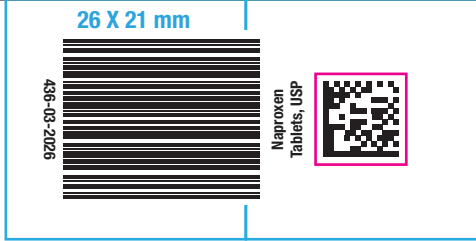


17.0" W

8.268" W (210 mm)

Width: 17.0"
Length: 18.75"
Fold: 1.25" x 1.25"



1.25"H x 1.25"W

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NAPROXEN TABLETS safely and effectively. See full prescribing information for NAPROXEN TABLETS.

NAPROXEN tablets, for oral use
Initial U.S. Approval: 1976

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 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. (5.1)
• Naproxen tablets are 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 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. (5.2)

RECENT MAJOR CHANGES
Warnings and Precautions (5.9) 11/2024

INDICATIONS AND USAGE
Naproxen tablets are non-steroidal anti-inflammatory drugs indicated for:

- the relief of the signs and symptoms of:
• rheumatoid arthritis
• osteoarthritis
• ankylosing spondylitis
• polyarticular juvenile idiopathic arthritis
• tendonitis
• bursitis
• acute gout

- the management of:
• pain
• primary dysmenorrhea

DOSEAGE AND ADMINISTRATION
Use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. (2.1)

Table with 3 columns: Indication, Dosage, Frequency. Includes Rheumatoid Arthritis, Osteoarthritis, and Ankylosing Spondylitis.

The dose may be adjusted up or down depending on the clinical response of the patient. In patients who tolerate lower doses well, the dose may be increased to naproxen 1,500 mg/day for up to 6 months.

Polyarticular Juvenile Idiopathic Arthritis
Naproxen tablets may not allow for the flexible dose titration needed in pediatric patients with polyarticular juvenile idiopathic arthritis. A liquid formulation may be more appropriate. Recommended total daily dose of naproxen is approximately 10 mg/kg given in 2 divided doses. Dosing with naproxen tablets is not appropriate for children weighing less than 50 kilograms.

Acute Gout
Recommended starting dose 750 mg of naproxen tablets followed by 250 mg every 8 hours until the attack has subsided.

DOSEAGE FORMS AND STRENGTHS
Naproxen tablets: 250 mg, 375 mg and 500 mg (3)

CONTRAINDICATIONS
• Known hypersensitivity to naproxen or any components of the drug product (4)
• History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs (4)
• In the setting of CABG surgery (4)

FULL PRESCRIBING INFORMATION: CONTENTS
WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS
1 INDICATIONS AND USAGE
2 DOSEAGE AND ADMINISTRATION
2.1 General Dosing Instructions
2.2 Rheumatoid Arthritis, Osteoarthritis and Ankylosing Spondylitis
2.3 Polyarticular Juvenile Idiopathic Arthritis
2.4 Management of Pain, Primary Dysmenorrhea, and Acute Tendonitis and Bursitis
2.5 Acute Gout
2.6 Non-Interchangeability of Other Formulations of Naproxen
3 DOSEAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Cardiovascular Thrombotic Events
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5.3 Hepatotoxicity
5.4 Hypertension
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5.11 Fetal Toxicity
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5.13 Masking of Inflammation and Fever
5.14 Long-Term Use and Laboratory Monitoring

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 and Precautions (5.1)).
• Naproxen tablets are contraindicated in the setting of coronary artery bypass graft (CABG) surgery [see Contraindications (4), Warnings and Precautions (5.1)].

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 and Precautions (5.2)].

1 INDICATIONS AND USAGE
Naproxen tablets are indicated for:
the relief of the signs and symptoms of:
• rheumatoid arthritis
• osteoarthritis
• ankylosing spondylitis
• Polyarticular Juvenile Idiopathic Arthritis
• tendonitis
• bursitis
• acute gout
the management of:
• pain
• primary dysmenorrhea

2 DOSEAGE AND ADMINISTRATION
2.1 General Dosing Instructions
Carefully consider the potential benefits and risks of naproxen tablets and other treatment options before deciding to use naproxen tablets. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals [see Warnings and Precautions (5)].

2.2 Rheumatoid Arthritis, Osteoarthritis and Ankylosing Spondylitis
The recommended dosages of naproxen tablets are shown in Table 1.

Table 1: Recommended dosages for Naproxen Tablets. Columns: Naproxen Tablets, 250 mg, 375 mg, 500 mg. Rows: twice daily, twice daily, twice daily.

During long-term administration, the dose of naproxen may be adjusted up or down depending on the clinical response of the patient. A lower daily dose may be sufficient for long-term administration. The morning and evening doses do not have to be equal in size and administration of the drug more frequently than twice daily does not generally make a difference in response.

2.3 Polyarticular Juvenile Idiopathic Arthritis
Naproxen solid-oral dosage forms may not allow for the flexible dose titration needed in pediatric patients with polyarticular juvenile idiopathic arthritis. A liquid formulation may be more appropriate for weight-based dosing and due to the need for dose flexibility in children.

2.4 Management of Pain, Primary Dysmenorrhea, and Acute Tendonitis and Bursitis
The recommended starting dose of naproxen tablets is 500 mg followed by 250 mg (one half of a 500 mg naproxen tablet) every 6-8 hours as required. The total daily dose should not exceed 1,250 mg of naproxen.

