NAPROXEN - naproxen capsule
Lake Erie Medical DBA Quality Care Products LLC

DESCRIPTION
Naproxen is a member of the arylacetic acid group of nonsteroidal anti-inflammatory drugs.
The chemical name for naproxen is (S)-6-methoxy-α-methyl-2-naphthaleneacetic acid. Naproxen has the following structure:
Naproxen is an odorless, white to off-white crystalline substance. It is lipid-soluble, practically insoluble in water at low pH and freely soluble in water at high pH. The octanol/water partition coefficient of naproxen at pH 7.4 is 1.6 to 1.8.
Each tablet, for oral administration, contains 250 mg, 375 mg or 500 mg of naproxen. In addition, each tablet contains the following inactive ingredients: colloidal silicon dioxide, magnesium stearate, povidone, and sodium starch glycolate.

CLINICAL PHARMACOLOGY
Pharmacodynamics: Naproxen is a nonsteroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties.
The sodium salt of naproxen has been developed as a more rapidly absorbed formulation of naproxen for use as an analgesic.
The mechanism of action of the naproxen anion, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition.
Pharmacokinetics: Naproxen itself is rapidly and completely absorbed from the gastrointestinal tract with an in vivo bioavailability of 95%. The different dosage forms of naproxen are bioequivalent in terms of extent of absorption (AUG) and peak concentration (C_{max}); however, the products do differ in their pattern of absorption. These differences between naproxen products are related to both the chemical form of naproxen used and its formulation. Even with the observed differences in pattern of absorption, 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. This suggests that the differences in pattern of release play only a negligible role in the attainment of steady-state plasma levels.
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 C_{ss} 36.5, 49.2 and 56.4 mg/L with 500, 1000 and 1500 mg daily doses of naproxen). The naproxen anion has been found in the milk of lactating women at a concentrations equivalent to approximately 1% of maximum naproxen concentration in plasma (see PRECAUTIONS: Nursing Mothers).
Metabolism:
Naproxen is extensively metabolized to 6-0-desmethyl naproxen, and both parent and metabolites do not induce metabolizing enzymes.
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 (less than 1%), 6-0-desmethyl naproxen (less than 1%) or their conjugates (66% 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 disappearance from the plasma. In patients with renal failure metabolites may accumulate (see WARNINGS: Renal Effects).
Special Populations:
Pediatric Patients: 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) 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 Patients: 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 less than 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. 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.
Race: Pharmacokinetic differences due to race have not been studied.
Hepatic Insufficiency: Naproxen pharmacokinetics has not been determined in subjects with hepatic insufficiency.
Renal Insufficiency: 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. Naproxen-containing products are not recommended for use in patients with moderate to severe renal impairment (creatinine less than 30 ml/min) (see WARNINGS: Renal Effects).
INDICATIONS AND USAGE
Carefully consider the potential benefits and risks of naproxen 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).

Naproxen is indicated:
* For reduction of fever
* For relief of mild to moderate pain
* For relief of signs and symptoms of juvenile arthritis.
* For relief of the signs and symptoms of rheumatoid arthritis
* For relief of the signs and symptoms of osteoarthritis.
* For treatment of primary dysmenorrhea.
* For acute or long-term use in the relief of signs and symptoms of the following:
  1. Ankylosing spondylitis
  2. Acute painful shoulder (Acute subacromial bursitis/supraspinatus tendinitis)
  3. Acute gouty arthritis

Naproxen tablets are also indicated
• For the relief of the signs and symptoms of tendinitis
• For the relief of the signs and symptoms of bursitis
• For the relief of the signs and symptoms of acute gout

CONTRAINDICATIONS
Naproxen is contraindicated in patients with known hypersensitivity to prescription as well as to over-the-counter products containing naproxen.

Naproxen should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients (see WARNINGS - Anaphylactoid Reactions, and PRECAUTIONS - Preexisting Asthma).

Naproxen is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

WARNINGS
CARDIOVASCULAR EFFECTS
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, myocardial infarction, and stroke, which can be fatal. All NSAIDs, both COX-2 selective and nonselective, may have a similar risk. Patients with known CV disease or risk factors for CV disease may be at greater risk. To minimize the potential risk for an adverse CV event in patients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and/or 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 does increase the risk of serious GI events (see GI WARNINGS). 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 (see CONTRAINDICATIONS).

Hypertension
NSAIDs, including naproxen, can lead to onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including naproxen, should be used with caution in patients with hypertension. Blood pressure (BP) should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.

