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Directions for Use **Please Read Carefully!**

SONAP 275MG & SONAP FORTE 550MG CAPLET

CONTENT
Each oblong tablet / caplet contains:
Sonap: Naproxen sodium 275mg (equiv. to Naproxen 250mg)
Sonap Forte: Naproxen sodium 550mg (equiv. to Naproxen 500mg)

DESCRIPTION
Sonap: Blue, oval, biconvex film coated caplet.
Sonap Forte: Opaque violet-blue, oval, biconvex film coated caplet with bisect on both sides and embossed with "SPS", "S13" on one side.

INDICATIONS
Sonap / Sonap Forte is used to treat signs and symptoms of primary acute gout, dysmenorrhoea, menorrhagia, headache, acute migraine attack, signs and symptoms of mild to moderately severe, acute or chronic musculoskeletal and soft tissue inflammation.
Sonap / Sonap Forte is also used to relieve mild and moderate pain including post-partum pain, pain following IUD insertion, post-operative pain and pain due to orthopedic surgery.

RECOMMENDED DOSAGE
After assessing the risk/benefit ratio in each individual patient, the lowest effective dose for the shortest possible duration should be used.

Naproxen and naproxen sodium have pharmacokinetic differences in terms of onset of action. Onset of pain relief can be obtained within 30 minutes in patients taking naproxen sodium and within 1 hour in patients taking naproxen. As the sodium salt of naproxen is more rapidly absorbed, ***Sonap/Sonap Forte*** is recommended for management of acute painful conditions when prompt onset of pain relief is desired. ***Sonap/Sonap Forte*** may be given orally either in fasting state (with antacids) or with meals.

Adult:
For post-operative pain (analgesia), pain due to IUD insertion, pain due to orthopedic surgery, dysmenorrhoea, acute musculoskeletal conditions, acute pain accompanied by inflammation:
The starting dose is 550mg of naproxen sodium, followed by 275mg of naproxen sodium every 6 to 8 hours as required.
A total daily dose of 1375mg per day should not be exceeded.

For acute gout: 825mg are given initially, followed by 275mg every 8 hours as required.

For menorrhagia: 825 to 1375 mg per day taken in 2 doses on the first day of menstrual bleeding. Thereafter, the total daily dose should not exceed 1100mg.

For acute migraine attack: 825mg to be given at the first symptom of an impending attack and, if necessary, followed by doses of 275 to 550 mg throughout the day, after at least half an hour after the initial dose.

For prophylaxis of migraine: 550mg are given twice daily. If no improvement is seen in 4 – 6 weeks, the treatment should be discontinued. A total daily dose of 1375 mg should not be exceeded.

Children
Sonap / Sonap Forte is not recommended for use in children under 16 years of age.

Renal/Hepatic Impairment & Elderly
A lower dose should be considered in patients with renal or hepatic impairment and also elderly patients. ***Sonap/Sonap Forte*** is not recommended in patients with baseline creatinine clearance less than 30 ml/min because accumulation of naproxen metabolites has been seen in patients with severe renal failure or those on dialysis.

CONTRAINDICATIONS
Sonap / Sonap Forte is contraindicated in children under 2 years of age since safety in this age group has not been established.
Also contraindicated in patients who:
- Are hypersensitive to naproxen sodium and any of its excipients. Severe anaphylactic-like reactions to naproxen have been reported in such patients.
- Have had allergic reactions to aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) inducing symptoms of asthma, rhinitis and nasal polyps.
- Have active or a history of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.
- Have known or suspected peptic ulceration or intestinal inflammatory disease.
- Have severe heart failure, hepatic failure and renal failure.
- At the third trimester of pregnancy.

WARNINGS AND PRECAUTIONS

Risk of GI Ulceration, Bleeding and Perforation with NSAID

Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAID therapy. Although minor upper GI problems (e.g. dyspepsia) are common, usually developing early in therapy, prescribers should remain alert for ulceration and bleeding in patients treated with NSAIDs even in the absence of previous GI tract symptoms.

Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Patients with prior history of serious GI events and other risk factors associated with peptic ulcer disease (e.g. alcoholism, smoking, and corticosteroid therapy) are at increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less than other individuals and account for most spontaneous reports for fatal GI events.

