Naproxen Oral Suspension, USP

125 mg/5 mL

Carefully consider the potential benefits and risks of Naproxen Suspension and other treatment options before deciding to use Naproxen Suspension. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see WARNINGS; Gastrointestinal Bleeding, Ulceration, and Perforation).

NAPROXEN SUSPENSION IS INDICATED FOR THE FOLLOWING:

THE RELIEF OF THE SIGNS AND SYMPTOMS OF:

- Rheumatoid Arthritis
- Ankylosing Spondylitis
- Tendonitis
- Osteoarthritis
- Acute Gout
- Bursitis
- Juvenile Rheumatoid Arthritis (Also recommended in order to obtain the maximum dosage flexibility based on the patient’s weight)

THE MANAGEMENT OF:

- Pain
- Primary Dysmenorrhea

KEY therapeutics

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

- Cardiovascular Thrombotic Events
- Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use (see WARNINGS).
- Naproxen Suspension is contraindicated in the setting of coronary artery bypass graft (CABG) surgery (see CONTRAINDICATIONS, WARNINGS).

Gastrointestinal Bleeding, Ulceration, and Perforation
- 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 can 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 (see WARNINGS).

INDICATIONS AND USAGE

Carefully consider the potential benefits and risks of Naproxen Suspension and other treatment options before deciding to use Naproxen Suspension. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see WARNINGS; Gastrointestinal Bleeding, Ulceration, and Perforation).

Naproxen Suspension is indicated:
- For the relief of the signs and symptoms of rheumatoid arthritis
- For the relief of the signs and symptoms of osteoarthritis
- For the relief of the signs and symptoms of ankylosing spondylitis
- For the relief of the signs and symptoms of juvenile rheumatoid arthritis

Naproxen Suspension is recommended for juvenile rheumatoid arthritis in order to obtain the maximum dosage flexibility based on the patient’s weight.

Naproxen Suspension is also indicated:
- For relief of the signs and symptoms of tendonitis
- For relief of the signs and symptoms of bursitis
- For relief of the signs and symptoms of acute gout
- For the management of pain
- For the management of primary dysmenorrhea

CONTRAINDICATIONS

Naproxen Suspension is contraindicated in the following patients:
- Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to naproxen or any components of the drug product (see WARNINGS; Anaphylactic Reactions, Serious Skin Reactions).
- History of asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, sometimes fatal, anaphylactic-reactions to NSAIDs have been reported in such patients (see WARNINGS; Anaphylactic Reactions, Exacerbation of Asthma Related to Aspirin Sensitivity).
- In the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS; Cardiovascular Thrombotic Events).

PLEASE SEE ADDITIONAL IMPORTANT SAFETY INFORMATION ON PAGES 2-4 AND ENCLOSED FULL PRESCRIBING INFORMATION BEFORE PRESCRIBING NAPROXEN SUSPENSION.
Cardiovascular Thrombolytic Events
Clinical trials of COX-2 selective and nonselective NSAIDs of up to three years duration 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 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, patients with known CV 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 week of treatment. The increase in CV thrombotic risk has been observed most consistently at higher doses.

To minimize the potential risk for an adverse CV event in NSAID-treated patients, use the lowest effective dose for the shortest duration possible. Physicians and patients should remain alert for the development of such events, throughout the entire treatment course, even in the absence of previous CV symptoms. Patients should be informed about the symptoms of serious CV events and the steps to take if they occur.

There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. The concurrent use of aspirin and an NSAID, such as naproxen, increases the risk of serious gastrointestinal (GI) events (see WARNINGS; Gastrointestinal Effects – Risk of Ulceration, Bleeding, and Perfusion).

Status Post Coronary Artery Bypass Graft (CABG) Surgery
Two large, controlled, clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke. NSAIDs are contraindicated in the setting of CABG (see CONTRAINDICATIONS).