Congestive Heart Failure and Edema
Fluid retention and edema have been observed in some patients taking NSAIDs. Naproxen should be used with caution in patients with fluid retention, hypertension, or heart failure.

Gastrointestinal Effects - Risk of Ulceration, Bleeding, and Perforation
NSAIDs, including naproxen, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the 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. These trends continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.

NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or gastrointestinal bleeding. Patients with a prior history of peptic ulcer disease and/or gastrointestinal bleeding who use NSAIDs have a greater than 10-fold increased risk for developing a GI bleed compared to patients with neither of these risk factors. Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include concomitant use of oral corticosteroids or anticoagulants, longer duration of NSAID
therapy, smoking, use of alcohol, older age, and poor general health status. Most spontaneous reports of fatal GI events are in elderly or debilitated patients and therefore, special care should be taken in treating this population. To minimize the potential risk for an adverse GI event in patients treated with an NSAID, the lowest effective dose should be used for the shortest possible duration. Patients and physicians should remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected. This should include discontinuation of the NSAID until a serious GI adverse event is ruled out. For high risk patients, alternate therapies that do not involve NSAIDs should be considered.

Renal Effects
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 has a compensatory role in the maintenance of renal perfusion. In these patients, administration of a nonsteroidal anti-inflammatory drug 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, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state (see WARNINGS: Advanced Renal Disease).

Advanced Renal Disease
No information is available from controlled clinical studies regarding the use of naproxen in patients with advanced renal disease. Therefore, treatment with naproxen is not recommended in these patients with advanced renal disease. If naproxen therapy must be initiated, close monitoring of the patient's renal function is advisable.

Anaphylactoid Reactions
As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to naproxen. Naproxen should not be given to patients with the aspirin triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs (see CONTRAINDICATIONS and PRECAUTIONS - Preexisting Asthma). Emergency help should be sought in cases where an anaphylactoid reaction occurs.

Skin Reactions
NSAIDs including naproxen, can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Pregnancy
In late pregnancy, as with other NSAIDs, naproxen should be avoided because it may cause premature closure of the ductus arteriosus.

PRECAUTIONS
General
Naproxen 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 10g or less who are to receive long-term therapy should have hemoglobin values determined periodically.

The pharmacological activity of naproxen in reducing [fever and] inflammation may diminish the utility of these diagnostic signs in detecting complications of presumed noninfectious, noninflammatory painful conditions. 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.

Hepatic Effects
Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs including naproxen. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy. Notable elevations of ALT or AST (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes have been reported. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with naproxen. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), naproxen should be discontinued. Chronic alcoholic liver disease and probably other diseases with decreased or abnormal plasma proteins (albumin) reduced the total plasma concentration of naproxen, but the plasma concentrations of unbound naproxen is increased. 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.

Hematological Effects
Anemia is sometimes seen in patients receiving NSAIDs, including naproxen. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including naproxen, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia.
NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible. Patients receiving naproxen who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants, should be carefully monitored.

Preexisting Asthma
Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in such aspirin-sensitive patients, naproxen should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.

ADVERSE REACTIONS

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.

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
- flatulence, gross bleeding/perforation, GI ulcers (gastric/duodenal), vomiting

**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:**
- flatus, 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 less than 1% of patients taking naproxen during clinical trials and through post-marketing reports. Those adverse reactions observed through post-marketing 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:**
- gastrointestinal bleeding and/or perforation, hematemesis, jaundice, pancreatitis, vomiting, colitis, abnormal liver function tests, nonpeptic gastrointestinal ulceration, ulcerative stomatitis

**Hepatobiliary:**
- jaundice, abnormal liver function tests, hepatitis (some cases have been fatal)

**Hemic and Lymphatic:**
- eosinophilia, leucopenia, melena, thrombocytopenia, agranulocytosis, granulocytopenia, hemolytic anemia, aplastic anemia

**Metabolic and Nutritional:**
- hyperglycemia, hypoglycemia

**Nervous System:**
- inability to concentrate, depression, dream abnormalities, insomnia, malaise, myalgia, muscle weakness, aseptic meningitis, cognitive dysfunction, convulsions

**Respiratory:**
- eosinophilic pneumonitis, asthma

**Dermatologic:**
- alopecia, urticaria, skin rashes, toxic epidermal necrolysis, erythema multiforme, erythema nodosum fixed drug eruption, lichen planus pustular reaction, systemic lupus erythematoses, Stevens-Johnson syndrome, photosensitive dermatitis, photosensitivity reactions, including rare cases resembling porphyria cutanea tarda (psuedoporphyria) 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 less than 1% of patients.