Cardiovascular and cerebrovascular events
Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and edema have been reported in association with NSAID therapy. The use of COXIBs and some NSAIDs may also be associated with small increased risk of arterial thrombotic events (myocardial infarction or stroke).

Patients with uncontrolled hypertension, congestive heart failure, established ischemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with naproxen after careful consideration and the lowest effective dose should be used for the shortest possible duration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidemia, diabetes mellitus, smoking).

Gastrointestinal ulceration, bleeding and perforation
GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events. The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer (particularly if complicated with haemorrhage or perforation), in elderly, alcoholism and smoking patients.

These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk.

Patients with a history of GI toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment. Caution should be advised in patients receiving concomitant medications which could increase risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin. When GI bleeding or ulceration occurs in patients receiving naproxen, the treatment should be withdrawn.

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated.

Use in elderly
Elderly and debilitated patients are more prone to gastrointestinal ulceration than others. Most of the fatal gastrointestinal events associated with NSAIDs have occurred in this patient population. Hence, the lowest effective dosage is recommended.

Elderly patients in whom impaired renal function may be expected should have renal function assessed before and during naproxen therapy. A reduction in daily dosage should be considered to avoid the possibility of excessive drug accumulation in this group of patients.

Skin reactions
NSAIDs may very rarely cause serious cutaneous adverse events such as exfoliative dermatitis, toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS), which can be fatal and occur without warning. Patients appear to be at highest risk early in the course of therapy, onset of reaction for majority of cases starts within the first month of treatment. ***Sonap/Sonap Forte*** should be discontinued at the first appearance of skin rash, mucosal lesions, or any sign of hypersensitivity.

Impaired renal function
As with other NSAIDs, ***Sonap/Sonap Forte*** should be used with caution in patients with impaired renal function or a history of kidney disease as naproxen is an inhibitor of prostaglandin synthesis. Caution should be observed in patients with conditions leading to a reduction in blood volume and/or renal blood flow as renal prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients, it may lead to a dose-dependent reduction in renal prostaglandin formation and may precipitate overt renal decompensation or failure. Therefore, patients at greater risk should have their serum creatinine and/or creatinine clearance monitored and should be adequately hydrated. A reduction in daily dosage should be considered to avoid the possibility of excessive accumulation of naproxen metabolites.

Sonap/Sonap Forte is not recommended in patients with baseline creatinine clearance less than 30ml/min to prevent accumulation of naproxen metabolites in these patients.

Haemodialysis does not decrease plasma concentration of naproxen because of the high degree of its protein binding.

Impaired liver function
In patients with impaired hepatic function, the lowest dose is recommended. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver function test has occurred, should be evaluated for evidence of the development of more severe hepatic reactions while on therapy with this drug. If abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if system manifestations occur, this drug should be discontinued. Hepatic abnormalities may be the result of hypersensitivity rather than direct toxicity.

Haematological effects
Naproxen may decrease platelet aggregation and prolong bleeding time. This effect should be kept in mind when bleeding times are determined. Thrombocytopenia, granulocytopenia, haemolytic anaemia, and aplastic anaemia have been reported rarely and particular care is required when prescribing naproxen for patients with history of blood dyscrasias.

Respiratory disorders
Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients.

Precautions related to fertility
The use of drug known to inhibit cyclooxygenase /prostaglandin synthesis may impair fertility and is not recommended in women attempting to conceive. In women who have difficulty conceiving or are undergoing investigation of infertility, withdrawal of ***Sonap/ Sonap Forte*** should be considered.

Combination with other NSAIDs
The combination of ***Sonap/Sonap Forte*** and other NSAIDs is not recommended, because of the cumulative risks of inducing serious NSAID-related adverse events.

Effects on Ability to Drive and Use Machine
Some patients may experience drowsiness, dizziness, vertigo, insomnia or depression with the use of ***Sonap/Sonap Forte***. If patients experience any of these or similar symptoms, they should exercise caution in carrying out activities that require alertness.