Post-MI Patients
Observational studies conducted in the Danish National Registry have demonstrated that patients treated with NSAIDs in the post-MI period were at increased risk of reinfection, CV-related death, and all-cause mortality beginning in the first week of treatment. In this same cohort, the incidence of death in the first year post MI was 20 per 100 person years in NSAID-treated patients compared to 12 per 100 person years in non-NSAID exposed patients. Although the absolute rate of death declined somewhat after the first year post-MI, the increased relative risk of death in NSAID users persisted over at least the next 4 years of follow-up. Avoid the use of Naproxen Suspension in patients with a recent MI unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If Naproxen Suspension is used in patients with a recent MI, monitor patients for signs of cardiac ischemia.

Gastrointestinal Bleeding, Ulceration, and Perforation
NSAIDs, including naproxen, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the esophagus, stomach, small intestine, or large intestine, which can be fatal.

These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Only one in five patients, who develop a serious upper GI adverse event on NSAID therapy, is symptomatic. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year. However, even short-term therapy is not without risk.

Risk Factors for GI Bleeding, Ulceration, and Perforation
Patients with a prior history of peptic ulcer disease and/or GI bleeding who used NSAIDs had a greater than 10-fold increased risk of developing a GI bleed compared to patients without these risk factors. Other factors that increase the risk of GI bleeding in patients treated with NSAIDs include longer duration of NSAID therapy; concomitant use of oral corticosteroids, aspirin, anticoagulants, antiplatelet agents, and selective serotonin reuptake inhibitors (SSRIs), smoking, use of alcohol, older age, and poor general health status. Most postmarketing reports of fatal GI events occurred in elderly or debilitated patients. Additionally, patients with advanced liver disease and/or coagulopathy are at increased risk for GI bleeding.

Strategies to Minimize the GI Risks in NSAID-treated patients:
- Use the lowest effective dosage for the shortest possible duration.
- Avoid administration of more than one NSAID at a time.
- Avoid use in patients at higher risk unless benefits are expected to outweigh the increased risk of bleeding. For such patients, as well as those with active GI bleeding, consider alternate therapies other than NSAIDs.
- Remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy.
- If a serious GI adverse event is suspected, promptly initiate evaluation and treatment, and discontinue Naproxen Suspension until a serious GI adverse event is ruled out.

- In the setting of concomitant use of low-dose aspirin for cardiac prophylaxis, monitor patients more closely for evidence of GI bleeding (see PRECAUTIONS; Drug Interactions).

Hepatic Effects
Elevations of ALT or AST (three or more times the upper limit of normal [ULN]) have been reported in approximately 1% of patients in clinical trials. In addition, rare, sometimes fatal, cases of severe hepatic injury, including fulminant hepatitis, liver necrosis and hepatic failure have been reported. Elevations of ALT or AST (less than three times ULN) may occur in up to 15% of patients taking NSAIDs including naproxen.

Inform patients of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, diarrhea, pruritus, jaundice, right upper quadrant tenderness, and “flu-like” symptoms). If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), discontinue Naproxen Suspension immediately, and perform a clinical evaluation of the patient.

Hypertension
NSAIDs, including Naproxen Suspension, can lead to new onset of hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking angiotensin converting enzyme (ACE) inhibitors, thiazide diuretics, or loop diuretics may have impaired response to these therapies when taking NSAIDs (see PRECAUTIONS; Drug Interactions).

Monitor blood pressure (BP) during the initiation of NSAID treatment and throughout the course of therapy.

Heart Failure and Edema
The Coxib and traditional NSAID Trialists’ Collaboration meta-analysis of randomized controlled trials demonstrated an approximately two-fold increase in hospitalizations for heart failure in COX-2 selective-treated patients and nonselective NSAID-treated patients compared to placebo-treated patients. In a Danish National Registry study of patients with heart failure, NSAID use increased the risk of MI, hospitalization for heart failure, and death.

Additionally, fluid retention, and edema have been observed in some patients treated with NSAIDs. Use of naproxen may blunt the CV effects of several therapeutic agents used to treat these medical conditions (e.g., diuretics, ACE inhibitors, or angiotensin receptor blockers (ARBs)) (see PRECAUTIONS; Drug Interactions).

