6</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea NOS</td>
<td>5</td>
<td>4</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
<td>4</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>13</td>
<td>11</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>8</td>
<td>9</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>25</td>
<td>20</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injury and Poisoning</td>
<td>4</td>
<td>6</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Investigations*</td>
<td>3</td>
<td>11</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>10</td>
<td>8</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>3</td>
<td>7</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous System</td>
<td>17</td>
<td>11</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache NOS</td>
<td>13</td>
<td>10</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness (excl vertigo)</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>8</td>
<td>15</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>7</td>
<td>7</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin &amp; Subcutaneous</td>
<td>10</td>
<td>7</td>
<td>18</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Abnormal laboratory tests, which include: Prolonged activated partial thromboplastin time, Bacteremia NOS present, Blood glucose increased, Blood pressure increased, Blood uric acid increased, Hematocrit decreased, Hematrauma present, Hemoglobin decreased, Liver function tests NOS abnormal, Prothrombin present. Transaminasis NOS increased, Urine analysis abnormal NOS.

Other Pre-Accord Studies

Adverse Events from Arthritis Studies

A total of 378 patients were treated with celecoxib in placebo- and active-controlled ankylosing spondylitis studies. Doses up to 400 mg once daily were studied. The types of adverse events reported in the ankylosing spondylitis studies were similar to those reported in the celecoxib/rheumatoid arthritis studies.

Adverse Events from Angina and Dysmenorrhea Studies

Approximately 1,700 patients were treated with celecoxib in angina and dysmenorrhea studies. All patients in post-or oral surgery pain studies received a single dose of study medication. Doses up to 600 mg/day of celecoxib were studied in primary dysmenorrhea and post-orthopedic surgery pain studies. The types of adverse events seen in the angina and dysmenorrhea studies were similar to those reported in arthritis studies. The only additional adverse event reported was post-dental extraction alveolar osteitis (dry socket) in the post-or oral surgery pain studies.

The APC and Pre-ASP Trials

Adverse Reactions from Long-Term, Placebo-Controlled Polypl Prevention Studies

Exposure to celecoxib in the Adenoma Prevention with Celecoxib (APC) and Prevention of Spontaneous Adenomatous Polyps (Pre-ASP) trials was 400 to 800 mg daily for up to 3 years (see Clinical Studies [14.3]) Some adverse reactions occurred in higher percentages of patients than in the arthritis pre-marketing trials (treatment durations up to 12 weeks); see Adverse Events from celecoxib during controlled arthritis trials, above). The adverse reactions for which these differences in patients treated with celecoxib were greater as compared to the arthritis pre-marketing trials were as follows:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Celecoxib 400 to 800 mg daily</th>
<th>Placebo N=265</th>
<th>Placebo N=265</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>10.5%</td>
<td>7.0%</td>
<td></td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>4.7%</td>
<td>3.1%</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>6.8%</td>
<td>5.3%</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>3.2%</td>
<td>2.1%</td>
<td></td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>2.8%</td>
<td>1.6%</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>12.5%</td>
<td>9.8%</td>
<td></td>
</tr>
<tr>
<td>Nephrolithiasis</td>
<td>2.1%</td>
<td>0.8%</td>
<td></td>
</tr>
</tbody>
</table>

The following additional adverse reactions occurred in ≥0.1% and <1% of patients taking celecoxib, at an incidence greater than placebo in the long-term placebo-controlled pain prevention studies, and were either not reported during the controlled arthritis pre-marketing trials or occurred with greater frequency in the long-term, placebo-controlled polypl prevention studies:

Nervous system disorders: Cerebral infarction
Eye disorders: Vitreous floaters, conjunctival hemorrhage
Ear and labyrinth: Labyrinthitis
Cardiac disorders: Angina unerta, aortic valve incompetence, coronary artery athereosclerosis, sinus bradycardia, ventricular hypertrophy

Vascular disorders: Deep vein thrombosis
Respiratory system and breast disorders: Ovarian cyst
Investigations: Blood potassium increased, blood sodium increased, blood testosterone increased

Injury, poisoning and procedural complications: Epididymitis, tendon rupture

Amlodipine Clinical Trials

Amlodipine has been evaluated for safety in more than 11,000 patients in U.S. and foreign clinical trials. In general, treatment with amlodipine was well-tolerated at doses up to 10 mg daily. Most adverse reactions reported during therapy with amlodipine were of mild or moderate severity. In controlled clinical trials directly comparing amlodipine (N=1730) at doses up to 10 mg to placebo (N=1250), decreases in blood pressure of amlodipine was required in only about 1.5% of patients and was not significantly different from placebo (about 1%). The most commonly reported side effects more frequent in amlodipine than placebo are reflected in the table below. The incidence (%) of side effects that occurred in a dose related manner are as follows:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Amlodipine (%) (N=1730)</th>
<th>Placebo (%) (N=1250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edema</td>
<td>1.8</td>
<td>3.0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1.1</td>
<td>3.4</td>
</tr>
<tr>
<td>Flushing</td>
<td>0.7</td>
<td>1.4</td>
</tr>
<tr>
<td>Palpitation</td>
<td>0.7</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Other adverse reactions that were not clearly dose related but were reported with an incidence greater than 1.5% in placebo-controlled clinical trials include the following:

