1. Sonaflam (275mg Film-Coated Tablet)

Sonaflam, 275 mg, film-coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Film-coated tablets containing naproxen sodium 275 mg (equivalent to 250mg naproxen).

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Oval, blue, film-coated, biconvex tablets, plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Pharmacy Only Medicine

Temporary relief of pain and/or inflammation associated with:

- Muscular aches and pains
- Sprains and strains
- Backache
- Osteoarthritis
- Rheumatic pain
- Arthritis
- Headache
- Period pain
- Dental pain
- Reduces fever.

Pharmacist Only (Restricted) Medicine

For temporary relief from:

- Gout
- Migraine and headaches
- Period pain
- Back and neck pain
- Muscle pain and inflammation
- Post-operative pain (eg. dental or minor surgery)
- Sinus pain
- Reduces fever.

Prescription Medicine

Sonaflam is indicated for the treatment of:

- Acute musculoskeletal disorders (such as sprains and strains, direct trauma, lumbo-sacral pain, cervical spondylitis, fibrositis, bursitis and tendonitis)
- Dysmenorrhoea, uterine pain following I.U.D. insertion;
- Dental pain
- Migraine headaches, prophylaxis and acute treatment
- Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and acute gout
- Juvenile arthritis

4.2 Dose and method of administration

General

After assessing the risk/benefit ratio in each individual patient, the lowest effective dose for the shortest possible duration should be used (see Warnings and Precautions).

Although naproxen and naproxen-sodium-containing products all circulate in the plasma as naproxen, they have pharmacokinetic differences that may affect onset of action. Onset of pain relief can begin within 30 minutes in patients taking naproxen sodium and within 1 hour in patients taking naproxen.

The recommended strategy for initiating therapy is to choose a formulation and a starting dose likely to be effective for the patient and then adjust the dosage based on observation of benefit and/or adverse events.

A lower dose should be considered in patients with renal or hepatic impairment or in elderly patients. Sonaflam is not recommended in patients with baseline creatinine clearance less than 30 mL/minute because accumulation of naproxen metabolites has been seen in patients with severe renal failure or those on dialysis.

During long-term administration the dose of naproxen may be adjusted up or down depending on the clinical response of the patient. A lower daily dose may suffice for long-term administration. In patients who tolerate lower doses well, the dose may be increased to 1000mg per day when a higher level of anti-inflammatory/analgesic activity is required. When treating patients with naproxen 1000 mg/day, the physician should observe sufficient increased clinical benefit to offset the potential increased risk (see section 4.4).

The morning and evening doses do not have to be equal in size and administration of the medicine more frequently than twice daily does not generally make a difference in response.

Because the sodium salt of naproxen is more rapidly absorbed, naproxen sodium is recommended for the management of acute painful conditions when prompt onset of pain relief is desired.

Sonaflam may be given orally either in fasting state or with meals and/or antacids.

Caution is required with dosage in the elderly and also in patients with renal impairment.

Adults

Acute musculoskeletal disorders

The recommended dosage is 550mg at once (two tablets), then 275 mg three or four times daily as needed; most patients will require only seven days treatment but some patients may require up to fourteen days treatment.

Dysmenorrhoea

The recommended dosage is 550 mg (two tablets) initially followed by 275 mg three or four times daily as needed.

Post-operative pain

The recommended regimen is 550 mg (two tablets) initially, followed by 275 mg three to four times daily as needed, with a maximum daily dose after the first day of 1375 mg (five tablets).

Acute treatment of migraine

The recommended dosage is 825 mg (three tablets) at the first symptom of an impending attack. An additional 275-550 mg (one to two tablets) can be taken throughout the day, if necessary, but not within 30 minutes of administration of the initial dose. The total dose of 1375 mg (five tablets) per day should not be exceeded.

Prophylaxis of common or classical migraine

The recommended starting dose is 275 mg twice daily. Adjustment of dosage (within the range of 275 mg – 550 mg twice daily), to establish the optimum dose, should be attempted within the first 2 weeks of therapy. If evidence of efficacy is not demonstrated after 3 weeks therapy, treatment should be discontinued.

Rheumatoid arthritis, osteoarthritis and ankylosing spondylitis

Maintenance dose is usually 550 mg per day (two tablets) taken in two doses at 12-hour intervals i.e. 275 mg usually given with the morning meal and 275 mg about 12 hours later. Dosage adjustment within the range 550-1100 mg/day (two to four tablets) maintaining 12-hourly administration may be employed.