Avoid the use of Naproxen Suspension in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If Naproxen Suspension is used in patients with severe heart failure, monitor patients for signs of worsening heart failure.

Each 5 mL of Naproxen Suspension contains 39 mg of sodium. This should be considered in patients whose overall intake of sodium must be severely restricted.

Renal Toxicity and Hyperkalemia
Long term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandin have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, dehydration, hypovolemia, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors or ARBs, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.

No information is available from controlled clinical studies regarding the use of Naproxen Suspension in patients with advanced renal disease. The renal effects of Naproxen Suspension may hasten the progression of renal disease in patients with pre-existing renal disease.

Correct volume status in dehydrated or hypovolemic patients prior to initiating Naproxen Suspension. Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia during use of Naproxen Suspension (see PRECAUTIONS; Drug Interactions). Avoid the use of Naproxen Suspension in patients with advanced renal disease unless the benefits are expected to outweigh the risk of worsening renal function. If Naproxen Suspension is used in patients with advanced renal disease, monitor patients for signs of worsening renal function.

Advanced Renal Disease
Increases in serum potassium concentration, including hyperkalemia, have been reported with use of NSAIDs, even in some patients without renal impairment. In patients with normal renal function, these effects have been attributed to a hyperreninemic-hypoaldosteronism state.

Anaphylactoid Reactions
Naproxen Suspension has been associated with anaphylactoid reactions in patients with and without known hypersensitivity to naproxen and in patients with aspirin-sensitive asthma (see CONTRAINDICATIONS, WARNINGS;
Exacerbation of Asthma Related to Aspirin Sensitivity

As a subpopulation of patients with asthma may have aspirin-sensitive asthma which may include chronic rhinosinusitis complicated by nasal polyps; severe, potentially fatal bronchospasm; and/or intolerance to aspirin and other NSAIDs. Because cross-reactivity between aspirin and other NSAIDs has been reported in such aspirin-sensitive patients, Naproxen Suspension is contraindicated in patients with this form of aspirin sensitivity (see CONTRAINDICATIONS). When Naproxen Suspension is used in patients with preexisting asthma (without known aspirin sensitivity), monitor patients for changes in the signs and symptoms of asthma.

Serious Skin Reactions

NSAIDs, including naproxen, can cause serious skin adverse reactions such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur with or without warning. Inform patients about the signs and symptoms of serious skin reactions and to discontinue use of Naproxen Suspension at the first appearance of skin rash or any other sign of hypersensitivity. Naproxen Suspension is contraindicated in patients with previous serious skin reactions to NSAIDs (see CONTRAINDICATIONS).

Premature Closure of Fetal Ductus Arteriosus

Naproxen may cause premature closure of the fetal ductus arteriosus. Avoid use of NSAIDs, including Naproxen Suspension, in pregnant women starting at 30 weeks of gestation (third trimester) (see PRECAUTIONS; Pregnancy).

Hematologic Toxicity

Anemia has occurred in NSAID-treated patients. This may be due to occult or gross blood loss, fluid retention, or an incompletely described effect on erythropoiesis. If a patient treated with Naproxen Suspension has any signs or symptoms of anemia, monitor hemoglobin or hematocrit.

NSAIDs, including Naproxen Suspension, may increase the risk of bleeding events. Co-morbid conditions such as coagulation disorders, or concomitant use of warfarin, other anticoagulants, antiplatelet agents (e.g., aspirin), serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) may increase this risk. Monitor these patients for signs of bleeding (see PRECAUTIONS; Drug Interactions).

PRECAUTIONS

General

Naproxen Suspension should not be used concomitantly with other naproxen-containing products since they all circulate in the plasma as the naproxen anion.

Naproxen Suspension cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids and the patient should be observed closely for any evidence of adverse effects, including adrenal insufficiency and exacerbation of symptoms of arthritis.

Patients with initial hemoglobin values of 10 g or less who are to receive long-term therapy should have hemoglobin values determined periodically. Because of adverse eye findings in animal studies with drugs of this class, it is recommended that ophthalmic studies be carried out if any change or disturbance in vision occurs.