Placeto Amlodipine

<table>
<thead>
<tr>
<th>Condition</th>
<th>Male%</th>
<th>Female%</th>
<th>Male%</th>
<th>Female%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edema</td>
<td>5.6</td>
<td>14.6</td>
<td>1.4</td>
<td>5.1</td>
</tr>
<tr>
<td>Flushing</td>
<td>1.5</td>
<td>4.5</td>
<td>0.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Palpitations</td>
<td>1.4</td>
<td>3.3</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Somnolence</td>
<td>1.3</td>
<td>1.6</td>
<td>0.8</td>
<td>0.3</td>
</tr>
</tbody>
</table>

For several adverse experiences that appear to be drug and dose related, there was a greater incidence in women than men associated with amlodipine treatment as shown in the following table:

Theappendix

The following postmarketing event has been reported infrequently where a causal relationship is uncertain: gynecomastia. In postmarketing experience, jaundice and hepatic enzyme elevations (mostly consistent with cholestasis or hepatitis), in some cases severe enough to require discontinuation of therapy or death. It is important to keep in mind that these reports are post-marketing and not placebo-controlled studies, but the incidence of these side effects was between 1% and 2% in all multiple dose studies. Amlodipine therapy has not been associated with clinically significant changes in routine laboratory tests. No clinically relevant changes were noted in serum potassium, serum glucose, total triglycerides, total cholesterol, high-density lipoprotein (HDL) cholesterol, uric acid, BUN, or creatinine.

In patients with angiographically documented coronary artery disease (PREVENT study: 825 patients randomized to amlodipine (5-10 mg once daily) or placebo and followed for 3 years; CAMELOT study: 1318 patients randomized to amlodipine (5-10 mg once daily) or placebo in addition to standard care as determined by mean event rate of 19 months), the adverse event profile was similar to that reported previously (see above), with the most common adverse event being peripheral edema.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of either celecoxib or amlodipine. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Celecoxib

Thromboembolic: Vasculitis, deep venous thrombosis
General: Anaphylactic reaction, angioedema
Hypertension: Liver necrosis, hepatitis, jaundice, hepatic failure
Musculoskeletal: Agranulocytosis, aplastic anemia, pancreatitis, leucopenia
Renal: Interstitial nephritis

Amlodipine

The following postmarketing event has been reported infrequently where a causal relationship is uncertain: gynecomastia. In postmarketing experience, jaundice and hepatic enzyme elevations (mostly consistent with cholestasis or hepatitis), in some cases severe enough to require hospitalization, have been reported in association with use of amlodipine.

Postmarketing reporting has also revealed a possible association between extrapyramidal disorder and amlodipine. Amlodipine has been used safely in patients with chronic obstructive pulmonary disease, well-compensated congestive heart failure, coronary artery disease, peripheral vascular disease, diabetes mellitus, and abnormal lipid profiles.
**DRUG INTERACTIONS**

**Cyclophosphamide**

**CYP2D6 Substrates**

**Clinical Impact:** In vitro studies indicate that celecoxib, although not a substrate, is an inhibitor of CYP2D6. Therefore, there is a potential for in vivo drug interaction with drugs that are metabolized by CYP2D6 (e.g., atomoxetine) and celecoxib may enhance the exposure of these drugs.

**Intervention:** Evaluate each patient's medical history when consideration is given to prescribing celecoxib. A dosage adjustment may be warranted when celecoxib is co-administered with CYP2D6 substrates [see Clinical Pharmacology (12.3)].

**Clinical Impact:** Concomitant use of corticosteroids with celecoxib may increase the risk of GI ulceration or bleeding.

**Intervention:** Monitor patients concomitantly using corticosteroids with celecoxib for signs of bleeding [see Warnings and Precautions (5.2)].

**Amiodarone**

**Clinical Impact:** Adverse drug interactions with amiodarone include systemic exposure to amiodarone and may require dose reduction. Monitor for symptoms of hypotension and edema when amiodarone is co-administered with CYP3A inhibitors to determine the need for dose adjustment [see Clinical Pharmacology (12.3)].

**Intervention:** Monitor patients concomitantly using corticosteroids with amiodarone for signs of bleeding [see Warnings and Precautions (5.2)].

**NSAIDs and Corticosteroids**

**Clinical Impact:** Adverse drug interactions with corticosteroids include systemic exposure to corticosteroids and may require dose reduction. Monitor for symptoms of hypotension and edema when corticosteroids are co-administered with CYP3A inhibitors to determine the need for dose adjustment [see Clinical Pharmacology (12.3)].

**Intervention:** Monitor patients concomitantly using corticosteroids with corticosteroids for signs of bleeding [see Warnings and Precautions (5.2)].

**Amiodarone**

**Clinical Impact:** High-risk other drugs on amiodarone include systemic exposure to amiodarone and may require dose reduction. Monitor for symptoms of hypotension and edema when amiodarone is co-administered with CYP3A inhibitors to determine the need for dose adjustment [see Clinical Pharmacology (12.3)].

**Intervention:** Monitor patients concomitantly using corticosteroids with amiodarone for signs of bleeding [see Warnings and Precautions (5.2)].