WARNINGS AND PRECAUTIONS
Hepatotoxicity: Inform patients of warning signs and symptoms of hepatotoxicity. Discontinue if abnormal liver tests persist or worsen or if clinical signs and symptoms of liver disease develop. (5.3)

Hypertension: Patients taking some antihypertensive medications may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure. (5.4,7)

Heart Failure and Edema: Avoid use of naproxen tablets in patients with severe heart failure unless benefits are expected to outweigh risk of worsening heart failure. (5.5)

Renal Toxicity: Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia. Avoid use of naproxen tablets in patients with advanced renal disease unless benefits are expected to outweigh risk of worsening renal function. (5.6)

Anaphylactic Reactions: Seek emergency help if an anaphylactic reaction occurs. (5.7)

Exacerbation of Asthma Related to Aspirin Sensitivity: Naproxen tablets are contraindicated in patients with aspirin-sensitive asthma. Monitor patients with preexisting asthma (without aspirin sensitivity). (5.8)

Serious Skin Reactions: Discontinue naproxen tablets at first appearance of skin rash or other signs of hypersensitivity. (5.9)

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): Discontinue and evaluate clinically (5.10).

Fetal Toxicity: Limit use of NSAIDs, including naproxen tablets, between about 20 to 30 weeks in pregnancy due to the risk of oligohydramnios/fetal dysfunction. Avoid use of NSAIDs in women at about 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/fetal renal dysfunction and premature closure of the fetal ductus arteriosus. (5.11, 8.1)

Hematologic Toxicity: Monitor hemoglobin or hematocrit in patients with any signs or symptoms of anemia. (5.12,7)

ADVERSE REACTIONS
Most common adverse reactions to naproxen were dyspepsia, abdominal pain, nausea, headache, rash, ecchymosis, and edema. (6.1)

Report SUSPECTED ADVERSE REACTIONS, contact SciGen Pharmaceuticals, Inc. at 1-855-724-3436 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS
Drugs that Interfere with Hemostasis (e.g., warfarin, aspirin, SSRIs/SNRIs)
• Monitor patients for bleeding who are concomitantly taking naproxen tablets with drugs that interfere with hemostasis. Concomitant use of naproxen tablets and analgesic doses of aspirin is not generally recommended. (7)

ACE Inhibitors, Angiotensin Receptor Blockers (ARB), or Beta-Blockers: Concomitant use with naproxen tablets may diminish the antihypertensive effect of these drugs. Monitor blood pressure. (7)

ACE Inhibitors and ARBs: Concomitant use with naproxen tablets in elderly, volume depleted, or those with renal impairment may result in deterioration of renal function. In such high risk patients, monitor for signs of worsening renal function. (7)

Diuretics: NSAIDs can reduce natriuretic effect of furosemide and thiazide diuretics. Monitor patients to assure diuretic efficacy including antihypertensive effects. (7)

Digoxin: Concomitant use with naproxen tablets can increase serum concentration and prolong half-life of digoxin. Monitor serum digoxin levels. (7)

USE IN SPECIFIC POPULATIONS
Infertility: NSAIDs are associated with reversible infertility. Consider withdrawal of naproxen tablets in women who have difficulties conceiving. (8.3)

Renal Impairment: Naproxen-containing products are not recommended for use in patients with moderate to severe and patient renal impairment (creatinine clearance <30 mL/min). (8.7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 3/2026

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Postmarketing Experience
6.3 Hematologic Toxicity
6.4 Pediatric Use
6.5 Geriatric Use
6.6 Hepatic Impairment
6.7 Renal Impairment
6.8 Fetal Toxicity
6.9 Hematologic Toxicity
6.10 OVERDOSAGE
10 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Reproductive Toxicology
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

2.5 Acute Gout
The recommended starting dose is 750 mg of naproxen tablets followed by 250 mg every 8 hours until the attack has subsided.

2.6 Non-Interchangeability with Other Formulations of Naproxen
Different dosages and formulations (e.g., tablets, suspension) of naproxen are not interchangeable. This difference should be taken into consideration when changing strengths or formulations.

3 DOSEAGE FORMS AND STRENGTHS
Naproxen Tablets USP, 250 mg are light yellow, round shaped tablets debossed with "SG" along with break-line on one side and "341" on the other side.
Naproxen Tablets USP, 375 mg are light yellow, capsule shaped tablets debossed with "SG" on one side and "435" on the other side.
Naproxen Tablets USP, 500 mg are light yellow, oblong shaped tablets debossed with "SG" along with break-line on one side and "436" on the other side.

CONTRAINDICATIONS
Naproxen tablets are 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 and Precautions (5.7, 5.9)]
• History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients [see Warnings and Precautions (5.7, 5.8)]
• In the setting of coronary artery bypass graft (CABG) surgery [see Warnings and Precautions (5.1)]

5 WARNINGS AND PRECAUTIONS

5.1 Cardiovascular Thrombotic Events
Clinical trials of several 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 weeks 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 and Precautions (5.2)].
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 to 14 days following CABG surgery found an increased incidence of myocardial infarction and stroke. NSAIDs are contraindicated in the setting of CABG [see Contraindications (4)].

Post-MI Patients
Observational studies conducted in the Danish National Registry have demonstrated that patients treated with NSAIDs in the post-operative period were at increased risk of reinfarction, 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 four years of follow-up.
Avoid the use of naproxen tablets in patients with a recent MI unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If naproxen tablets are used in patients with a recent MI, monitor patients for signs of cardiac ischemia.

5.2 Gastrointestinal Bleeding, Ulceration, and Perforation
NSAIDs, including naproxen, 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 occurred in approximately 1% of patients treated for 3 to 6 months, and in about 2% to 4% of patients treated for one year. However, even short-term NSAID therapy is not without risk.

