Relev rapid®

Naproxen Sodium 550 mg Tablets

swipha

Composition
Each tablet contains: Naproxen Sodium 550mg

Description
An oblong half scored white tablet, inscribed 'swipha' on one side and 'RLV/550' on the other side.

Clinical pharmacology
Naproxen is a nonsteroidal anti-inflammatory drug (NSAID), with analgesic and antipyretic properties. As with other nonsteroidal anti-inflammatory drugs (NSAIDs), its mode of action is not fully understood; however, its ability to inhibit prostaglandin synthesis may be involved in the anti-inflammatory effect.

Pharmacokinetics

Absorption: Naproxen sodium is rapidly and completely absorbed from the GI tract with an in vivo bioavailability of 95%. After oral administration of **Relev Rapid®**, peak plasma levels are attained in 1 to 2 hours. The difference in rates between Naproxen and Naproxen sodium is due to the increased aqueous solubility of the sodium salt of Naproxen used in **Relev Rapid®**.

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 a less than proportional increase in plasma levels due to an increase in clearance caused by saturation of plasma protein binding at higher doses. However, the concentration of unbound naproxen continues to increase proportionally to dose.
Relev Rapid® Tablets exhibit similar dose proportional characteristics.

Biotransformation: Naproxen is extensively metabolized 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 acylgluconide conjugated metabolites
Elimination: The elimination half-life of **Relev Rapid** Tablets® and conventional naproxen is approximately 15 hours. Steady state conditions are attained after 2-3 doses of **Relev Rapid®** Tablets. Most of the drug is excreted in the urine, primarily as unchanged naproxen (less than 1%), 6-0-desmethyl naproxen (less than 1%) and their glucuronide or other conjugates (66-92%). A small amount of the drug is excreted in the faeces. The rate of excretion has been found to coincide closely with the rate of clearance from the plasma. In patients with renal failure, metabolites may accumulate.

Indications

Relev Rapid® is indicated in the following conditions:

The relief of the signs and symptoms of:
- rheumatoid arthritis
- osteoarthritis
- ankylosing spondylitis
- polyarticular juvenile idiopathic arthritis

The relief of signs and symptoms of:
- tendonitis
- bursitis
- acute gout

The management of:
- pain
- primary dysmenorrhea

Dosage and Administration

Adults: The usual dosage is 550mg to 1100mg daily taken in two administrations at 12 hours intervals, may be increased to 1650mg/day depending on the response and tolerance.
Dental pain, strains, sprains: the recommended dose is 550mg initially, then 275mg every 6-8 hours as needed. The total dose in one day should not exceed 1375mg.

Migraine headache

Prophylaxis: the recommended dose is 550mg twice daily, if no improvement is seen within 4-6 weeks, the drug should be discontinued.

Treatment: 825mg at the first symptom of an impending attack. Additional 275-550mg can be taken throughout the day, if necessary, but not before 30 minutes after the initial dose.

Uterine relaxation and analgesia in postpartum non-nursing mother, in dysmenorrhea and following IUD insertion: 550 mg initially, followed thereafter by 275mg at 6-8 hours intervals.

Reduce menstrual blood loss: 825-1375mg per day taken in two doses on the first day of menstrual bleeding. 550-1100 mg per day thereafter, in two doses, as needed, for no longer than 5 days.

Acute gout: 825mg should be given initially, followed in 8 hours with 550mg and thereafter 275mg at 8 hours interval until the attack has passed.

Rheumatoid Arthritis, Osteoarthritis, And Ankylosing Spondylitis: The recommended starting dose of **Relev Rapid®** Tablets in adults is 550 to 1100 mg daily in two divided doses at 12 hours intervals.

Maintenance treatment: 550 to 1100mg per day, in 2 divided doses at 12 hours intervals. Adjustment of morning and evening doses should be based on predominant symptoms. i.e. nighttime pain or morning stiffness. Alternatively, 550-1100mg given as a single dose in the morning or evening.

Children

Analgesic and antipyretic use: 11mg/kg as an initial dose followed by 2.75-5.5mg/kg at 8 hours interval. The dosage should not exceed 16.5mg/kg/day after the first day.

Elderly
A lower dose should be considered in patients with renal or hepatic impairment or in elderly 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.

Interactions
Due to the high plasma protein binding of **Relev Rapid®**, patients simultaneously receiving hydantoins, should be closely monitored for adjustment of dose if required.
Naproxen may decrease platelet aggregation and prolong bleeding time. This effect should be kept in mind when bleeding times are determined.