**8.1 Pregnancy**

**NSAIDs and CONSENSI**

**Clinical Considerations**

Serotonin release by platelets plays an important role in hemostasis. Drugs that interfere with serotonin reuptake (e.g., selective serotonin reuptake inhibitors or serotonin 5HT1A agonists) may potentiate the risk of bleeding more than an NSAID alone. Rifampin may lead to compromised efficacy of celecoxib. Flucloxacillin (e.g., fluconazole) may enhance the exposure and toxicity of pemetrexed whereas co-administration with CYP2C9 inducers (e.g., rifampin) may lead to compromised efficacy of pemetrexed.

### Signs of worsening renal function

- Monitor for signs of worsening renal function [see Warnings and Precautions (5.8)].
- When these drugs are administered concomitantly, patients should be adequately hydrated. Assess renal function at the beginning of the concomitant treatment and periodically thereafter.

### Clinical Considerations

*Serotonin release by platelets plays an important role in hemostasis.* Drugs that interfere with serotonin reuptake (e.g., selective serotonin reuptake inhibitors or serotonin 5HT1A agonists) may potentiate the risk of bleeding more than an NSAID alone. Rifampin may lead to compromised efficacy of celecoxib. Flucloxacillin (e.g., fluconazole) may enhance the exposure and toxicity of pemetrexed whereas co-administration with CYP2C9 inducers (e.g., rifampin) may lead to compromised efficacy of pemetrexed.

### Signs of worsening renal function

- Monitor for signs of worsening renal function [see Warnings and Precautions (5.8)].
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### Clinical Considerations

*Serotonin release by platelets plays an important role in hemostasis.* Drugs that interfere with serotonin reuptake (e.g., selective serotonin reuptake inhibitors or serotonin 5HT1A agonists) may potentiate the risk of bleeding more than an NSAID alone. Rifampin may lead to compromised efficacy of celecoxib. Flucloxacillin (e.g., fluconazole) may enhance the exposure and toxicity of pemetrexed whereas co-administration with CYP2C9 inducers (e.g., rifampin) may lead to compromised efficacy of pemetrexed.

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- Monitor for signs of worsening renal function [see Warnings and Precautions (5.8)].
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### Clinical Considerations

*Serotonin release by platelets plays an important role in hemostasis.* Drugs that interfere with serotonin reuptake (e.g., selective serotonin reuptake inhibitors or serotonin 5HT1A agonists) may potentiate the risk of bleeding more than an NSAID alone. Rifampin may lead to compromised efficacy of celecoxib. Flucloxacillin (e.g., fluconazole) may enhance the exposure and toxicity of pemetrexed whereas co-administration with CYP2C9 inducers (e.g., rifampin) may lead to compromised efficacy of pemetrexed.
Methodological limitations of these postmarketing studies and reports include lack of a control group; limited information regarding dose, duration, and timing of drug exposure, and concomitant use of other medications. These limitations preclude establishing a reliable estimate of the risk of adverse events among the elderly with concomitant diseases that may have influenced the results. Because the published studies are observational, they cannot be considered randomized trials, and therefore cannot establish whether the results would be obtained under clinical conditions.

Coelexib
Coelexib is available in oral doses 215 mg/kg/day (approximately 2 times the human exposure at 200 mg twice daily as measured by AUC[0-24]), caused an increased incidence of ventricular septal defects, a rare event, seen as rhabdomyolysis, amino-terminal prohormone, and creatine kinase abnormalities at doses ≥30 mg/kg/day (approximately 6 times human exposure based on the AUC[0-24] at 200 mg twice daily for rheumatoid arthritis) throughout organogenesis. In rats, exposure to coelexib during early embryonic development resulted in a decreased number of pregnant dams and a delayed fertility in rats at oral doses 50 mg/kg (approximately 6 times human exposure based on the AUC[0-24] at 200 mg twice daily for rheumatoid arthritis) without any evidence of fetal malformations. In mice, coelexib caused a delayed labor or parturition at oral doses up to 100 mg/kg in rats (approximately 7-fold human exposure as measured by the AUC[0-24] at 200 mg twice daily).

Amloidine
No evidence of teratogenicity or other embryofetal toxicity was found when pregnant rats and rabbits were treated from before mating to midgestation with oral doses 10 mg/kg/day (approximately 10 and 20 times the MRHD based on body surface area, respectively) during their pregnancy. Amlodipine maleate has been shown to cause maternal toxicity (by about 50%) and the number of intrauterine deaths was significantly increased (about 5-fold) in rats receiving amloidine maleate at a dose equal to 10 mg amloidine/kg/day for 14 days before mating and throughout mating and gestation. Amloidine maleate has been shown to prolong both the gestation period and the duration of labor in rats at this dose.

8.2 Lactation

Because amloidine is highly protein bound, hemodialysis is not likely to be of benefit.