**Body as a Whole:**
- fever, infection, sepsis, anaphylactic reactions, appetite changes, death

**Cardiovascular:**
- hypertension, tachycardia, syncope, arrhythmia, hypotension, myocardial infarction

**Gastrointestinal:**
- dry mouth, esophagitis, gastric/peptic ulcers, gastritis, glossitis, hepatitis, eructation, liver failure

**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

OVERDOSAGE
Significant naproxen overdosage may be characterized by lethargy, dizziness, drowsiness, epigastric pain, abdominal discomfort, heartburn, indigestion, nausea, transient alterations in liver function, hypoproteinemia, renal dysfunction, metabolic acidosis, apnea, disorientation or vomiting. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression, and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose. Because naproxen sodium may be rapidly absorbed, high and early blood levels should be anticipated. A few patients have experienced convulsions, but it is not clear whether or not these were drug-related. It is not known what dose of the drug would be life-threatening. The oral LD₅₀ of the drug is 543 mg/kg in rats, 1234 mg/kg in mice, 4110 mg/kg in hamsters, and greater than 1000 mg/kg in dogs. Patients should be managed by symptomatic and supportive care following a NSAID overdose. There are no specific antidotes. Hemodialysis does not decrease the plasma concentration of naproxen because of the high degree of its protein binding. Emesis and/or activated charcoal (60 to 100 g in adults, 1 to 2 g/kg in children) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose. Forced diuresis, alkalinization of urine or hemoperfusion may not be useful due to high protein binding.

DOSAGE AND ADMINISTRATION:
Carefully consider the potential benefits and risks of naproxen and other treatment options before deciding to use naproxen. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see WARNINGS). After observing the response to initial therapy with naproxen, the dose and frequency should be adjusted to suit an individual patient's needs. Naproxen Tablets
250 mg twice daily or 375 mg twice daily or 500 mg twice daily
Although naproxen circulates in the plasma they have pharmacokinetic differences that may affect onset of action. Onset of pain relief can begin within 30 minutes in patients taking naproxen sodium and within 1 hour in patients taking naproxen (see CLINICAL PHARMACOLOGY).

The recommended strategy for initiating therapy is to choose a formulation and a starting dose likely to be effective for the patient and then adjust the dosage based on observation of benefit and/or adverse events. A lower dose should be considered in patients with renal or hepatic impairment or in elderly patients (see WARNINGS and PRECAUTIONS).
Geriatric Patients: 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. In patients who tolerate lower doses well, the dose may be increased to naproxen 1500 mg/day for limited periods of up to 6 months when a higher level of anti-inflammatory/analgesic activity is required. When treating such patients with naproxen 1500 mg/day, the physician should observe sufficient increased clinical benefits to offset the potential increased risk. The morning and evening doses do not have to be equal in size and administration of the drug more frequently than twice the daily doses do not generally make a difference in response (See CLINICAL PHARMACOLOGY).

Acute Gout: The recommended starting dose is 750 mg of naproxen followed by 250 mg every 8 hours until the attack has HOW SUPPLIED
Naproxen Tablets USP, 250 mg are white, round, unscored tablet; embossed "West-ward 346" and are available in:
Bottles of 30 tablets. Bottles of 100 tablets. Bottles of 500 tablets.
Naproxen Tablets USP, 375 mg are white, oblong, unscored tablet; embossed "West-ward 347" and are available in:
Bottles of 30 tablets. Bottles of 100 tablets. Bottles of 500 tablets.
Naproxen Tablets USP, 500 mg are white, oblong, unscored tablet; embossed "West-ward 348" and are available in:
Bottles of 30 tablets. Bottles of 100 tablets. Bottles of 500 tablets.

Manufactured By:
West-ward Pharmaceutical Corp.
Eatontown, NJ 07724
Revised March 2007
Information for Patients
Patients should be informed of the following information before initiating therapy with an NSAID and periodically during the course of ongoing therapy. Patients should also be encouraged to read the NSAID Medication Guide that accompanies each prescription dispensed.
1. Naproxen, like other NSAIDs, may cause serious CV side effects, such as MI or stroke, which may result in hospitalization and even death. Although serious CV events can occur without warning symptoms, patients should be alert for the signs and symptoms of chest pain, shortness of breath, weakness, slurring of speech, and should ask for medical advice when observing any indicative sign or symptoms. Patients should be apprised of the importance of this follow-up (see WARNINGS, Cardiovascular Effects).