Masking of Inflammation and Fever

The pharmacological activity of Naproxen in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infections.

Laboratory Monitoring

Because serious GI bleeding, hepatotoxicity, and renal injury can occur without warning symptoms or signs consider monitoring patients on long-term NSAID treatment with a CBC and a chemistry profile periodically (see WARNINGS; Gastrointestinal Bleeding, Ulceration, and Perforation, and Hepatotoxicity).

DRUG INTERACTIONS

Drugs That Interfere with Hemostasis

**Clinical Impact:**
- Naproxen and anticoagulants such as warfarin have a synergistic effect on bleeding. The concomitant use of naproxen and anticoagulants has an increased risk of serious bleeding compared to the use of either drug alone.
- Serotonin release by platelets plays an important role in hemostasis. Case-control and cohort epidemiological studies showed that concomitant use of drugs that interfere with serotonin reuptake and an NSAID may potentiate the risk of bleeding more than an NSAID alone.

**Intervention:** Monitor patients with concomitant use of Naproxen Suspension with anticoagulants (e.g., warfarin), antiplatelet agents (e.g., aspirin), selective serotonin reuptake inhibitors (SSRIs), and serotonin norepinephrine reuptake inhibitors (SNRIs) for signs of bleeding (see WARNINGS; Hematologic Toxicity).

Aspirin

**Clinical Impact:** Controlled clinical studies showed that the concomitant use of NSAIDs and analgesic doses of aspirin does not produce any greater therapeutic effect than the use of NSAIDs alone. In a clinical study, the concomitant use of an NSAID and aspirin was associated with a significantly increased incidence of GI adverse reactions as compared to use of the NSAID alone (see WARNINGS; Gastrointestinal Bleeding, Ulceration and Perforation).

**Intervention:** Concomitant use of Naproxen Suspension and analgesic doses of aspirin is not generally recommended because of the increased risk of bleeding (see WARNINGS; Hematologic Toxicity). Naproxen Suspension is not a substitute for low dose aspirin for cardiovascular protection.

ACE Inhibitors, Angiotensin Receptor Blockers, and Beta-Blockers

**Clinical Impact:**
- NSAIDs may diminish the antihypertensive effect of angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), or beta-blockers (including beta-blockers used for cardiovascular protection).
- In patients who are elderly, volume-depleted (including those on diuretic therapy), or have renal impairment, co-administration of an NSAID with ACE inhibitors or ARBs may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible.

**Intervention:**
- During concomitant use of Naproxen Suspension and ACE-inhibitors, ARBs, or beta-blockers, monitor blood pressure to ensure that the desired blood pressure is obtained.
- During concomitant use of Naproxen Suspension and ACE-inhibitors or ARBs in patients who are elderly, volume-depleted, and have impaired renal function, monitor for signs of worsening renal function (see WARNINGS; Renal Toxicity and Hyperkalemia). When these drugs are administered concomitantly, patients should be adequately hydrated. Assess renal function at the beginning of the concomitant treatment and periodically thereafter.

Diuretics

**Clinical Impact:** Clinical studies, as well as post-marketing observations, showed that NSAIDs reduced the natriuretic effect of loop diuretics (e.g., furosemide) and thiazide diuretics in some patients. This effect has been attributed to the NSAID inhibition of renal prostaglandin synthesis.

**Intervention:**
- During concomitant use of Naproxen Suspension with diuretics, observe patients for signs of worsening renal function, in addition to assuring diuretic efficacy including antihypertensive effects (see WARNINGS; Renal Toxicity and Hyperkalemia).

Digoxin

**Clinical Impact:** The concomitant use of naproxen with digoxin has been reported to increase the serum concentration and prolong the half-life of digoxin.

**Intervention:**
- During concomitant use of Naproxen Suspension and digoxin, monitor serum digoxin levels.

Lithium

**Clinical Impact:** NSAIDs have produced elevations in plasma lithium levels and reductions in renal lithium clearance. The mean minimum lithium concentration increased 15%, and the renal clearance decreased by approximately 20%. This effect has been attributed to NSAID inhibition of renal prostaglandin synthesis.