8.3 Females and Males of Reproductive Potential

Amloidine
An observational clinical lactation study of 31 lactating women who were receiving amloidine within 3 weeks after delivery for pregnancy-induced hypertension showed a median concentration of amloidine in milk 24 hours after a mean maternal oral dose of approximately 6 mg/day for 7 to 9 days of 11.5 ng/mL (interquartile range of 9.84-18.0 ng/mL). The mean maternal body weight-adjusted dose was 0.0987 ± 0.0369 mg/kg. The median plasma concentration of amloidine in the infant was 0.25 ng/mL (mean 0.18 ng/mL). The estimated mean relative infant dose was 1.7 to 3.3% of the recommended dose for an average 6-year-old child (20 kg) (see Data). No adverse effects of amloidine were observed in the breastfed infants. There is no available information on the effects of celexib or amloidine on milk production.

8.4 Pediatric Use

Amloidine
Safely and effectiveness of CONSENSI in pediatric patients have not been established.

8.5 Contraindications

Combination of Celecoxib and Amloidine
In the clinical trials of the combination of coelexib and amloidine in patients with newly diagnosed hypertension who required pharmaceutical therapy to control their hypertension (Study No. KIT-302-03-01), 24.5% of patients treated with the combination were ≥65 years of age. No examinations of age subgroups were planned by protocol or performed, because of the limited sample size. Coelexib
Elderly patients, compared to younger patients, are at greater risk for NSAID-associated serious CV, GI, and other adverse effects. This is generally attributed to the elderly population having more potential risk factors, starting dosing at the low end of the dosage range, and monitoring for adverse events (see Warnings and Precautions [5.1, 5.2, 5.3, 5.4, 5.5, 5.6]). Because CONSENSI is not available in lower strengths of celecoxib, CONSENSI is not recommended in patients that require dosages other than 200 mg of coelexib once daily.

Amloidine
Clinical studies of amloidine did not include sufficient numbers of subjects aged 65 or over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, geriatric patients should be monitored for adverse reactions and dose adjustment based on body weight. The effects of concomitant disease or other drug therapy. Elderly patients have decreased clearance of amloidine and are more sensitive to drug-induced and acute renal failure in the elderly than in younger patients [see Warnings and Precautions (5.4, 5.8)].

Amloidine
Amloidine has anagrace, anti-inflammatory, and antipruritic properties.

12.2 CLINICAL PHARMACOLOGY

Amloidine
Amloidine is a white crystalline powder. It is slightly soluble in water and sparingly soluble in ethanol.

12.1 Description

Amloidine
Amloidine is chemically designated as 3-Ethyl-5-methyl-2-[2-(benzenesulfonamido)-5-(1H-pyrazol-1-yl)benzenesulfonamido] with the molecular weight is 381.36; the chemical structure is as follows:

Amloidine besylate is a white crystalline powder. It is slightly soluble in water and sparingly soluble in ethanol.

Celecoxib
Celecoxib is a white to off-white powder with a pKa of 11.1 (sulfonamide moiety). Celecoxib is hydrophobic (log P is 3.5) and is practically insoluble in aqueous media at physiological pH range.

Celecoxib has analgesic, anti-inflammatory, and antipyretic properties.

10 OVERDOSAGE

Celecoxib
No overdoses of celecoxib were reported during clinical trials. Doses up to 2400 mg/day for up to 12 days in 12 patients did not result in toxic effects. No information is available regarding the removal of celecoxib by hemodialysis, but based on its high degree of plasma protein binding (>97%) dialysis is unlikely to be useful in overdose.

Manage patients by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. Consider emesis and/or activated charcoal (60 to 100 grams in adults, 1 to 2 grams per kg of body weight in pediatric patients) and/or osmotic cathartic in symptomatic patients seen within four hours of ingestion or in patients with a large overdose (5 to 10 times the recommended dosage). Forced diuresis, alkalization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding. Consider whether the presence of severe renal insufficiency may impact the management of an overdose.

Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia. In humans, experience with intentional overdosage of amloidine is limited.

Symptoms following acute NSAID overdosages have been typically limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which have been generally reversible with supportive care. Symptomatic and supportive treatment are generally appropriate in almost all cases of overdose, except in cases of life-threatening or unusual overdose.

If massive overdose should occur, initiate active cardiac and respiratory monitoring. Frequent blood pressure measurements are indicated until stable. If hypotension occurs, supportive care should be given. If hypotension is severe and persistent despite adequate circulating volume and urine output, then use of vasoactive agents (such as dopamine) with attention to circulating volume and urine output. As amloidine is highly protein bound, hemodialysis is not likely to be of benefit.

For additional information about overdosage treatment contact a poison control center (1-800-222-1222).

12.3 Hematologic Use

Amloidine
All components of CONSENSI (coelexib, celecoxib and amlodipine) are used in the treatment of arterial hypertension. In patients who are known or suspected to be poor CYP2C9 metabolizers (i.e., CYP2C9*3/*3), based on genotype or previous history/experience with other CYP2C9 substrates (such as warfarin, phenytion), administer coelexib starting with half the lowest recommended dose. This dose reduction is not recommended in patients who are known or suspected to be poor CYP2C9 metabolizers (see Clinical Pharmacology [12.3]).

10 OVERDOSAGE

Celecoxib
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Celecoxib is a white to off-white powder with a pKa of 11.1 (sulfonamide moiety). Celecoxib is hydrophobic (log P is 3.5) and is practically insoluble in aqueous media at physiological pH range.