5.3 Hematologic Toxicity
Patients with a prior history of 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 for 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, or 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.
• Such 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.
• Such 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.
• In the setting of concomitant use of low-dose aspirin for cardiac prophylaxis, monitor patients more closely for evidence of GI bleeding [see Drug Interactions (7)].

5.4 Hypertension
NSAIDs, including naproxen tablets 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 antihypertensive or diuretic (ACE) inhibitors, thiazide diuretics, or loop diuretics may have impaired response to these therapies when taking NSAIDs [see Drug Interactions (7)].
Monitor blood pressure (BP) during the initiation of NSAID treatment and throughout the course of therapy.

5.5 Heart Failure and Edema
The Food and Drug Administration (FDA) Collaborative 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 Drug Interactions (7)].

5.6 Renal Toxicity and Hyperkalemia
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. NSAIDs can also cause fixed drug eruption (FDE). FDE may present as a more severe variant known as generalized bullous fixed drug eruption (GBFDE), which can be life-threatening. These serious events may occur without warning. Inform patients about the signs and symptoms of serious skin reactions and discontinue use of naproxen tablets at the first appearance of skin rash or any other sign of hypersensitivity. Naproxen tablets are contraindicated in patients with previous serious skin reactions to NSAIDs [see Contraindications (4)].

5.7 Anaphylactic Reactions
Naproxen has been associated with anaphylactic reactions in patients with and without known hypersensitivity to naproxen and in patients with aspirin-sensitive asthma [see Contraindications (4) and Warnings and Precautions (5.8)].
Seek emergency help if an anaphylactic reaction occurs.

5.8 Exacerbation of Asthma Related to Aspirin Sensitivity
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 patients with aspirin-sensitive asthma, patients with asthma should be monitored for asthma symptoms [see Contraindications (4)]. When naproxen tablets are used in patients with preexisting asthma (without known aspirin sensitivity), monitor patients for changes in the signs and symptoms of asthma.

5.9 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. NSAIDs can also cause fixed drug eruption (FDE). FDE may present as a more severe variant known as generalized bullous fixed drug eruption (GBFDE), which can be life-threatening. These serious events may occur without warning. Inform patients about the signs and symptoms of serious skin reactions and discontinue use of naproxen tablets at the first appearance of skin rash or any other sign of hypersensitivity. Naproxen tablets are contraindicated in patients with previous serious skin reactions to NSAIDs [see Contraindications (4)].

5.10 Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
NSAIDs, including naproxen tablets, have been reported in patients taking NSAIDs such as naproxen tablets. Some of these reactions have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this is a variable in its presentation and other organ systems not noted here may be involved, it is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue naproxen tablets and evaluate the patient immediately.

5.11 Fetal Toxicity
Premature Closure of Fetal Ductus Arteriosus
Avoid use of NSAIDs, including naproxen tablets in pregnant women at about 30 weeks of gestation and later. NSAIDs, including naproxen tablets increase the risk of premature closure of the fetal ductus arteriosus at approximately the same gestational age.
Oligohydramnios/Neonatal Renal Impairment
Use of NSAIDs, including naproxen tablets, at about 20 weeks gestation or later in pregnancy may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. These adverse outcomes are associated with increased days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation. Complications of prolonged oligohydramnios may, for example, include limb contractures and delayed lung maturation. In some postmarketing cases of impaired neonatal renal function, renal replacement therapy was necessary, and in some cases, dialysis was required.
If NSAID treatment is necessary between about 20 weeks and 30 weeks gestation, limit naproxen tablets use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if naproxen treatment extends beyond 48 hours. Discontinue naproxen tablets if oligohydramnios occurs and follow up according to clinical practice [see Use in Specific Populations (8.1)].

5.12 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 tablets has any signs or symptoms of anemia, monitor hemoglobin or hematocrit.
NSAIDs, including naproxen tablets may increase the risk of bleeding events. Co-morbid conditions such as coagulation disorders or concomitant use of warfarin and 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 Drug Interactions (7)].

5.13 Masking of Inflammation and Fever
The pharmacological activity of naproxen tablets in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infections.
5.14 Long-Term Use and Laboratory Monitoring
Because of the potential for serious GI adverse reactions, 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 and Precautions (5.2,5.3, 5.6)].
Patients with initial hemoglobin values of 10g or less who are to receive long-term therapy should have hemoglobin and hematocrit determined separately. If clinically warranted, consider periodic monitoring of hemoglobin values if any change or disturbance in vision occurs.

6 ADVERSE REACTIONS
The following adverse reactions are discussed in greater detail in other sections of the labeling:
• Cardiovascular Thrombotic Events [see Warnings and Precautions (5.1)]
• GI Bleeding, Ulceration, and Perforation [see Warnings and Precautions (5.2)]
• Hepatotoxicity [see Warnings and Precautions (5.3)]
• Hypertension [see Warnings and Precautions (5.4)]
• Heart Failure and Edema [see Warnings and Precautions (5.5)]
• Renal Toxicity and Hyperkalemia [see Warnings and Precautions (5.6)]
• Anaphylactic Reactions [see Warnings and Precautions (5.7)]
• Serious Skin Reactions [see Warnings and Precautions (5.8)]
• Hematologic Toxicity [see Warnings and Precautions (5.12)]

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.
Adverse reactions reported in controlled clinical trials in 960 patients treated for rheumatoid arthritis or osteoarthritis are listed below. In general, reactions in patients treated chronically were reported 2 to 10 times more frequently than they were in short-term studies in the 962 patients treated for mild to moderate pain or for dysmenorrhea. The most frequent complaints reported related to the gastrointestinal tract.
A clinical study found gastrointestinal reactions to be more frequent and more severe in rheumatoid arthritis patients taking daily doses of 1,500 mg naproxen compared to those taking 750 mg naproxen.
In controlled clinical trials with about 80 pediatric patients and in well-monitored, open-label studies with about 400 pediatric patients with polyarticular juvenile idiopathic arthritis treated with naproxen, the incidence of rash and prolonged bleeding times were greater, the incidence of gastrointestinal and central nervous system reactions were about the same, and the incidence of other reactions were lower in pediatric patients than in adults.