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DRUG INTERACTIONS

Drugs	Interactions
Albumin-bound drugs	Naproxen is highly bound to plasma albumin; thus have potential to interact with other albumin-bound drugs such as coumarin-type anticoagulants, sulphonylureas, hydantoins, other NSAIDs and aspirin. Simultaneous treatment should be observed for toxicity and adjustment of dose if required.
Coumarin-type anticoagulants	NSAIDs may enhance effects of anticoagulants, such as warfarin, by decreasing platelet aggregation and prolongs bleeding time.
Probenecid	Simultaneous administration will cause increase in naproxen plasma concentration and an increased half-life of naproxen.
Methotrexate	Naproxen and other prostaglandin synthesis-inhibiting drugs have been reported to reduce the clearance of methotrexate, and thus enhance its toxicity. Concomitant administration should be done in caution.
Antihypertensive drugs	Naproxen reduces the anti-hypertensive effects of beta-blockers, angiotensin converting enzyme inhibitors (ACE inhibitors) and angiotensin receptor blockers (ARBs). Concomitant use of NSAIDs with ACE inhibitors and ARBs may increase the risk of renal dysfunction, especially in patients with pre-existing poor renal function.
Diuretic	Concomitant administration inhibits natriuretic effect of furosemide.
Lithium	Inhibition of renal lithium clearance leading to increase in plasma lithium concentrations has been reported.
Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs)	Combination with NSAIDs leads to an increased risk of gastrointestinal bleeding.
Clinical Laboratory Tests	Naproxen should be temporarily discontinued 48 hours before adrenal function tests are performed, because naproxen may artefactually interfere with some tests for 17-ketogenic steroids. Similarly Naproxen may interfere with some urinary assays of 5-hydroxy indoleacetic acid (5HIAA).

PREGNANCY AND LACTATION

Pregnancy

Naproxen readily crosses the placenta barrier and may affect the human foetal cardiovascular system (closure of the ductus arteriosus). Hence, it should not be administered during known or suspected pregnancy unless considered essential by physician.

Labour and delivery

Sonap/Sonap Forte is not recommended in labour and delivery because, through their prostaglandin synthesis inhibitory effect, they may adversely affect foetal circulation and inhibit uterine contractions, thus increasing the risk of uterine haemorrhage.

Nursing mothers

The use of ***Sonap/Sonap Forte*** in nursing mothers should be avoided, as the drug is excreted in breast milk.

SIDE EFFECTS

Blood and lymphatic system disorders
Rare: Haemolytic anaemia
Very rare: Granulocytopenia, thrombocytopenia, agranulocytosis
Not known: Aplastic anaemia, neutropenia

Immune system disorders
Rare: Allergic and hypersensitivity reactions, anaphylaxis

Metabolism and nutritional disorders
Rare: Hyperkalaemia

Psychiatric disorders
Uncommon: Depression, cognitive dysfunction, insomnia, loss of concentration, abnormal dreams
Not known: Hallucinations

Nervous system disorders
Common: Confusion, dizziness, drowsiness, headache
Very rare: Convulsions, aseptic meningitis
Not known: Vertigo, paraesthesia, malaise, exacerbation of Parkinson's disease

Eye disorders
Common: Visual disturbances
Not known: Optic neuritis, papilloedema

Ear and labyrinth disorders
Common: Tinnitus
Rare: Hearing impairment

Cardiac disorders
Uncommon: Palpitations
Not known: Cardiac failure

Vascular disorders
Rare: Vasculitis
Very rare: Arterial thrombotic events (e.g. myocardial infarction or stroke)
Not known: Hypertension

Respiratory thoracic and mediastinal disorders
Rare: Aggravated asthma, eosinophilic pneumontitis.
Not known: Bronchospasm, dyspnea, rhinitis, pulmonary oedema

Gastrointestinal disorders
Very rare: Pancreatitis
Not known: Thirst, peptic ulcers, perforation or GI bleeding, nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomasis, exacerbation of colitis and Crohn's disease, gastritis.

Hepatobiliary
Rare: Hepatitis (sometimes fatal), jaundice
Not known: Abnormal liver function

Skin and subcutaneous tissue disorders
Common: Rash, pruritis, purpura
Uncommon: Urticaria, photosensitivity
Rare: Alopecia, pseudoporphyria
Very rare: Erythema, multiforme, Steven Johnson's syndrome, toxic epidermal necrosis, epidermolysis bullosa.
Not known: Angio-edema, epidermal necrosis, exfoliative and bullous dermatoses, linchen planus.