Celecoxib is chemically designated as 3-Ethyl-5-methyl-2-[2-(benzenesulfonamido)-5-(1H-pyrazol-1-yl)benzenesulfonamido] with the molecular weight is 381.36; the chemical structure is as follows:
Amlodipine therapy did not alter electrocardiographic intervals or produce higher degrees of AV block. Amlodipine produces vasodilation resulting in a reduction of supine and standing blood pressures. These decreases in blood pressure are not accompanied by a significant change in heart rate. In controlled clinical trials, amlodipine has shown no effect on blood pressure in normotensive patients. Although the antihypertensive effect of amlodipine is dose-related, no evidence of a lack of further reductions in blood pressure exists in patients whose blood pressures were not adequately controlled on lower doses of amlodipine. In clinical trials, amlodipine has not been associated with a negative inotropic effect when administered in the therapeutic dose range to intact animals and man, even when co-administered with beta-blockers. In clinical studies in which amlodipine was administered in combination with beta-blockers, amlodipine did not influence the hypotensive response to beta-blockers. In patients with chronic stable angina, administration of amlodipine produced vasodilation resulting in a reduction of supine and standing blood pressures in normotensive patients. In patients with chronic stable angina, intravenous administration of amlodipine has been shown to reduce systemic vascular resistance and increase cardiac output. Both peak and trough free plasma concentrations of celecoxib are less than 1% of the total plasma concentrations. The pharmacokinetics of celecoxib are robust to the low solubility of the drug in aqueous media. Absolute bioavailability has been estimated to be 60-75% from 200 mg tablets and 39% from 400 mg tablets. The AUC after the administration of celecoxib at 200 mg or 400 mg is roughly dose-proportional up to 400 mg. Celecoxib is well absorbed following oral administration. At steady state, elderly subjects (over 65 years old) had a 40% higher Cmax and a 50% higher AUC compared to the young subjects. In elderly females, celecoxib and AUC are slightly lower compared to young females. The elimination half-life of celecoxib and its metabolite, MPA, is longer in elderly males. The observed decrease in renal vascular resistance and an increase in GFR and effective renal plasma flow is not accompanied by changes in heart rate or plasma catecholamine levels with chronic dosing. Although the acute intravenous interaction of the calcium channel receptor is characterized by a gradual rate of association and dissociation process. The interaction with the calcium channel receptor is characterized by a gradual rate of association and dissociation process. Plasma concentrations of celecoxib were increased by 40-50% in the presence of food. Celecoxib is not a substitute for aspirin for cardiovascular prophylaxis. Celecoxib is not a substitute for aspirin for cardiovascular prophylaxis. Celecoxib is not contraindicated in patients with severe renal insufficiency (see Warnings and Precautions (5.6) and Drug Interactions (7)). Other Drugs: The effects of celecoxib on the pharmacokinetics and/or pharmacodynamics of drugs with a similar site of action (e.g., clopidogrel) and celecoxib have not been studied in vivo and clinically important interactions have not been found. After oral administration of therapeutic doses of amlodipine, absorption produces peak plasma concentrations within 2-6 hours. The absolute bioavailability of amlodipine following oral administration of therapeutic doses is approximately 30-40%. In elderly patients and patients with hepatic insufficiency have decreased clearance of amlodipine with a resulting increase in AUC of approximately 40-60%, and a lower initial dose may be required. A similar increase in AUC was observed in patients with moderate to severe heart failure. In a 2-year hypertensive patients aged 6 to 17 years received doses of amlodipine between 1.25 mg and 20 mg. Weight-adjusted clearance and volume of distribution were similar to values in infants.
50 mg/kg for females (approximately equal to human exposure as measured by the AUC0-24 of 200 mg/day in adult males) by oral gavage. In clinical studies, celecoxib had two prespecified analysis populations:

- Intent-to-treat population (ITT): Comprised of all randomized subjects followed for a maximum duration of 120 months
- Modified intent-to-treat population (mITT): Comprised of all randomized subjects who received at least one dose of study medication and had at least one post-baseline visit followed until the time of treatment discontinuation or up to 120 months.

Celecoxib, at the 100 mg twice daily dose, as compared with either naproxen or ibuprofen at the 800 mg three-times daily dose, had a significantly lower risk of non-renal serious adverse events (p = 0.03). This was also true for gastrointestinal serious adverse events (p < 0.001) and all-cause mortality (p = 0.001) as compared with ibuprofen and naproxen.

Primary Endpoint

### Summary of the Adjudicated APTC Components*

*Patient may have experienced more than one component; therefore, the sum of the components is larger than the number of patients who experienced the composite outcome in the ITT analysis population through 30 months, all-cause mortality was 1.6% in the celecoxib group, 1.8% in the ibuprofen group, and 2.0% in the naproxen group.

Primary Endpoint: Cardiovascular Death (CV Death), Myocardial Infarction (MI), or Stroke (together or alone) with celecoxib compared to placebo over 12 months.