**Intervention:**
- During concomitant use of Naproxen Suspension and lithium, monitor patients for signs of lithium toxicity.

Methotrexate

**Clinical Impact:** Concomitant use of NSAIDs and methotrexate may increase the risk for methotrexate toxicity (e.g., neutropenia, thrombocytopenia, renal dysfunction).

**Intervention:**
- During concomitant use of Naproxen Suspension and methotrexate, monitor patients for methotrexate toxicity.

Cyclosporine

**Clinical Impact:**
- Concomitant use of Naproxen Suspension and cyclosporine may increase cyclosporine’s nephrotoxicity.

**Intervention:**
- During concomitant use of Naproxen Suspension and cyclosporine, monitor patients for signs of worsening renal function.
NSAIDs and Salicylates

**Clinical Impact:** Concomitant use of naproxen with other NSAIDs or salicylates (e.g., ibuprofen, aspirin) increases the risk of GI toxicity with little or no increase in efficacy (see WARNINGS; Gastrointestinal Bleeding, Ulceration, and Perforation).

**Intervention:** During concomitant use of Naproxen Suspension and cyclosporine, monitor patients for signs of worsening renal function.

**Pemetrexed**

**Clinical Impact:** Concomitant use of Naproxen Suspension may increase the risk of pemetrexed-associated myelosuppression, renal, and GI toxicity (see the pemetrexed prescribing information).

**Intervention:** During concomitant use of Naproxen Suspension and pemetrexed, in patients with renal impairment whose creatinine clearance ranges from 45 to 79 mL/min, monitor for myelosuppression, renal, and GI toxicity. NSAIDs with short elimination half-lives (e.g., diclofenac, indomethacin) should be avoided for a period of two days before, the day of, and two days following administration of pemetrexed. In the absence of data regarding potential interaction between pemetrexed and NSAIDs with longer half-lives (e.g., meloxicam, nabumetone), patients taking these NSAIDs should interrupt dosing for at least five days before, the day of, and two days following pemetrexed administration.

**Antacids and Sucralfate**

**Clinical Impact:** Concomitant administration of some antacids (magnesium oxide or aluminum hydroxide) and sucralfate can delay the absorption of naproxen.

**Intervention:** Concomitant administration of antacids such as magnesium oxide or aluminum hydroxide, and sucralfate with Naproxen Suspension is not recommended.

**Cholestyramine**

**Clinical Impact:** Concomitant administration of cholestyramine can delay the absorption of naproxen.

**Intervention:** Concomitant administration of cholestyramine with Naproxen Suspension is not recommended.

**Probenecid**

**Clinical Impact:** Probenecid given concurrently increases naproxen anion plasma levels and extends its plasma half-life significantly.

**Intervention:** Patients simultaneously receiving Naproxen Suspension and probenecid should be observed for adjustment of dose if required.

**Other albumin-bound drugs**

**Clinical Impact:** Naproxen is highly bound to plasma albumin; it thus has a theoretical potential for interaction with other albumin-bound drugs such as coumarin-type anticoagulants, sulphonylureas, hydantoins, other NSAIDs, and aspirin (see WARNINGS; Gastrointestinal Bleeding, Ulceration, and Perforation).

**Intervention:** Patients simultaneously receiving Naproxen Suspension and a hydantoin, sulphonamide or sulphonylurea should be observed for adjustment of dose if required.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

Use of NSAIDs, including Naproxen Suspension, during the third trimester of pregnancy increases the risk of premature closure of the fetal ductus arteriosus. Avoid use of NSAIDs, including Naproxen Suspension, in pregnant women starting at 30 weeks of gestation (third trimester) (see WARNINGS; Premature Closure of Fetal Ductus Arteriosus).

