PROXEN®
250mg Tablets
500mg Tablets

(Naproxen)

PRESENTATION:

(i) A yellow, half-scored tablet containing 250mg of Naproxen USP inscribed **'PROXEN 250'** on one side.
(ii) An oblong, scored, yellow tablet containing 500mg of Naproxen USP inscribed **'PROXEN 500'** on one side.

USES:

PROXEN is a non-steroidal, anti-inflammatory agent for the treatment of the following:
Rheumatoid arthritis including juvenile rheumatoid arthritis.
Osteoarthritis (degenerative arthritis).
Ankylosing spondylitis.
Acute gout.
Acute musculoskeletal disorders (such as sprains, strains, direct trauma, lumbosacral pain, cervical spondylitis, tenosynovitis and fibrositis).

DOSAGE AND ADMINISTRATION:

Adults:
Rheumatoid arthritis, osteoarthritis and ankylosing spondylitis:
The usual dosage is 500mg to 1g per day taken in two doses at 12-hour intervals, or alternatively as a single administration of two tablets, morning or evening.
In the following cases a loading dose of 750mg or 1g per day for the acute phase is recommended:
(a) In patients reporting severe night-time pain and/or morning stiffness.
(b) In patients being switched to **PROXEN** from a high dose of another antirheumatic compound.
(c) In osteoarthritis where pain is the predominant symptom.
For the patient who requires 750mg per day the size of the morning and evening doses can be adjusted on the basis of the predominant symptoms - i.e. night-time pain or morning stiffness.

Acute gout:
The recommended dosage is 750mg initially, then 250mg every eight hours until the attack has passed.

Acute musculoskeletal disorders:
The recommended dosage is 500mg initially followed by 250mg at 6-8 hour intervals as needed, with a maximum daily dose after the first day of 1250mg.

Use in the elderly:
Studies indicate that although total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly. The implication of this finding for **PROXEN** dosing is unknown. As with other drugs used in the elderly it is prudent to use the lowest effective dose. For the effect of reduced elimination in the elderly refer to the section - 'Use in patients with impaired renal function'.

Children:
PROXEN is effective in the treatment of juvenile rheumatoid arthritis in children over five years of age, at a dose of 10mg/kg/day taken in two doses at 12-hour intervals. **PROXEN** is not recommended for use in any other indication in children under 16 years of age.

CONTRA-INDICATIONS, WARNINGS, ETC:

Contra-indications:
Active peptic ulceration. Hypersensitivity to naproxen or naproxen sodium formulations. Since the potential exists for cross-sensitivity reactions, **PROXEN** should not be given to patients in whom aspirin or other non- steroidal anti-inflammatory/analgesic drugs induce asthma, rhinitis or urticaria. Severe anaphylactic-like reactions to **PROXEN** have been reported in such patients.

Special precautions and warnings:
PROXEN should be given under close supervision to patients with a history of gastro-intestinal disease. Serious gastro-intestinal adverse reactions can occur at any time in patients on therapy with non-steroidal anti-inflammatory drugs. The risk of their occurrence does not seem to change with duration of therapy. Studies to date have not identified any subset of patients not at risk of developing peptic ulcer and bleeding, however elderly and debilitated patients tolerate gastro-intestinal ulceration or bleeding less well than others. Most of the fatal gastro-intestinal events associated with non-steroidal anti-inflammatory drugs occurred in this patient population.
The antipyretic and anti-inflammatory activities of **PROXEN** may reduce fever and inflammation, thereby diminishing their usefulness as diagnostic signs. Bronchospasm may be precipitated in patients suffering from, or with a history of, bronchial asthma or allergic disease.
Sporadic abnormalities in laboratory tests (e.g. liver function tests) have occurred in patients on **PROXEN** therapy, but no definite trend was seen in any test indicating toxicity. **PROXEN** decreases platelet aggregation and prolongs bleeding time. This effect should be kept in mind when bleeding times are determined. Mild peripheral oedema has been observed in a few patients receiving **PROXEN.** Although sodium retention has not been reproted in metabolic studies, it is possible that patients with questionable or compromised cardiac function may be at a greater risk when taking **PROXEN.**

Use in patients with impaired renal function:
As naproxen is eliminated to a large extent (95%) by urinary excretion via glomerular filtration, it should be used with great caution in patients with impaired renal function and the monitoring of serum creatinine and/ or creatinine clearance is advised in these patients. **PROXEN** is not recommended in patients having baseline creatinine clearance of less than 20ml/minute.
Certain patients, specifically those where renal blood flow is compromised, because of extracellular volume depletion, cirrhosis of the liver, sodium restriction, congestive heart failure and pre-existing renal disease, should have renal function assessed before and during **PROXEN** therapy. Some elderly patients in whom impaired renal function may be expected as well as patients using diuretics, may also fall within this category. A reduction in daily dosage should be considered to avoid the possibility of excessive accumulation of naproxen metabolites in these patients.

Use in patients with impaired liver function:
Chronic alcoholic liver disease and probably also other forms of cirrhosis reduce the total plasma concentration of naproxen but the plasma concentration of unbound naproxen is increased. The implication of this finding for **PROXEN** dosing is unknown, but it is prudent to use the lowest effective dose.