### Cardiovascular Outcomes Trial: Prospective Randomized Evaluation of Celecoxib Integrated Safety vs. Ibuprofen or Naproxen (PRECISION; NCT00346216) Design

The PRECISION trial was a double-blind randomized controlled trial of cardiovascular safety in osteoarthritis and rheumatoid arthritis patients with or at high risk for cardiovascular disease (including those taking aspirin), comparing celecoxib with naproxen and ibuprofen. Patients were randomized to a starting dose of 100 mg twice daily (celexoxib), 200 mg twice daily (naproxen), or 600 mg three times daily (ibuprofen) and were permitted to escalate their dose up to 200 mg twice daily for celecoxib or naproxen, with the option of escalating the dose as needed for pain management. Based on the results of the PRECISION trial, celecoxib was not associated with an increased risk of cardiovascular events compared to naproxen or ibuprofen.

### Cardiovascular Outcomes Study: Long-Term Arthritis Safety Study (CLASS) Design

The CLASS trial was a prospective, long-term, double-blind, randomized, placebo-controlled, double-dose parallel group study conducted post-marketing in approximately 5,800 osteoarthritis patients and 2,200 rheumatoid arthritis patients. Patients received celecoxib 400 mg twice daily (4-fold and 2-fold the recommended osteoarthritis and rheumatoid arthritis doses, respectively) or placebo. The primary endpoint of this study was the incidence of complicated ulcers (GI bleeding, perforation, obstruction, or complicated ulceration). Patients were randomized to take concomitant low-dose aspirin (≤325 mg/day) for CV prophylaxis (ASA subgroups: celecoxib, n = 882; diclofenac, n = 445; ibuprofen, n = 412). The Kaplan-Meier rate for complicated ulcers at 9 months was 1.12% versus 3.0% for those on low-dose ASA and those not on ASA, respectively (see Warnings and Precautions).
The estimated cumulative rates at 9 months of complicated and symptomatic ulcers for patients treated with celecoxib 400 mg twice daily are described in the table below. The table also displays results for patients less than or greater than 65 years of age. The difference in rates between celecoxib alone and celecoxib with ASA groups may be due to the higher risk for GI events in ASA users.

### Complicated and Symptomatic Ulcer Rates in Patients Taking Celecoxib 400 mg Twice Daily (Kaplan-Meier Rates at 9 months [%] Based on Risk Factors)

**All Patients**

<table>
<thead>
<tr>
<th>Celecoxib alone (n=3105)</th>
<th>0.78</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celecoxib with ASA (n=882)</td>
<td>2.19</td>
</tr>
</tbody>
</table>

**Patients ≤65 Years**

<table>
<thead>
<tr>
<th>Celecoxib alone (n=2025)</th>
<th>0.47</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celecoxib with ASA (n=479)</td>
<td>3.06</td>
</tr>
</tbody>
</table>

**Patients >65 Years**

<table>
<thead>
<tr>
<th>Celecoxib alone (n=1080)</th>
<th>1.40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celecoxib with ASA (n=479)</td>
<td>3.06</td>
</tr>
</tbody>
</table>

In a small number of patients with a history of ulcer disease, the complicated and symptomatic ulcer rates in patients taking celecoxib alone or celecoxib with ASA were, respectively, 2.56% (n=445) and 17.9% (n=115) at 48 weeks. These results are expected to be in patients with a prior history of ulcer disease (see Warnings and Precautions (5.4) and Use in Specific Populations (8.6)).

**Cardiovascular Safety**

Kaplan-Meier cumulative rates for investigator-reported serious CV thromboembolic adverse events (including myocardial infarction, pulmonary embolism, deep venous thrombosis, unstable angina, transient ischemic attacks, and ischemic cerebrovascular accidents) demonstrated no differences between the placebo, celecoxib, diclofenac, or ibuprofen treatment groups. The cumulative rates in all patients at nine months for celecoxib, diclofenac, and ibuprofen were 1.2%, 1.4%, and 1.1%, respectively. The cumulative rates in non-ASA users at nine months in each of the three treatment groups were less than 1%. The cumulative rates for myocardial infarction in non-ASA users at nine months in each of the three treatment groups were less than 0.2%. There was no placebo group in the CLASS trial, which limits the ability to determine whether the three drugs tested had no increased risk of CV events or if they all increased the risk to a similar degree. In the CLASS study, the Kaplan-Meier cumulative rates at 9 months of peripheral edema in patients on celecoxib 400 mg twice daily (4-fold and 2-fold the recommended osteoarthritis and rheumatoid arthritis doses, respectively), ibuprofen 800 mg three times daily and diclofenac 75 mg twice daily were 4.5%, 6.9% and 4.7%, respectively. The rates of hypertension from the CLASS trial in the celecoxib, ibuprofen and diclofenac-treated patients were 2.4%, 4.2% and 2.5%, respectively.

**Endoscopic Studies**

The correlation between findings of short-term endoscopic studies with celecoxib and the relative incidence of clinically significant serious upper GI events with long-term use has not been established. Serious clinically significant upper GI bleeding has been observed in patients receiving celecoxib in controlled and open-labeled trials (see Warnings and Precautions (5.4) and Clinical Studies [14.3]).

A randomized, double-blind study in 430 rheumatoid arthritis patients was conducted in which an endoscopic examination was performed at 6 months. The incidence of endoscopic ulcers in patients taking celecoxib 200 mg twice daily was 4% vs. 15% for patients taking diclofenac SR 75 mg twice daily. However, celecoxib was not statistically different than diclofenac for clinically relevant GI outcomes in the CLASS trial (see Clinical Studies [14.3]).