**Labor and Delivery**

There are no studies on the effects of Naproxen Suspension during labor or delivery. In animal studies, NSAIDs, including naproxen, inhibit prostaglandin synthesis, cause delayed parturition, and increase the incidence of stillbirth.

**Nursing Mothers**

The naproxen anion has been found in the milk of lactating women at the concentration equivalent to approximately 1% of maximum naproxen concentration in plasma. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Naproxen Suspension and any potential adverse effects on the breastfed infant from the Naproxen Suspension or from the underlying maternal condition.

**Females and Males of Reproductive Potential**

Based on the mechanism of action, the use of prostaglandin-mediated NSAIDs, including Naproxen Suspension, may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women. Published animal studies have shown that administration of prostaglandin synthesis inhibitors has the potential to disrupt prostaglandin-mediated follicular rupture required for ovulation. Small studies in women treated with NSAIDs have also shown a reversible delay in ovulation. Consider withdrawal of NSAIDs, including Naproxen Suspension, in women who have difficulties conceiving or who are undergoing investigation of infertility.

**Pediatric Use**

Safety and effectiveness in pediatric patients below the age of 2 years have not been established. Pediatric dosing recommendations for juvenile arthritis are based on well-controlled studies (see DOSAGE AND ADMINISTRATION). There are no adequate effectiveness or dose-response data for other pediatric conditions, but the experience in juvenile arthritis and other use experience have established that single doses of 2.5 to 5 mg/kg (as naproxen suspension), with total daily dose not exceeding 15 mg/kg/day, are well tolerated in pediatric patients over 2 years of age. (see DOSAGE AND ADMINISTRATION).

**Geriatric Use**

Elderly patients, compared to younger patients, are at greater risk for NSAID-associated serious cardiovascular, gastrointestinal, and/or renal adverse reactions. If the anticipated benefit for the elderly patient outweighs these potential risks, start dosing at the low end of the dosing range, and monitor patients for adverse effects (see WARNINGS; Cardiovascular Thrombotic Events, Gastrointestinal Bleeding, Ulceration, and Perforation, Hepatotoxicity, Renal Toxicity and Hyperkalemia, PRECAUTIONS; Laboratory Monitoring).

Studies indicate that although total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly. Caution is advised when high doses are required and some adjustment of dosage may be required in elderly patients. As with other drugs used in the elderly, it is prudent to use the lowest effective dose. Experience indicates that geriatric patients may be particularly sensitive to certain adverse effects of nonsteroidal anti-inflammatory drugs. Elderly or debilitated patients seem to tolerate peptic ulceration or bleeding less well when these events do occur. Most spontaneous reports of fatal GI events are in the geriatric population (see WARNINGS; Gastrointestinal Bleeding, Ulceration, and Perforation).

Naproxen is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. Geriatric patients may be at a greater risk for the development of a form of renal toxicity precipitated by reduced prostaglandin formation during administration of nonsteroidal anti-inflammatory drugs (see WARNINGS; Renal Toxicity and Hyperkalemia).

**ADVERSE REACTIONS**

In patients taking naproxen in clinical trials, the most frequently reported adverse experiences in approximately 1% to 10% of patients are:

**Gastrointestinal (GI) Experiences**, including: heartburn*, abdominal pain*, nausea*, constipation*, diarrhea, dyspepsia, stomatitis

**Central Nervous System**: headache*, dizziness*, drowsiness*, lightheadedness, vertigo

**Dermatologic**: pruritus (itching)*, skin eruptions*, ecchymoses*, sweating, purpura

**Special Senses**: tinnitus*, visual disturbances, hearing disturbances

**Cardiovascular**: edema*, palpitations

**General**: dyspnea*, thirst

*Incidence of reported reaction between 3% and 9%. Those reactions occurring in less than 3% of the patients are unmarked.