The patients taking naproxen in clinical trials, the most frequently reported adverse experiences in approximately 1% to 10% of patients were:
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, ecchymosis, sweating, purpura
Special Senses: tinnitus, visual disturbances, hearing disturbances
Cardiovascular: edema, palpitations
Respiratory: dyspnea, rhinitis
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
The following are additional adverse experiences reported in <1% of patients taking naproxen during clinical trials:
Gastrointestinal (GI) Experiences, including: flatulence, gross bleeding/perforation, GI ulcers (gastric/duodenal), vomiting
Hepatic: jaundice
Hemic and Lymphatic: melena, thrombocytopenia, agranulocytosis
Nervous System: inability to concentrate

Dermatologic: skin rashes
6.2 Postmarketing Experience
The following adverse reactions have been identified during post approval use of naproxen. 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.

The following are additional adverse experiences reported in <1% of patients taking naproxen during clinical trials and through postmarketing reports. Those adverse reactions observed through postmarketing reports are italicized.
Body as a Whole: anaphylactoid reactions, angioneurotic edema, menstrual disorders, pyrexia (chills and fever)
Cardiovascular: congestive heart failure, vasculitis, hypertension, pulmonary edema
Gastrointestinal: inflammatory bleeding (sometimes fatal, particularly in the elderly), ulceration, perforation and obstruction of the upper or lower gastrointestinal tract, Esophagitis, stomatitis, hematemesis, colitis, exacerbation of inflammatory bowel disease (ulcerative colitis, Crohn's disease),
Hepatobiliary: abnormal liver function tests, hepatitis (some cases have been fatal)
Hemic and Lymphatic: eosinophilia, leukopenia, granulocytopenia, hemolytic anemia, aplastic anemia
Metabolic and Nutritional: hyperglycemia, hypoglycemia
Nervous System: depression, dream abnormalities, insomnia, malaise, myalgia, muscle weakness, aseptic meningitis, cognitive dysfunction, convulsions
Respiratory: eosinophilic pneumonitis, asthma
Dermatologic: alopecia, urticaria, toxic epidermal necrolysis, erythema multiforme, erythema nodosum, lichen planus, pustular reaction, systemic lupus erythematosus, bullous reactions, including Stevens-Johnson syndrome, fixed drug eruption (FDE), photosensitive dermatitis, photosensitivity reactions, including rare cases resembling porphyria cutanea tarda (pseudoporphyria) or epidermolysis bullosa. If skin fragility, blistering or other symptoms suggestive of pseudoporphyria occur, treatment should be discontinued and the patient monitored.

Special Senses: hearing impairment, corneal opacity, papillitis, retrobulbar optic neuritis, papilledema
Urogenital: glomerular nephritis, hematuria, hyperkalemia, interstitial nephritis, nephrotic syndrome, renal disease, renal failure, renal papillary necrosis, raised serum creatinine
Reproduction (female): infertility
In patients taking NSAIDs, the following adverse experiences have also been reported in <1% of patients.
Body as a Whole: fever, infection, sepsis, anaphylactic reactions, apopleptic changes, death
Cardiovascular: hypertension, tachycardia, syncope, arrhythmia, hypertension, myocardial infarction
Gastrointestinal: dry mouth, esophagitis, gastric/peptic ulcers, gastritis, glossitis, eructation
Hepatobiliary: hepatitis, liver failure
Hemic and Lymphatic: rectal bleeding, lymphadenopathy, pancytopenia
Metabolic and Nutritional: weight changes
Nervous System: anxiety, asthenia, confusion, nervousness, paresthesia, somnolence, tremors, convulsions, coma, hallucinations
Respiratory: asthma, respiratory depression, pneumonia
Dermatologic: exfoliative dermatitis
Special Senses: blurred vision, conjunctivitis
Urogenital: cystitis, dysuria, oliguria/polyuria, proteinuria

7 DRUG INTERACTIONS
See Table 1 for clinically significant drug interactions with naproxen.

Table 1: Clinically Significant Drug Interactions with naproxen

Table with 2 columns: Drug Interaction, Clinical Impact. Includes Drugs That Interfere with Hemostasis, ACE Inhibitors, Angiotensin Receptor Blockers, Diuretics, Digoxin, Lithium, Methotrexate, Cyclosporine, NSAIDs and Salicylates, Penicillins, and Antacids and Sucralfate.

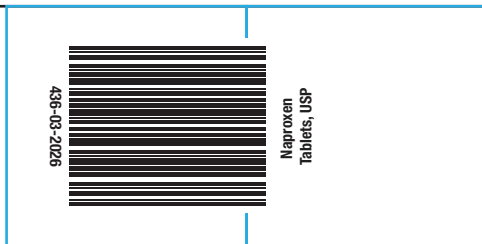
18.75" L

9.125"

17.0" W

8.268" W (210 mm)

Width: 17.0"
Length: 18.75"
Fold: 1.25" x 1.25"



1.25"H x 1.25"W

Table 1 continued

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, sulphonyureas, hydantoins, other NSAIDs, and aspirin.
Intervention:	Patients simultaneously receiving naproxen tablets and a hydantoin, sulphonamide or sulphonyurea should be observed for adjustment of dose if required.