For the patient who requires 825 mg per day (three tablets) and whose night-time pain and/or morning stiffness are most troublesome, 550 mg (two tablets) should be taken before retiring and 275 mg upon awakening. For the patient whose day-time pain and reduced mobility are most troublesome, 550 mg (two tablets) should be taken upon awakening and 275 mg upon retiring.

Gout

The recommended dosage is 825 mg (three tablets) at once, then 275 mg every eight hours, as needed, until the attack has passed.

Special Dosage Instructions

Dose in Children

Safety and effectiveness in children below the age of 2 years have not been established.

Juvenile arthritis

Naproxen sodium has been reported to be effective in the treatment of juvenile arthritis in children over five years of age at a dosage of 10 mg/kg/day. As safety and efficacy studies in children are not yet complete, naproxen sodium is not recommended for use in other indications in children under sixteen years of age.

4.3 Contraindications

Sonaflam is contraindicated in patients:

- who are hypersensitive to naproxen or naproxen sodium or in whom acetylsalicylic acid (aspirin) or other non-steroidal anti-inflammatory/analgesic agents induce allergic manifestations, e.g. asthma, nasal polyps, rhinitis and urticaria. Severe anaphylactic-like reactions to naproxen have been reported in such patients.
- with either active, or a history of peptic or gastrointestinal ulceration, chronic dyspepsia or active gastrointestinal bleeding or perforation, related to previous NSAID therapy.
- with active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding) unrelated to previous NSAIDs therapy.
- under 2 years of age since safety in this age group has not been established.
- with severe heart failure.
- undergoing treatment of perioperative pain in setting of coronary artery surgery (CABG).
- with severe hepatic impairment.
- during the 3rd trimester of pregnancy.

4.4 Special warnings and precautions for use

Cardiovascular thrombotic events

Observational studies have indicated that non-selective NSAIDs may be associated with an increased risk of serious cardiovascular events, including myocardial infarction and stroke, which may increase with dose or duration of use. Patients with cardiovascular disease, history of atherosclerotic cardiovascular disease or cardiovascular risk factors may also be at greater risk. To minimise the potential risk of an adverse cardiovascular event in patients taking an NSAID, especially in those with cardiovascular risk factors, the lowest effective dose should be used for the shortest possible duration (see section 4.2).

Physicians and patients should remain alert for such CV events even in the absence of previous CV symptoms. Patients should be informed about signs and/or symptoms of serious CV toxicity and the steps to take if they occur.

There is no consistent evidence that the concurrent use of aspirin mitigates the possible increased risk of serious cardiovascular thrombotic events associated with NSAID use. Clinical trial and epidemiological data suggest that the use of coxibs and some NSAIDs (particularly at high doses and with either short or long-term treatment) may be associated with a small increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke).

Hypertension

NSAIDS may lead to the onset of new hypertension or worsening of pre-existing hypertension, and patients taking anti-hypertensives with NSAIDs may have an impaired anti-hypertensive response. Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals thereafter.

Heart failure

Fluid retention and oedema have been observed in some patients taking NSAIDs; therefore, caution is advised in patients with fluid retention or heart failure.

Gastrointestinal events

All NSAIDs can cause gastrointestinal discomfort and rarely serious, potentially fatal, gastrointestinal effects such as ulcers, irritation, bleeding and perforation, which may increase with dose or duration of use, but can occur at any time without warning symptoms. Upper gastrointestinal ulcers, gross bleeding or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3 – 6 months and in about 2 - 4% patients treated for one year. These trends continue with longer duration

of use, increasing the likelihood of developing a serious gastrointestinal event at some time during the course of therapy. However, even short-term therapy is not without risk.

Caution is advised in patients with risk factors for gastrointestinal events who may be at greater risk of developing serious gastrointestinal events, e.g. elderly, debilitated patients, those with a history of serious gastrointestinal events, smoking and alcoholism.

NSAIDs should be given with care to patients with a history of inflammatory bowel disease (ulcerative colitis; Crohn's disease) as their condition may be exacerbated. Patients with a history of gastrointestinal toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding) particularly in the initial stages of treatment. When gastrointestinal bleeding or ulceration occurs in patients receiving NSAIDs, treatment should be withdrawn immediately. Physicians should warn patients about the signs and symptoms of serious gastrointestinal toxicity.