The incidence of endoscopic ulcers was studied in two 12-week, placebo-controlled studies in 2157 osteoarthritis and rheumatoid arthritis patients in whom baseline endoscopies revealed no ulcers. There was no dose relationship for the incidence of gastroduodenal ulcers and the dose of celecoxib (50 mg to 400 mg twice daily). The incidence for naproxen 500 mg twice daily was 16.2% and 17.9% in the two studies, for placebo was 2.0% and 2.3%, and for all doses of celecoxib, the incidence ranged between 2.7%–9%. There have been no large clinical outcome studies to comparatively evaluate GI outcomes with celecoxib and naproxen.

In the endoscopic studies, approximately 11% of patients were taking aspirin (≤ 325 mg/day). In patients with a history of ulcer disease, the complication and symptomatic ulcer rates observed in the active comparator groups, with or without aspirin, were 2.56%, respectively. The correlation between findings of short-term endoscopic studies with celecoxib and the relative incidence of clinically significant serious upper GI events with long-term use has not been established. Serious clinically significant upper GI bleeding has been observed in patients receiving celecoxib in controlled and open-labeled trials (see Warnings and Precautions (5.4) and Clinical Studies [14.3]).

**Fetal Toxicity**

Inform pregnant women to avoid use of CONSENSI and other NSAIDs starting at 30 weeks gestation because of the risk of the premature closing of the fetal ductus arteriosus. If treatment with CONSENSI is needed for a pregnant woman between about 20 to 30 weeks gestation, advise her that she may need to be monitored for oligohydramnios, if treatment continues for longer than 48 hours (see Warnings and Precautions (5.13) and Use in Specific Populations (8.1)).

**Avoid Concomitant Use of NSAIDs**

Inform patients that the concomitant use of CONSENSI with other NSAIDs or salicylates (e.g., ibuprofen, ibuprofen acid, aspirin) is not recommended due to the increased risk of GI toxicity, and little or no increase in efficacy (see Warnings and Precautions (5.2) and Drug Interactions (7)). Alert patients that NSAIDs may be present in “over-the-counter” medications for treatment of colds, fever, or insomnia.

**Use of NSAIDS and Low-Dose Aspirin**

Inform patients not to use low-dose aspirin concomitantly with CONSENSI until they talk to their healthcare provider [see Drug Interactions (7)].

**Discontinuation of CONSENSI**

Inform patients not to discontinue CONSENSI without discussing with their healthcare provider because an alternative blood pressure lowering drug should be started to control blood pressure [see Dosage and Administration (2.2)].

**How Supplied/Storage and Handling**

CONSENSI tablets are white and biconvex, non-coated, non-scored, with the tablet strength debossed on one side, available as follows:

<table>
<thead>
<tr>
<th>Amlodipine</th>
<th>Celecoxib</th>
<th>Shape</th>
<th>NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 mg</td>
<td>0.5 mg</td>
<td>Bottle of 30 tablets</td>
<td>69101-505-50</td>
</tr>
<tr>
<td>0.5 mg</td>
<td>1 mg</td>
<td>Bottle of 500 tablets</td>
<td>69101-505-50</td>
</tr>
</tbody>
</table>

**Storage**

Store at room temperature 20°C to 25°C (68°F to 77°F); [see USP Controlled Room Temperature]. Dispense in tight, light-resistant containers (USP).
What is the most important information I should know about CONSENSI?
CONSENSI contains celecoxib, a nonsteroidal anti-inflammatory drug (NSAID), and amlodipine, a calcium channel blocker (CCB). NSAIDs can cause serious side effects, including:

- **Increased risk of a heart attack or stroke that can lead to death.** This risk may happen early in treatment and may increase:
  - with increasing doses of NSAIDs
  - with longer use of NSAIDs

Do not take CONSENSI right before or after a heart surgery called a “coronary artery bypass graft” (CABG).

Avoid taking CONSENSI after a recent heart attack, unless your healthcare provider tells you to. You may have an increased risk of another heart attack if you take NSAIDs after a recent heart attack.

- **Increased risk of bleeding, ulcers, and tears (perforation) of the esophagus (tube leading from the mouth to the stomach), stomach, and intestines:**
  - anytime during use
  - without warning symptoms
  - that may cause death

The risk of getting an ulcer or bleeding increases with:

  - past history of stomach ulcers, or stomach or intestinal bleeding with use of NSAIDs
  - taking medicines called “corticosteroids”, “antiplatelet drugs”, “anticoagulants”, “selective serotonin reuptake inhibitors (SSRIs)”, or “serotonin norepinephrine reuptake inhibitors (SNRIs)”
  - increasing doses of NSAIDs
  - older age
  - longer use of NSAIDs
  - poor health
  - smoking
  - advanced liver disease
  - drinking alcohol
  - bleeding problems

You should not take other medicines that contain NSAIDs or salicylates during treatment with CONSENSI because of increased risk of stomach problems. Taking other medicines that contain NSAIDs or salicylates during treatment with CONSENSI will not provide increased relief of symptoms of osteoarthritis.