Drug/Laboratory Test Interactions

Bleeding Times	
Clinical Impact:	Naproxen may decrease platelet aggregation and prolong bleeding time.
Intervention:	This effect should be kept in mind when bleeding times are determined.
Porter-Silber test	
Clinical Impact:	The administration of naproxen may result in increased urinary values for 17-ketogenic steroids because of an interaction between the drug and/or its metabolites with m-d-nitrobenzene used in this assay.
Intervention:	Although 17-hydroxy-corticosteroid measurements (Porter-Silber test) do not appear to be artifactually altered, it is suggested that therapy with naproxen be temporarily discontinued 72 hours before adrenal function tests are performed if the Porter-Silber test is to be used.
Urinary assays of 5-hydroxy indoleacetic acid (5HIAA)	
Clinical Impact:	Naproxen may interfere with some urinary assays of 5-hydroxy indoleacetic acid (5HIAA).
Intervention:	This effect should be kept in mind when urinary 5-hydroxy indoleacetic acid is determined.

8 USE IN SPECIFIC POPULATIONS**8.1 Pregnancy**

Risk Summary: Use of NSAIDs, including naproxen tablets can cause premature closure of the fetal ductus arteriosus and fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, limit dose and duration of naproxen tablets use between about 20 and 30 weeks of gestation, and avoid naproxen tablets use at about 30 weeks of gestation and later in pregnancy (see Clinical Considerations, Data). **Premature Closure of Fetal Ductus Arteriosus:** Use of NSAIDs, including naproxen tablets at about 30 weeks gestation or later in pregnancy increases the risk of premature closure of the fetal ductus arteriosus.

Oligohydramnios/Neonatal Renal Impairment: Use of NSAIDs at about 20 weeks gestation or later in pregnancy has been associated with cases of fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Data from observational studies regarding other potential embryofetal risks of NSAID use in women in the first or second trimesters of pregnancy are inconclusive. In animal reproduction studies in rats, rabbits, and mice no evidence of teratogenicity or fetal harm when naproxen was administered during the period of organogenesis at doses 0.13, 0.26, and 0.6 times the maximum recommended human daily dose of 1,500 mg/day, respectively (see Data). Based on animal data, prostaglandins have been shown to have an important role in endometrial vascular permeability, blastocyst implantation, and decidualization. In animal studies, administration of prostaglandin synthesis inhibitors such as naproxen, resulted in increased pre- and post-implantation loss. Prostaglandins also have been shown to have an important role in fetal kidney development. In published animal studies, prostaglandin synthesis inhibitors have been reported to impair kidney development when administered at clinically relevant doses. The estimated background risk of major birth defects and miscarriage for the indicated population(s) is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

8.2 Lactation

Risk Summary: The naproxen anion has been found in the milk of lactating women at a 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 tablets and any potential adverse effects on the breastfed infant from the naproxen tablets or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Fertility: In animal studies, naproxen 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 tablets, in women who have difficulties conceiving or who are undergoing investigation of infertility.

8.4 Pediatric Use: Safety and effectiveness in pediatric patients below the age of 2 years have not been established. Pediatric dosing recommendations for polyarthral juvenile idiopathic arthritis are based on well-controlled studies (see Dosage and Administration (2)). There are no adequate effectiveness or dose-response data for other pediatric conditions, but the experience in polyarthral juvenile idiopathic arthritis and other use experience have established that single doses of 2.5 mg/kg 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.

8.5 Geriatric Use: The hepatic and renal tolerability of long-term naproxen administration was studied in two double-blind clinical trials involving 586 patients. Of the patients studied, 98 patients were age 65 and older and 10 of the 98 patients were age 75 and older. NAPROXEN was administered at doses of 375 mg twice daily or 750 mg twice daily for up to 6 months. Transient abnormalities of laboratory tests assessing hepatic and renal function were noted in some patients, although there were no differences noted in the occurrence of abnormal values among different age groups.

Elderly patients, compared to younger patients, are at a 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 and Precautions (5.1, 5.2, 5.3, 5.6, 5.14)).

Studies indicate that although total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly. The clinical significance of this finding is unclear, although it is possible that the increase in free naproxen concentration could be associated with an increase in the rate of adverse events per a given dosage in some elderly patients. 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 and Precautions (5.2)).

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 (see Clinical Pharmacology (12.3)). 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 and Precautions (5.6)).

8.6 Hepatic Impairment: Caution is advised when high doses are required and some adjustment of dosage may be required in these patients. It is prudent to use the lowest effective dose (see Clinical Pharmacology (12.3)).

8.7 Renal Impairment: Naproxen-containing products are not recommended for use in patients with moderate to severe and severe renal impairment (creatinine clearance <30 mL/min) (see Warnings and Precautions (5.6), Clinical Pharmacology (12.3)).

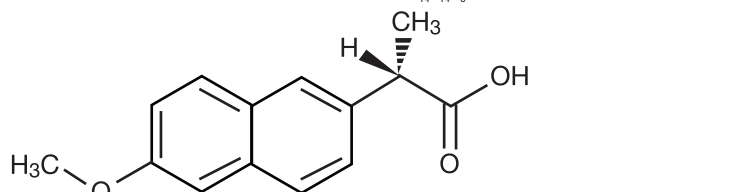
16 HOW SUPPLIED/STORAGE AND HANDLING
Naproxen Tablets USP, 250 mg are light yellow, round shaped tablets debossed with "S & G" on either side of functional score on one side and "434" on the other side.

Bottles of 100 NDC 77771-434-01
Bottles of 500 NDC 77771-434-05

Naproxen Tablets USP, 375 mg are light yellow, capsule shaped tablets debossed with "SG" on one side and "435" on the other side.