Interactions with other drugs:
Due to the high plasma protein binding of **PROXEN,** patients simultaneously receiving hydantoins, anticoagulants or a highly protein-bound sulphonamide should be observed for signs of overdosage of these drugs. No interactions have been observed in clinical studies with **PROXEN** and anticoagulants or sulphonylureas, but caution is nevertheless advised since interaction has been seen with other non-steroidal agents of this class.
The natriuretic effect of frusemide has been reported to be inhibited by some drugs of this class. Inhibition of renal lithium clearance leading to increases in plasma lithium concentrations has also been reported. **PROXEN** and other non-steroidal anti-inflammatory drugs can reduce the anti hypertensive effect of propranolol and other beta-blockers.
Probenecid given concurrently increases **PROXEN** plasma levels and extends its half-life considerably. As with other non-steroidal anti-inflammatory drugs, **PROXEN** may increase the risk of renal impairment associated with the use of ACE (angiotensin I-converting enzyme) inhibitors.
Caution is advised where methotrexate is administered concurrently because of possible enhancement of its toxicity, since **PROXEN,** among other non-steroidal anti-inflammatory drugs, has been reported to reduce the tubular secretion of methotrexate in an animal model.
In vitro studies have shown that naproxen may interfere with the metabolism of zidovudine, resulting in higher zidovudine plasma levels. Therefore, consideration should be given to reducing zidovudine doses to avoid the potential of increased side-effects associated with increased zidovudine plasma levels.
It is suggested that **PROXEN** therapy be temporarily discontinued 48 hours before adrenal function tests are performed, because **PROXEN** may artifactually interfere with some tests for 17-ketogenic steroids. Similarly, **PROXEN** may interfere with some assays of urinary 5-hydroxyindoleacetic acid.

Side-effects:
Gastro-intestinal: The more frequent reactions are nausea, vomiting, abdominal discomfort and epigastric distress. More serious reactions which may occur occasionally are gastro-intestinal bleeding and/or perforation, non-peptic, gastro-intestinal ulceration, peptic ulceration and colitis.
Dermatological/hypersensitivity: Skin rashes, urticaria, angio-oedema. Anaphylactic reactions to naproxen and naproxen sodium formulations, eosinophilic pneumonitis, alopecia, erythema multiforme, Stevens Johnson syndrome, epidermal necrolysis and photosensitive dermatitis in which the skin resembles porphyria cutanea tarda (pseudoporphyria) or epidermolysis bullosa may occur rarely.
Renal: Glomerular nephritis, interstitial nephritis, nephrotic syndrome, haematuria, renal papillary necrosis, renal failure.
CNS: Headache, insomnia, convulsions, inability to concentrate and cognitive dysfunction have been reported.
Haematological: Thrombocytopenia, granulocytopenia (including agranulocytosis), aplastic anaemia and haemolytic anemia may occur rarely.
Other: Tinnitus, hearing impairment, vertigo, mild peripheral oedema, Jaundice, fatal hepatitis, haematuria, visual disturbances, vasculitis and ulcerative stomatitis have been rarely reported.

Use in pregnancy and in breast-feeding:
Teratology studies in rats and rabbits at dose levels equivalent on a human multiple basis to those which have produced fetal abnormality with certain other non-steroidal anti-inflammatory agents, e.g. aspirin, have not produced evidence of fetal damage with **PROXEN.** As with other drugs of this type **PROXEN** delays parturition in animals (the relevance of this finding to human patients is unknown) and also affects the human fetal cardiovascular system (closure of the ductus arteriosus). Good medical practice indicates minimal drug usage in pregnancy, and use of this class of therapeutic agent requires cautious balancing of possible benefit against potential risk to the mother and fetus especially in the first and third trimesters. **PROXEN** has been found in the milk of lactating mothers. The use of **PROXEN** should be avoided in patients who are breast-feeding.

Overdosage:
Significant overdosage of the drug may be characterised by drowsiness, heartburn, indigestion, nausea or vomiting. A few patients have experienced seizures, but it is not clear whether these were naproxen-related or not. It is not known what dose of the drug would be life-threatening.
Should a patient ingest a large amount of **PROXEN** accidentally or purposefully, the stomach may be emptied and usual supportive measures employed. Animals studies indicate that the prompt administration of activated charcoal in adequate amounts would tend to reduce markedly the absorption of the drug. Haemodialysis does not decrease the plasma concentration of naproxen because of its high degree of protein binding. However, haemodialysis may still be appropriate in a patient with renal failure who has taken naproxen.

PACKS:
PROXEN 250mg tablets are supplied in packs of 30 tablets.
PROXEN 500mg tablets are supplied in packs of 20 tablets.

INSTRUCTIONS:
Keep all medicines out of the reach of children.
Protect from light, heat and moisture.
Store below 30°C.
To be sold on prescription of a registered medical practitioner only.

ہدایات:
تمام ادویات بچوں کی پہنچ سے دور رکھیں۔
روشنی، گرمی اور نمی سے محفوظ رکھیں۔
۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر فروخت کی جائے۔

Further information is available from:
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