2. Naproxen, like other NSAIDs, can cause GI discomfort and, rarely, serious GI side effects, such as ulcers and bleeding, which may result in hospitalization and even death. Although serious GI tract ulcerations and bleeding can occur without warning symptoms, patients should be alert for the signs and symptoms of ulcerations and bleeding, and should ask for medical advice when observing any indicative sign or symptoms including epigastric pain, dyspepsia, melena, and hematemesis. Patients should be apprised of the importance of this follow-up (see WARNINGS, Gastrointestinal Effects: Risk of Ulceration, Bleeding, and Perforation).

3. Naproxen, like other NSAIDs, can cause serious skin side effects such as exfoliative dermatitis, SJS, and TEN, which may result in hospitalizations and even death. Although serious skin reactions may occur without warning, patients should be alert for the signs and symptoms of skin rash and blisters, fever, or other signs of hypersensitivity such as itching, and should ask for medical advice when observing any indicative signs or symptoms. Patients should be advised to stop the drug immediately if they develop any type of rash and contact their physicians as soon as possible.

4. Patients should promptly report signs or symptoms of unexplained weight gain or edema to their physicians.

5. Patients should be informed of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, pruritus, jaundice, right upper quadrant tenderness, and "flu-like" symptoms). If these occur, patients should be instructed to stop therapy and seek immediate medical therapy.

6. Patients should be informed of the signs of an anaphylactoid reaction (e.g. difficulty breathing, swelling of the face or throat). If these occur, patients should be instructed to seek immediate emergency help (see WARNINGS).

7. In late pregnancy, as with other NSAIDs, naproxen should be avoided because it will cause premature closure of the ductus arteriosus.

8. Caution should be exercised by patients whose activities require alertness if they experience drowsiness, dizziness, vertigo or depression during therapy with naproxen.

Medication Guide for Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
(See the end of this Medication Guide for a list of prescription NSAID medicines.)

What is the most important information I should know about medicines called Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)?

NSAID medicines may increase the chance of a heart attack or stroke that can lead to death. This chance increases:
- with longer use of NSAID medicines
- in people who have heart disease

NSAID medicines should never be used right before or after a heart surgery called a "coronary artery bypass graft (CABG)."

NSAID medicines can cause ulcers and bleeding in the stomach and intestines at any time during treatment. Ulcers and bleeding:
- can happen without warning symptoms
- may cause death

The chance of a person getting an ulcer or bleeding increases with:
- taking medicines called "corticosteroids" and "anticoagulants"
- longer use
- smoking
- drinking alcohol
- older age
- having poor health

NSAID medicines should only be used:
• exactly as prescribed

• at the lowest dose possible for your treatment

**What are Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)?**
NSAID medicines are used to treat pain and redness, swelling, and heat (inflammation) from medical conditions such as:
• different types of arthritis

• menstrual cramps and other types of short-term pain

**Who should not take a Non-Steroidal Anti-Inflammatory Drug (NSAID)?**
Do **not take an NSAID medicine:**
• if you had an asthma attack, hives, or other allergic reaction with aspirin or any other NSAID medicine

• for pain right before or after heart bypass surgery

**Tell your healthcare provider:**
• about all of your medical conditions.

• about all of the medicines you take. NSAIDs and some other medicines can interact with each other and cause serious side effects. **Keep a list of your medicines to show to your healthcare provider and pharmacist.**

• if you are pregnant. **NSAID medicines should not be used by pregnant women late in their pregnancy.**

• if you are breastfeeding. **Talk to your doctor.**

**Get emergency help right away if you have any of the following symptoms:**
• shortness of breath or trouble breathing

• slurred speech

• chest pain

• swelling of the face or throat

• weakness in one part or side of your body

These are not all the side effects with NSAID medicines. **Talk to your healthcare provider or pharmacist for more information about NSAID medicines.**

**Other information about Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**
• Aspirin is an NSAID medicine 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 of these NSAID medicines 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.**

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**Cardiovascular Risk**
• NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. (See WARNINGS).

• Naproxen is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

**Gastrointestinal Risk**
• NSAIDs cause an increased risk of serious gastrointestinal 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 are at greater risk for serious gastrointestinal events. (See WARNINGS).**
NAPROXEN 500 MG
# 20 TABLETS
Each tablet contains 500 mg of naproxen

Item # 0001842FL  Rx

Take___ tablets every___ hours or___ times a day.
Take as directed.
Tome___ tabletas cada___ horas o___ veces al dia.
Tome como indicado.

WHITE, OBLONG, UNSCORED TABLET; EMBOSSED "WEST-WARD 348"