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For additional information about overdose treatment contact a poison control center (1-800-222-1222).
11 DESCRIPTION
Naproxen tablets, USP are nonsteroidal anti-inflammatory drugs and available as follows: Naproxen tablets, USP are available as light yellow round shaped tablets containing 250 mg naproxen, light yellow capsule shaped tablets containing 375 mg naproxen, and light yellow oblong shaped tablets containing 500 mg naproxen for oral administration.



Naproxen is white or almost white crystalline powder. It is insoluble in water, soluble in chloroform, dehydrated ethanol and methanol. Sparingly soluble in ether. The octanol/water partition coefficient of Naproxen at pH < 2.18 is 3.18.

Each naproxen tablet, USP contains the following inactive ingredients: croscarmellose sodium, yellow iron oxide, povidone and magnesium stearate

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Naproxen has analgesic, anti-inflammatory, and antipyretic properties. The mechanism of action of naproxen, like that of other NSAIDs, is not completely understood but involves inhibition of cyclooxygenase (COX-1 and COX-2). Naproxen is a potent inhibitor of prostaglandin synthesis in vitro. Naproxen concentrations reached during therapy have produced in vivo effects. Prostaglandins sensitize afferent nerves and potentiate the action of bradykinin in inducing pain in animal models. Prostaglandins are mediators of inflammation. Because naproxen is an inhibitor of prostaglandin synthesis, its mode of action may be due to a decrease of prostaglandins in peripheral tissues.

12.2 Pharmacodynamics
In a healthy volunteer study, 10 days of concomitant administration of naproxen 220 mg once-daily with low-dose immediate-release aspirin (81 mg) showed an interaction with the antiplatelet activity of aspirin as measured by % serum thromboxane B2 inhibition at 24 hours following the day 10 dose (98.7% (aspirin alone) vs 93.1% (naproxen and aspirin)). The interaction was observed even following discontinuation of naproxen on day 11 (while aspirin dose was continued) but normalized by day 13. In the same study, the interaction was greater when naproxen was administered 30 minutes prior to aspirin (98.7% vs 87.7%) and minimal when aspirin was administered 30 minutes prior to naproxen (98.7% vs 95.4%).

Following administration of naproxen 220 mg twice-daily with low-dose immediate-release aspirin (first naproxen dose given 30 minutes prior to aspirin), the interaction was minimal at 24 h following day 10 dose (98.7% vs 95.7%). However, the interaction was more prominent after discontinuation of naproxen (washout) day 11 (98.7% vs 84.3%) and did not normalize completely by day 13 (98.5% vs 90.7%). (see Drug Interactions (7)).

12.3 Pharmacokinetics
Naproxen is rapidly and completely absorbed from the gastrointestinal tract with an in vivo bioavailability of 91%. The elimination half-life of naproxen is unchanged across products ranging from 12 to 17 hours. Steady-state levels of naproxen are reached in 4 to 5 days, and the degree of naproxen accumulation is consistent with this half-life.

Absorption: After administration of naproxen tablets, peak plasma levels are attained in 2 to 4 hours.
Distribution: Naproxen has a volume of distribution of 0.16 L/kg. At therapeutic levels naproxen is greater than 99% albumin-bound. At doses of naproxen greater than 500 mg/day there is less than proportional increase in plasma levels due to an increase in clearance caused by saturation of plasma protein binding at higher doses (average trough C₀ 36.5, 49.2 and 56.4 mg/L with 500, 1,000 and 1,500 mg daily doses of naproxen, respectively). The naproxen anion has been found in the milk of lactating women at a concentration equivalent to approximately 1% of maximum naproxen concentration in plasma (see Use in Specific Populations (8.2)).

Elimination: Naproxen is extensively metabolized in the liver to 6-O-desmethyl naproxen, and both parent and metabolites do not induce metabolizing enzymes. Both naproxen and 6-O-desmethyl naproxen are further metabolized to their respective acylglucuronide conjugated metabolites.
Excretion: The clearance of naproxen is 0.13 mL/min/kg. Approximately 95% of the naproxen from any dose is excreted in the urine, primarily as naproxen (<1%), 6-O-desmethyl naproxen (<1%) or their conjugates (86% to 92%). The plasma half-life of the naproxen anion in humans ranges from 12 to 17 hours. The corresponding half-lives of both naproxen's metabolites and conjugates are shorter than 12 hours, and their rates of excretion have been found to coincide closely with the rate of naproxen clearance with the plasma. Small amounts, 3% or less of the administered dose, are excreted in the feces. In patients with renal failure metabolites may accumulate (see Warnings and Precautions (5.6)).

Specific Populations
Pediatric: In pediatric patients aged 5 to 16 years with arthritis, plasma naproxen levels following a 5 mg/kg single dose of naproxen suspension (see Dosage and Administration (2)) were found to be similar to those found in normal adults following a 500 mg dose. The terminal half-life appears to be similar in pediatric and adult patients. Pharmacokinetic studies of naproxen were not performed in pediatric patients younger than 5 years of age. Pharmacokinetic parameters appear to be similar following administration of naproxen suspension or tablets in pediatric patients.

Geriatric: Studies indicate that although total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly, although the unbound fraction is <1% of the total naproxen concentration. Unbound trough naproxen concentrations in elderly subjects have been reported to range from 0.12% to 0.19% of total naproxen concentration, compared with 0.05% to 0.075% in younger subjects.
Hepatic Impairment: Naproxen pharmacokinetics has not been determined in subjects with hepatic insufficiency. Chronic alcoholic liver disease and probably other diseases with altered or abnormal plasma proteins (albumin) reduce the total plasma concentration of naproxen, but the plasma concentration of unbound naproxen is increased.