Musculoskeletal and connective tissue disorders
Rare: Myalgia, muscle weakness

Renal and urinary disorders
Very rare: Glomerular nephritis, haematuria, interstitial nephritis, nephritic syndrome, renal papillary necrosis.
Not known: Renal failure, nephropathy, increased in serum creatinine.

Reproductive system and breast disorders
Not known: Impaired female fertility

General disorders and administration site complications
Common: Fatigue
Not known: Mild peripheral oedema, pyrexia

SYMPTOMS & TREATMENT OF OVERDOSE

Symptoms: Possible symptoms of overdose include dizziness, epigastric pain, indigestion, transient alterations in liver function, hypoprothrombinemia, renal dysfunction, metabolic acidosis, apnoea, nausea, disorientation, vomiting, heartburn, abdominal discomfort and drowsiness. Because ***Sonap/Sonap Forte*** may be rapidly absorbed, high and early blood levels should be anticipated. A few patients have experienced seizures, but it is not known whether these were naproxen-related or not. Gastrointestinal bleeding may occur. Hypertension, acute renal failure, respiratory depression and coma may occur after the ingestion of NSAIDs but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following as overdose.

Treatment: Patients should be managed by symptomatic and supportive care following NSAIDs overdose. There are no specific antidotes. Prevention of further absorption (e.g. activated charcoal) may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose. Forced diuresis, alkalinization of urine, haemodialysis, or hemoperfusion may not be useful due to high protein binding.

PHARMACODYNAMIC PROPERTIES

Sonap/Sonap Forte is a non-steroidal anti-inflammatory drug (NSAID) with analgesic, anti-inflammatory and antipyretic properties. It contains the active ingredient, naproxen sodium, which is more rapidly absorbed and have faster onset of pain relief than naproxen. Naproxen sodium acts by inhibiting the synthesis of prostaglandins as with other similar agents, however, the exact mechanism of its anti-inflammatory action is not known.

PHARMACOKINETIC PROPERTIES

Absorption: Naproxen and naproxen sodium are rapidly and completely absorbed from the gastrointestinal tract after oral administration. Naproxen sodium is more rapidly absorbed than naproxen. Peak plasma levels for naproxen is attained in 2 to 4 hours, whereas naproxen sodium is able to show significant plasma levels and pain relief within 30 minutes of oral administration with peak plasma levels attained in 1 to 2 hours (depending on food intake). The difference in rates between the two products is due to the increased aqueous solubility of the sodium salt of naproxen.

Distribution: Naproxen has a volume of distribution of 0.16 l/kg. At therapeutic levels naproxen is more than 99% bound to albumin (plasma protein). Plasma concentrations of naproxen increase proportionally with dose up to about 500mg daily. At higher doses, there is an increase in clearance caused by saturation of plasma proteins.

Metabolism: Naproxen is extensively metabolised in the liver to 6-0-desmethyl naproxen. The drug and metabolites do not induce metabolising enzymes.

Elimination: Naproxen has a plasma elimination half-life of about 13 hours. Steady state conditions are attained after 2 – 3 doses of naproxen sodium. Approximately 95% of naproxen sodium dose is excreted in the urine as unchanged naproxen, 6-0-desmethyl naproxen and their glucuronide or other conjugates. Small amounts, 3% or less, are excreted in the faeces. The rate of excretion of metabolites and conjugates has been found to coincide closely with the rate of clearance from the plasma. In patients with renal failure, metabolites may accumulate.

LIST OF EXCIPIENTS

Lactose, dicalcium phosphate anhydrous, sodium starch glycolate, pregelatinized starch, croscarmellose sodium, crospovidone, povidone K-30, sodium lauryl sulfate, talcum, magnesium stearate, coating solutions.

PACKING / PACK SIZES

Sonap: Amber Alu - PVC blister strip of 10 caplets per strip. Box of [10 x 10's] & [50 x 10's].
Sonap Forte: Amber Alu - PVC blister strip of 10 caplets per strip. Box of [5 x 10's], [10 x 10's] & [50 x 10's].

STORAGE CONDITIONS & PHARMACEUTICAL PRECAUTIONS

Do not store above 30°C.
Protect from moisture and light.
Keep out of reach of children.
Jauhi daripada kanak-kanak.

SHELF-LIFE: Please refer to the outer box label

MANUFACTURED BY:

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