In patients taking NSAIDs, the following adverse experiences have also been reported in approximately 1% to 10% of patients:

**Gastrointestinal (GI) Experiences**, including: flatulence, gross bleeding/ perforation, GI ulcers (gastric/duodenal), vomiting

**General**: abnormal renal function, anemia, elevated liver enzymes, increased bleeding time, rashes

**PLEASE SEE BOXED WARNINGS AND INDICATION ON FRONT, ADDITIONAL IMPORTANT SAFETY INFORMATION ON PAGES 2-4 AND ENCLOSED FULL PRESCRIBING INFORMATION BEFORE PRESCRIBING NAPROXEN SUSPENSION.**
Naproxen Oral Suspension, USP 125mg/5mL

In 150 to 300 mg daily divided into 2 or 3 doses or in 500 mg daily in a single dose, or as determined by the clinician's judgment, the use of NaP offers a wide margin of safety and effective antinflammatory, analgesic, and antipyretic activity. In general, patients respond well to NaP therapy and are usually asymptomatic when the above doses are continued for 2 to 3 days. The maximum daily dose for adults is 1500 mg.

In 500 mg tablets, the therapeutic action of NaP has been shown by a reduction in joint pain or inflammation in patients with arthritis. In patients with osteoarthritis, the therapeutic action has been shown by a reduction in joint pain. In patients with rheumatoid arthritis, the therapeutic action has been shown by a reduction in joint pain, morning stiffness, and swelling. In patients with ankylosing spondylitis, the therapeutic action has been shown by a reduction in joint pain, morning stiffness, and joint swelling.

In patients with osteoarthritis, the therapeutic action of NaP has been shown by a reduction in joint pain or inflammation. In patients with rheumatoid arthritis, the therapeutic action has been shown by a reduction in joint pain, morning stiffness, and swelling. In patients with ankylosing spondylitis, the therapeutic action has been shown by a reduction in joint pain, morning stiffness, and joint swelling.

In patients with acute gout, a favorable response to NaP was shown by a significant clearing of inflammatory signs and symptoms. In patients with acute gout, a favorable response to NaP was shown by a significant clearing of inflammatory signs and symptoms.

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Elderly patients, compared to younger patients, are at greater risk for NSAID-associated serious cardiovascular, gas-

Safety and effectiveness in pediatric patients below the age of 2 years have not been established. Pediatric dosing

Labor and Delivery

have an important role in endometrial vascular permeability, blastocyst implantation, and decidualization. In animal

mum recommended human daily dose, based on body surface area comparison), and mice at 170 mg/kg/day

persistent pulmonary hypertension, renal dysfunction and abnormal prostaglandin E levels in preterm infants. Because

There are no adequate and well-controlled studies of Naproxen Suspension in pregnant women.

A 2-year study was performed in rats to evaluate the carcinogenic potential of naproxen at rat doses of 8, 16, and

Studies to evaluate the impact of naproxen on male or female fertility have not been completed.

Naproxen is highly bound to plasma albumin; it thus has a theoretical potential for interaction

Expiration:

Naproxen is contraindicated in patients with suicidal tendencies or those with a history of a previous allergic reaction

overdose is treated with supportive and symptomatic measures. In an overdose situation, the physician should observe sufficient increased clinical benefits to offset the potential

There are no controlled studies in animals to evaluate possible teratogenic or embryotoxic effects. Animal studies
demonstrated that naproxen has induced fetal renal malformations at maternal doses of 1500 mg/kg/day (animal

Human Data

Studies, administration of prostaglandin synthesis inhibitors such as naproxen, resulted in increased pre- and post-

Clinical Impact:

Naproxen is a competitive inhibitor of cysteinyl leukotriene receptor.

Treatment of Overdose

Clinical studies conducted in patients with impaired renal function and in patients receiving diuretics have demonstrated

A 1-week study has been conducted in rats to evaluate the carcinogenic potential of naproxen at rat doses of 10, 100, and

Naproxen is not indicated for use in the prevention of angina pectoris and the management of unstable angina.

Naproxen is not indicated for use in the prevention of angina pectoris and the management of unstable angina.

Naproxen is highly bound to plasma albumin; it thus has a theoretical potential for interaction

Cardiovascular: (severe and life-threatening)

Hypertension (see

Clinical Impact:

Clinical Impact:

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General Pharmacology

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