Drugs that Interfere with Hemostasis (e.g. warfarin, aspirin, SSRIs/SNRIs): Monitor patients for bleeding who are concomitantly taking **Relev Rapid®** with drugs that interfere with hemostasis. Concomitant use of Relev Rapid® Tablets and analgesic doses of aspirin is not generally recommended. Naproxen may decrease platelet aggregation and prolong bleeding time. This effect should be kept in mind when bleeding times are determined.

ACE inhibitors, Angiotensin Receptor Blockers (ARB), or Beta-Blockers: Concomitant use with **Relev Rapid®** Tablets, may diminish the antihypertensive effect of these drugs. Monitoring of blood pressure is recommended.

ACE Inhibitors and ARBs: Concomitant use with **Relev Rapid®** 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.

Diuretics: NSAIDs can reduce natriuretic effect of furosemide and thiazide diuretics. Monitor patients to assure diuretic efficacy including antihypertensive effects.
Digoxin: Concomitant use with **Relev Rapid®** tablets can increase serum concentration and prolong half-life of digoxin. Monitor serum digoxin levels.

Contraindications
Relev Rapid® is contraindicated in patients with known hypersensitivity to naproxen.

Relev Rapid® 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.
Relev Rapid® is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

Warnings and Precautions

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.

Hypertension:
Relev Rapid ® can lead to onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of cardiovascular events.

Congestive Heart Failure and Edema:
Relev Rapid® should be used with caution in patients with fluid retention or heart failure.

Gastrointestinal Effects
Risk of Ulceration, Bleeding, and Perforation: Nonsteroidal anti-inflammatory drugs (NSAIDs), Including **Relev Rapid®** 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. 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.

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 prostaglandins have 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.

Skin Reactions
NSAIDs, including **Relev Rapid®**, 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.

Exacerbation of Asthma Related to Aspirin Sensitivity
Relev Rapid ® tablets is contraindicated in patients with aspirin-sensitive asthma. Monitor use in patients with preexisting asthma (without aspirin sensitivity).

Hematologic Toxicity
Monitor hemoglobin or hematocrit in patients with any signs or symptoms of anemia.

Anaphylactic Reactions
Discontinue drug, seek emergency care if an anaphylactic reaction occurs

Adverse Reaction

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, peptic ulceration (sometimes with haemorrhage and perforation) and colitis.

Dermatological/hypersensitivity:
Skin rashes, urticaria, angio-oedema. Anaphylactic reactions to naproxen and naproxen sodium formulations, eosinophilic pneumonitis, photosensitive dermatitis in which the skin resembles porphyria cutanea tarda ('pseudoporphyria'), and or epidermolysis bullosa may occur rarely.CNS: Headache, insomnia, inability to concentrate and cognitive dysfunction have been reported.

Haematological: Thrombocytopenia, granulocytopenia, aplastic anaemia and heamolytic anaemia may occur rarely.

Other: Tinnitus, hearing impairment, vertigo, mild peripheral oedema, jaundice, fatal hepatitis, nephropathy, haematuria, visual disturbances, vasculitis and ulcerative stomatitis have been reported rarely.

Use in Specific Populations

Pregnancy: Use of NSAIDs during the third trimester of pregnancy increases the risk of premature closure of the fetal ductus arteriosus. Avoid use of NSAIDs in pregnant women starting at 30 weeks gestation.

Breastfeeding: The Naproxen anion has been found in the milk of lactating women at a concentration equivalent too 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 **Relev Rapid®** Tablets and any potential adverse effects on the breastfed infant from the **Relev xRapid®** Tablets or from underlying maternal condition.

Infertility: NSAIDs are associated with reversible infertility. Consider withdrawal of **Relev Rapid®** Tablets in women who have difficulties conceiving.

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).

Symptoms of overdosage and Management
Significant naproxen overdosage may be characterized by drowsiness, heartburn, indigestion, nausea or vomiting. Because naproxen sodium may be rapidly absorbed, high and early blood levels should be anticipated. A few patients have experienced seizures, but it is unclear if these were drug related or dose specific. The oral LD50 of the drug is 500 mg/kg in rats, 1200 mg/kg in mice, 4000 mg/kg in hamsters and greater than 1000 mg/kg in dogs.

Management
In animals 0.5 g/kg of activated charcoal was effective in reducing plasma levels of naproxen. Patients should be managed by symptomatic and supportive care following an 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.

Storage Condition
Store below 30°C
Protect from light.

Pack sizes: 2 x 10, 10 x 10

NAFDAC REG NO.: 04 - 9829

Medicine: Keep out of reach of children

swipha

Manufactured by:
swiss pharma nigeria Ltd.,
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