CONSENSI should only be used:

- exactly as prescribed
- at the lowest dose possible for your treatment
- for the shortest time needed

What is CONSENSI?
CONSENSI is a prescription medicine used in adults who need treatment:

- with amlodipine for high blood pressure (hypertension), to lower blood pressure, and
- with celecoxib for the management of the signs and symptoms of osteoarthritis.

It is not known if CONSENSI is safe and effective in children.

Who should not take CONSENSI?

Do not take CONSENSI:

- if you are allergic to amlodipine, celecoxib or any of the inactive ingredients in CONSENSI. See the end of this Medication Guide for a complete list of ingredients in CONSENSI.
• if you have had an asthma attack, hives, or other allergic reaction with aspirin or any other NSAIDs.
• right before or after heart bypass surgery.
• if you have had an allergic reaction to sulfonamides.

Before taking CONSENSI, tell your healthcare provider about all your medical conditions, including if you:
• have heart problems.
• have liver or kidney problems.
• have asthma.
• are pregnant or plan to become pregnant. Talk to your healthcare provider if you are considering taking CONSENSI during pregnancy. Taking NSAIDs at about 20 weeks of pregnancy or later may harm your unborn baby. If you need to take NSAIDs for more than 2 days when you are between 20 and 30 weeks of pregnancy, your healthcare provider may need to monitor the amount of fluid in your womb around your baby. You should not take NSAIDs after about 30 weeks of pregnancy.
• are breastfeeding or plan to breastfeed. CONSENSI can pass into your breast milk. It is not known if CONSENSI will harm your baby. Talk with your healthcare provider about the best way to feed your baby if you take CONSENSI.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, or herbal supplements. CONSENSI and some other medicines can interact with each other and cause serious side effects. Do not start taking any new medicine without talking to your healthcare provider first.

How should I take CONSENSI?
• Take CONSENSI exactly as your healthcare provider tells you to.
• Take 1 CONSENSI tablet orally each day.
• If your pain stops, do not stop taking CONSENSI until your healthcare provider prescribes a different medicine to treat your blood pressure. Your healthcare provider will monitor your blood pressure when changing to the new medicine.
• If you take too much CONSENSI, call your healthcare provider or get medical help right away.

What are the possible side effects of CONSENSI?
CONSENSI can cause serious side effects, including:
See “What is the most important information I should know about CONSENSI?”.
• liver problems, including liver failure
• worsening chest pain (angina) or heart attack, particularly in people with severe obstructive coronary artery disease
• heart failure
• swelling of your arms, legs, hands and feet (peripheral edema) is common with CONSENSI but can sometimes be serious.
• kidney problems, including kidney failure
• increased potassium levels (hyperkalemia)
• life-threatening allergic reactions
• life-threatening skin reactions
• low red blood cells (anemia)

Your healthcare provider will monitor your blood pressure and do blood tests to check you for side effects during treatment with CONSENSI.

CONSENSI may cause fertility problems in females that is reversible when treatment with CONSENSI is stopped. Talk to your healthcare provider if this is a concern for you.

The most common side effects of CONSENSI include:
• swelling of the arms, legs, hands, and feet
• joint swelling
• headache
• frequent urination
• dizziness • hot or warm feeling in your face (flushing)
• stomach pain • gas
• diarrhea • tiredness
• heartburn • extreme sleepiness

Get emergency help right away if you get any of the following symptoms:
• shortness of breath or trouble breathing • slurred speech
• chest pain • swelling of the face or throat
• weakness in one part or side of your body

Stop taking CONSENSI and call your healthcare provider right away if you get any of the following symptoms:
• nausea • vomit blood
• more tired or weaker than usual • there is blood in your bowel movement or it is black and sticky like tar
• diarrhea • unusual weight gain
• itching • your skin or eyes look yellow
• indigestion or stomach pain • skin rash or blisters with fever
• flu-like symptoms • swelling of the arms, legs, hands and feet

These are not all the possible side effects of CONSENSI.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store CONSENSI?
• Store CONSENSI at room temperature between 68° and 77°F (20°C to 25°C).

Keep CONSENSI and all medicines out of the reach of children.

Other information about NSAIDs
• Aspirin is an NSAID but it does not increase the chance of a heart attack. Aspirin can cause bleeding in the brain, stomach, and intestines. Aspirin can also cause ulcers in the stomach and intestines.
• Some NSAIDs are sold in lower doses without a prescription (over-the-counter). Talk to your healthcare provider before using over-the-counter NSAIDs for more than 10 days.

General information about the safe and effective use of CONSENSI
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use CONSENSI for a condition for which it was not prescribed. Do not give CONSENSI to other people, even if they have the same symptoms that you have. It may harm them. If you would like more information about CONSENSI®, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about CONSENSI that is written for health professionals.

What are the ingredients in CONSENSI?
Active ingredients: amlodipine and celecoxib
Inactive ingredients: mannitol DC 200, croscarmellose sodium, povidone K-30, sodium lauryl sulfate, magnesium stearate, and colloidal silicon dioxide.

Manufactured by: Dexcel Pharma Technologies, Ltd., Yokneam, Israel
Distributed by: Burke Therapeutics, LLC., Hot Springs, AR 71913
For more information, go to www.consensi.com or call 1-888-275-1264

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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