Renal Impairment: Naproxen pharmacokinetics has not been determined in subjects with renal insufficiency. Given that naproxen, its metabolites and conjugates are primarily excreted by the kidney, the potential exists for naproxen metabolites to accumulate in the presence of renal insufficiency. Elimination of naproxen is decreased in patients with severe renal impairment.

Drug Interactions/Studies: Aspirin: When NSAIDs were administered with aspirin, the protein binding of NSAIDs were reduced, although the clearance of free NSAID was not altered. The clinical significance of this interaction is not known. See Table 1 for clinically significant drug interactions of NSAIDs with aspirin (see Drug Interactions (7)).

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis: A 2-year study was performed in rats to evaluate the carcinogenic potential of naproxen at rat doses of 8, 16, and 24 mg/kg/day (0.05, 0.1, and 0.16 times the maximum recommended human daily dose [MRHD] of 500 mg/day based on a body surface area comparison). No evidence of tumorigenicity was found.

Mutagenesis: Naproxen tested positive in the in vivo sister chromatid exchange assay for but was not mutagenic in the in vitro bacterial reverse mutation assay (Ames test).

Impairment of Fertility: Male rats were treated with 2, 5, 10, and 20 mg/kg naproxen by oral gavage for 60 days prior to mating and female rats were treated with the same doses for 14 days prior to mating and for the first 7 days of pregnancy. There were no adverse effects on fertility noted (up to 0.13 times the MRHD based on body surface area).

14 CLINICAL STUDIES
Naproxen has been studied in patients with rheumatoid arthritis, osteoarthritis, polyarthral juvenile idiopathic arthritis, ankylosing spondylitis, tendonitis and bursitis, and acute gout. Improvement in patients treated for rheumatoid arthritis was demonstrated by a reduction in joint swelling, a reduction in duration of morning stiffness, a reduction in disease activity as assessed by both patients and physicians, and by a reduction in mobility as demonstrated by a reduction in walking time. Generally, response to naproxen has not been found to be dependent on age, sex, severity or duration of rheumatoid arthritis.

In patients with osteoarthritis, the therapeutic action of naproxen has been shown by a reduction in joint pain or tenderness, an increase in range of motion in knee joints, increased mobility as demonstrated by a reduction in walking time, and improvement in capacity to perform activities of daily living impaired by the disease.

In a clinical trial comparing standard formulations of naproxen 375 mg twice a day (750 mg a day) vs 750 mg twice a day (1,500 mg/day), 9 patients in the 750 mg group terminated prematurely because of adverse events. Nineteen patients in the 1,500 mg group terminated prematurely because of adverse events. Most of these adverse events were gastrointestinal events.

In clinical studies in patients with rheumatoid arthritis, osteoarthritis, and polyarthral juvenile idiopathic arthritis, naproxen has been shown to be comparable to aspirin and indomethacin in controlling the aforementioned measures of disease activity, but the frequency and severity of the milder gastrointestinal adverse effects (nausea, dyspepsia, heartburn) and nervous system adverse effects (lumbago, dizziness, lightheadedness) were less in naproxen-treated patients than in those treated with aspirin or indomethacin.

In patients with ankylosing spondylitis, naproxen has been shown to decrease night pain, morning stiffness and pain at rest. In double-blind studies the drug was shown to be as effective as aspirin, but with fewer side effects.

In patients with acute gout, a favorable response to naproxen was shown by significant clearing of inflammatory changes (e.g. decrease in swelling, heat) within 24 to 48 hours, as well as by relief of pain and tenderness. Naproxen has been studied in patients with mild to moderate pain secondary to postoperative, orthopedic, postpartum episiotomy and uterine contraction pain and dysmenorrhea. Onset of pain relief can begin within 1 hour in patients taking naproxen. Analgesic effect was shown by such measures as reduction of pain intensity scores, increase in pain relief scores, decrease in numbers of patients requiring additional analgesic medication, and delay in time to remedication. The analgesic effect has been found to last for up to 12 hours. Naproxen may be used safely in combination with gold salts and/or corticosteroids; however, in controlled clinical trials, when added to the regimen of patients receiving corticosteroids, it did not appear to cause greater improvement over that seen with corticosteroids alone. Whether naproxen has a "steroid-sparing" effect has not been adequately studied. When added to the regimen of patients receiving gold salts, naproxen did result in greater improvement. Its use in combination with salicylates is not recommended because there is evidence that aspirin increases the rate of excretion of naproxen and data are inadequate to demonstrate that naproxen and aspirin produce greater improvement over that achieved with aspirin alone. In addition, as with other NSAIDs, the combination may result in higher frequency of adverse events than demonstrated for either product alone.

In ¹⁴Cr blood loss and gastroscopy studies with normal volunteers, daily administration of 1,000 mg of naproxen has been demonstrated to cause statistically significantly less gastric bleeding and erosion than 3,250 mg of aspirin.

16 HOW SUPPLIED/STORAGE AND HANDLING
Naproxen Tablets USP, 250 mg are light yellow, round shaped tablets debossed with "S & G" on either side of functional score on one side and "434" on the other side.

Bottles of 100 NDC 77771-434-01
Bottles of 500 NDC 77771-434-05

Naproxen Tablets USP, 375 mg are light yellow, capsule shaped tablets debossed with "SG" on one side and "435" on the other side.

Bottles of 100 NDC 77771-435-01
Bottles of 500 NDC 77771-435-05

Naproxen Tablets USP, 500 mg are light yellow, oblong shaped tablets debossed with "S & G" on either side of functional score on one side and "436" on the other side.

