SYNFLEX® 550mg Tablets

(Naproxen sodium)

PRESENTATION:

Opaque, blue, film-coated tablet containing Naproxen sodium (USP) 550mg.

USES:

Synflex is an anti-inflammatory analgesic for the treatment of the following:
Musculoskeletal disorders including sprains, strains, direct trauma, cervical spondylitis, fibrositis, bursitis, tendinitis, synovitis, tenosynovitis, lumbago.
Postoperative pain: orthopaedic manipulations, dental extractions and surgery.
Post-partum pain, uterine pain following IUD insertion.
Dysmenorrhoea.
Relief of migraine.

DOSAGE AND ADMINISTRATION:

Adults:
Musculoskeletal disorders, postoperative pain and pain following IUD insertion; 550 mg twice daily, maximum 1100mg per day.
Post-partum pain: a single dose of 550mg is recommended.
Dysmenorrhoea: 550mg initially, then 275mg (half a 550mg tablet) at 6-8 hour intervals as needed. This represents a maximum dose on the first day of 1375mg ($2\frac{1}{2}$ tablets) and 1100mg (2 tablets) per day thereafter.
Migraine: 825mg at the first symptom of an impending attack. Additional 275-550mg can be taken throughout the day, if necessary but not before $\frac{1}{2}$ hour after the initial dose. Maximum daily dose 1375mg ($2\frac{1}{2}$ tablets).

Use in the elderly:
Studies indicate that although the total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly. The implication of this finding for **Synflex** 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:
Synflex is not recommended for use in children under sixteen 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, **Synflex** 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 **Synflex** have been reported in such patients.

Special precautions and warnings:
Synflex 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 **Synflex** 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 (eg. liver function tests) have occurred in patients on **Synflex** therapy, but no definite trend was seen in any test indicating toxicity.
Synflex 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 **Synflex.** Although sodium retention has not been reported in metabolic studies, it is possible that patients with questionable or compromised cardiac function may be at a greater risk when taking **Synflex.** Each **Synflex** tablet contains approximately 50mg (about 2m Eq) sodium. This should be considered in patients whose overall intake of sodium must be markedly restricted.

Use in patients with impaired renal function :
As **Synflex** is eliminated to large extent (95%) by urinary excretion via glomerular filtration, it should be used with great caution in patients with significantly impaired renal function and the monitoring of serum creatinine and/or creatinine clearance is advised in these patients. **Synflex** is not recommended in patients having baseline creatinine clearance of less than 20ml/minute.
Certain patients, specifically those whose renal blood flow is compromised, as in 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 **Synflex** therapy. Some elderly patients in whom impaired renal function may be expected, as well as patients using diuretics, could 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 **Synflex** 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 **Synflex,** patients simultaneously receiving hydantoins,

of these drugs. No interactions have been observed in clinical studies with naproxen sodium or naproxen 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 increase in plasma lithium concentrations has also been reported. **Synflex** and other non-steroidal anti-inflammatory drugs can reduce the antihypertensive effect of propranolol and other beta-blockers.
Probenecid given concurrently increases **Synflex** plasma levels and extends its half-life considerably. Caution is advised when methotrexate is given concurrently because of possible enhancement of its toxicity, since **Synflex,** 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.
As with other non-steroidal anti-inflammatory drugs, **Synflex** may increase the risk of renal impairment associated with the use of ACE (angiotensin I-converting enzyme) inhibitors.
It is suggested that **Synflex** therapy be temporarily discontinued 48 hours before adrenal function tests are performed because **Synflex** may artifactually interfere with some tests for 17-ketogenic steroids. Similarly, **Synflex** 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 rash, urticaria, angio-oedema. Anaphylactic reactions to naproxen and naproxen sodium formulations, eosinophilic pneumonitis, alopecia, erythema multiforme, Stevens Johnson syndrome, epidermal necrolysis and photosensitivity reactions including rare cases 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 anaemia may occur rarely.
Other: Tinnitus, hearing impairment, vertigo, mild peripheral oedema. Anaphylactic reactions to naproxen and naproxen sodium formulations have been reported. Jaundice, fatal hepatitis, visual disturbances, vasculitis, aseptic meningitis, hyperkalemia 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, eg. aspirin, have not produced evidence of fetal damage with **Synflex**. As with other drugs of this type **Synflex** 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. Naproxen has been found in the milk of lactating mothers. The use of **Synflex** 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 **Synflex** accidentally or purposefully, the stomach may be emptied and usual supportive measures employed. Animal 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 **Synflex.**

PACKS:
Synflex 550mg film coated 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 دوائیں بچوں کی پہنچ سے دور رکھیں۔
روشنی، گرمی اور نمی سے محفوظ رکھیں۔
۳۰° 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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