DESCRIPTION:
Naproxen sodium is a nonsteroidal anti-inflammatory drug (NSAID) with an affinity for the cyclooxygenase enzyme and a molecular weight of 252.23.

CLINICAL PHARMACOLOGY:
(1) Pharmacodynamics: Naproxen sodium is rapidly and completely absorbed from the gastrointestinal tract with a bioavailability of 90%. After oral administration of naproxen sodium, peak plasma levels are attained in 1 to 2 hours. This fast action is due to the increased aqueous solubility of the sodium salt of naproxen.

(2) Distribution: Naproxen has a volume of distribution of 0.15 L/kg. At therapeutic levels, naproxen is greater than 99% albumin-bound. At doses of naproxen greater than 1000 mg/day, the increase in clearance caused by saturation of plasma protein binding at higher doses.

(3) Metabolism: Naproxen is extensively metabolized in the liver to 6-0-desmethyl naproxen, and both parent and metabolites do not induce metabolizing enzymes. Both naproxen and 6-0-desmethyl naproxen are further metabolized to their respective acetylcysteine conjugates and metabolites.

(4) Excretion: The clearance of naproxen is 0.12 mL/min/kg. Approximately 60% of the naproxen from any dose is excreted in the urine, primarily as naproxen (c. 1%), 6-0-desmethyl naproxen (c. 1%) or their conjugates (68% 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 rate of excretion have been found to coincide closely with the rate of naproxen disappearance from the plasma. Small amounts, 3% or less of the administered dose, are excreted unchanged as the drug. (6) Hepatic Insufficiency: After the administration of single doses of 10, 50, 100, and 150 mg to patients with severe 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 metabolism 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 and severe renal impairment (creatinine clearance < 30 mL/min).

INDICATIONS: For the management of pain and for the relief of the signs and symptoms of temporomandibular, acute tendinitis, bursitis, acute glaucoma and primary dysmenorrhea.

DOSAGE AND ADMINISTRATION: The recommended starting dose is 500 mg of naproxen sodium followed by every 12 hours. The initial total daily dose should not exceed 1500 mg/day in adults. The naproxen sodium may be adjusted up or down depending on the clinical response of the patient. A lower daily dose may suffice for long-term treatment. The morning and evening doses should not be to be equal in size and the administration of the drug more frequently than twice daily is not necessary. 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/cytostatic activity is required.

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

CONTRAINDICATIONS: Naproxen sodium should not be given to patients who have experienced aspirin-arthritis, urticaria, or allergy-like reactions after taking aspirin or other NSAIDs. Severe, rapidly life-threatening anaphylactic reactions to NSAIDs have been reported in such patients. Naproxen Sodium is contraindicated for the treatment of pruritus ani in the setting of coronary artery bypass graft (CABG) surgery.

DRUG INTERACTIONS: ACE-inhibitors, Amiodarone, Azathioprine, Dicoumarol, Lithium, Methotrexate, Warfarin. Selective Serotonin Reuptake Inhibitors, anticoagulants, ranitidine, thiacetarsamide, other NSAIDs, and aspirin. 

PRECAUTIONS: (1) Hepatic Effects: Because naproxen sodium is rapidly excreted in the urine, it may be excreted unchanged in the urine. (2) Absorption: Absorption of naproxen sodium is rapidly and completely absorbed from the gastrointestinal tract with a bioavailability of 90%. (3) Pregnancy: There are no adequate and well-controlled studies in pregnant women. Naproxen sodium should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus. (4) Nursing Mothers: 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. Because of the possible adverse effects of prostaglandin-inhibiting drugs on infants, use in nursing mothers should be avoided. (5) Pediatric Use: Safety and effectiveness in pediatric patients below the age of 2 years have not been established. Pediatric dosing recommendations for juvenile arthritis are based on well-controlled studies.

OVERDOSE: (1) Symptomatic and Signs: Significant overdose may be characterized by lethargy, dizziness, drowsiness, epigastric pain, abdominal discomfort, heartburn, indigestion, nausea, transient alterations in liver function, hypotension, bradycardia, renal dysfunction, metabolic acidosis, agitation, apnea, disorientation or vomiting. Gastrintestinal 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 are achieved. A few patients have experienced convulsions, but it is not clear whether these were drug-related. It is not known what dose of the drug would be life threatening. The oral LD₅₀ in rabbits was 60 to 100 g in adults, 1 to 2 g/kg in children and/or neonates. (6) Renal Insufficiency: For patients with mild to moderate renal insufficiency, the maximum daily dose should not exceed 1000 mg. For patients with severe renal insufficiency, doses should be reduced. Dose should be reduced when necessary in patients with severe renal impairment, particularly in patients with impaired renal function. (7) Renal Insufficiency: For patients with impaired renal function, the dose should be reduced in patients with moderate or severe renal impairment. (8) Gastrointestinal: For patients with a history of peptic ulcer disease, the dose should be reduced. (9) Edema, Central Nervous System: Aspirin, methotrexate, lithium. (10) Anticoagulants, aspirin, warfarin, selective serotonin reuptake inhibitors, anticoagulants, ranitidine, thiacetarsamide, other NSAIDs, and aspirin.