Bottles of 100 NDC 77771-436-01
Bottles of 500 NDC 77771-436-05

Store at 15°C to 30°C (59°F to 86°F) in well-closed containers; dispense in light-resistant containers.
17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Medication Guide) that accompanies each prescription dispensed. Inform patients, families, or their caregivers of the following information before initiating therapy with naproxen tablets and periodically during the course of ongoing therapy.

Cardiovascular Thrombotic Events
Advise patients to be alert for the symptoms of cardiovascular thrombotic events, including chest pain, shortness of breath, weakness, or slurring of speech, and to report any of these symptoms to their health care provider immediately (see Warnings and Precautions (5.1)).

Gastrointestinal Bleeding, Ulceration, and Perforation
Advise patients to report symptoms of ulcerations and bleeding, including epigastric pain, dyspepsia, melena, and hematemesis to their health care provider. In the setting of concomitant use of low-dose aspirin for cardiac prophylaxis, inform patients of the increased risk for and the signs and symptoms of GI bleeding (see Warnings and Precautions (5.2)).

Hepatotoxicity
Inform patients of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, pruritus, diarrhea, right upper quadrant tenderness, and "flu-like" symptoms). If these occur, instruct patients to stop naproxen tablets and seek immediate medical therapy (see Warnings and Precautions (5.3)).

Heart Failure and Edema
Advise patients to be alert for the symptoms of congestive heart failure including shortness of breath, unexplained weight gain, or edema and to contact their healthcare provider if such symptoms occur (see Warnings and Precautions (5.5)).

Anaphylactic Reactions
Inform patients of the signs of an anaphylactic reaction (e.g., difficulty breathing, swelling of the face or throat). Instruct patients to seek immediate emergency help if these occur (see Contraindications (4) and Warnings and Precautions (5.7)).

Serious Skin Reactions, including DRESS
Inform patients to stop taking naproxen tablets immediately if they develop any type of rash or fever and to contact their healthcare provider as soon as possible (see Warnings and Precautions (5.9, 5.10)).

Female Fertility
Advise females of reproductive potential who desire pregnancy that NSAIDs, including naproxen tablets, may be associated with a reversible delay in ovulation (see Use in Specific Populations (8.3)).

Fetal Toxicity
Inform pregnant women to avoid use of naproxen tablets and other NSAIDs starting at 30 weeks gestation because of the risk of the premature closing of the fetal ductus arteriosus. If treatment with naproxen tablets are 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 (5.11) and Use in Specific Populations (8.1)).

Avoid Concomitant Use of NSAIDs
Inform patients that the concomitant use of naproxen tablets with other NSAIDs or salicylates (e.g., diflunisal, ibuprofen) is not recommended due to the increased risk of gastrointestinal 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 naproxen tablets until they talk to their healthcare provider (see Drug Interactions (7)).

Manufactured by:
ScieGen Pharmaceuticals Inc
Hauppauge, NY 11788 USA

Distributed By:
Radha Pharmaceuticals, Inc.
Hauppauge, NY 11788 USA

Rev. 3/2026

Medication Guide for Nonsteroidal Anti-inflammatory Drugs (NSAIDs)
What is the most important information I should know about medicines called Nonsteroidal Anti-inflammatory Drugs (NSAIDs)? 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 NSAIDs right before or after a heart surgery called a "coronary artery bypass graft (CABG)."

Avoid taking NSAIDs 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", "anticoagulants", "SSRIs", or "SNRIs"
- increasing doses of NSAIDs
- longer use of NSAIDs
- smoking
- drinking alcohol
- advanced liver disease
- bleeding problems

NSAIDs should only be used:

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

Who should not take NSAIDs?
Do not take NSAIDs:

- 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.

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

- have liver or kidney problems
- have high blood pressure
- have asthma
- are pregnant or plan to become pregnant. 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 breast feed.

Tell your healthcare provider about all of the medicines you take, including prescription or over-the-counter medicines, vitamins or herbal supplements. NSAIDs 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 NSAIDs? NSAIDs can cause serious side effects, including:

See "What is the most important information I should know about medicines called Nonsteroidal Anti-inflammatory Drugs (NSAIDs)?"

- new or worse high blood pressure
- heart failure
- liver problems including liver failure
- kidney problems including kidney failure
- low red blood cells (anemia)
- life-threatening skin reactions
- life-threatening allergic reactions

Other side effects of NSAIDs include: stomach pain, constipation, diarrhea, gas, heartburn, nausea, vomiting, and dizziness. **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
- vomited blood
- more tired or weaker than usual
- there is blood in your bowel movement or it is black and sticky like tar
- unusual weight gain
- skin rash or blisters with fever
- swelling of the face or throat
- swelling of the arms, legs, hands and feet

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

- nausea
- more tired or weaker than usual
- diarrhea
- itching
- your skin or eyes look yellow
- indigestion or stomach pain
- flu-like symptoms

If you take too much of your NSAID, call your healthcare provider or get medical help right away.

These are not all the possible side effects of NSAIDs. For more information, ask your healthcare provider or pharmacist about NSAIDs. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

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 NSAIDs
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use NSAIDs for a condition for which it was not prescribed. Do not give NSAIDs to other people, even if they have the same symptoms that you have. It may harm them.

If you would like more information about NSAIDs, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about NSAIDs that is written for health professionals.

Manufactured by:
ScieGen Pharmaceuticals Inc
Hauppauge, NY 11788 USA

Distributed By:
Radha Pharmaceuticals, Inc.
Hauppauge, NY 11788 USA

For more information, call 1-855-724-3436

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

Revised: 3/2026

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