Studies to date have not identified any subset of patients not at risk of developing peptic ulcer and bleeding. However, the elderly have an increased frequency of adverse effects to NSAIDs, especially gastrointestinal bleeding and perforation which may be fatal. Debilitated patients do not seem to tolerate ulceration or bleeding as well as others. Most of the fatal gastrointestinal events associated with NSAIDs occurred with the elderly and/or debilitated patients.

In patients with active peptic ulcer or inflammatory disease of the gastrointestinal tract and active rheumatoid arthritis, an attempt might be made to treat the arthritis with a non-ulcerogenic drug.

Caution is advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding (see section 4.5). The concurrent use of aspirin and NSAIDs also increase the risk of serious gastrointestinal adverse events.

Patients with risk factors should commence treatment on the lowest dose available.

Use in renal impairment

There have been reported cases of impaired renal function, renal failure, acute interstitial nephritis, haematuria, proteinuria, renal papillary necrosis and occasionally nephritic syndrome associated with naproxen.

Naproxen should not be given to patients with creatinine clearance less than 30 mL/minute because accumulation of naproxen metabolites has been seen in such patients.

As with other NSAIDs, naproxen should be used with caution in patients with impaired renal function or a history of kidney disease because 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 prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients, administration of naproxen or other NSAIDs may cause a dose-dependent reduction in renal prostaglandin formation and may precipitate overt renal decompensation or failure. Patients at greatest risk are those with impaired renal function, hypovolaemia, heart failure, liver dysfunction, salt depletion, those taking diuretics, angiotensin converting enzyme inhibitors or angiotensin receptor blockers and the elderly. Discontinuation of naproxen is usually followed by recovery to the pre-treatment state; however serious adverse events may persist. Naproxen should be used with great caution in such patients and the monitoring of serum creatinine and/or creatinine clearance is advised and patients should be adequately hydrated. A reduction in daily dosage should be considered to avoid the possibility of excessive accumulation of naproxen metabolites in these patients.

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

Haematological

Naproxen decreases platelet aggregation and prolongs bleeding time. This effect should be kept in mind when bleeding times are determined (see section 4.4).

Patients who have coagulation disorders or are receiving drug therapy that interferes with haemostasis should be carefully observed if naproxen is administered. Patients at high risk of bleeding and those on anticoagulation therapy (e.g. heparin or dicoumarol derivatives) may be at increased risk of bleeding if given naproxen concurrently. Therefore, the benefits of prescribing naproxen should be weighed against these risks.

Patients with initial haemoglobin values of 10 grams or less, and who are to receive long-term therapy should have haemoglobin values determined frequently.

Patients on other drugs such as hydantoins, sulfonamides, sulfonylureas or methotrexate should be observed for increased effect or toxicity (see section 4.5).

Severe skin reactions

NSAIDs may very rarely cause serious cutaneous adverse events such as exfoliative dermatitis, toxic epidermal necrolysis (TEN), Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS) and Stevens-Johnson syndrome (SJS), which can be fatal and occur without warning. These serious adverse events are idiosyncratic and are independent of dose or duration of use. Patients should be advised of the signs and symptoms of serious skin reactions and to consult their doctor at the first appearance of a skin rash or any other sign of hypersensitivity.

DRESS has been reported in patients taking NSAIDs. Some of these events have been fatal or life- threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection.

Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue NSAID and evaluate the patient immediately.

Anaphylactic reactions

Hypersensitivity reactions may occur in susceptible individuals. Anaphylactic (anaphylactoid) reactions may occur both in patients with, and without, a history of hypersensitivity or exposure to aspirin, other NSAIDs or naproxen containing product. They may also occur in individuals with a history of angioedema, bronchospastic reactivity (e.g. asthma), rhinitis and nasal polyps. Anaphylactoid reactions, like anaphylaxis, may have a fatal outcome.

Bronchospasm may be precipitated in patients suffering from, or with a history of, asthma or allergic disease or aspirin sensitivity.

Use in hepatic impairment

As with other NSAIDs, elevations of one or more liver function tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially

unchanged, or may resolve with continued therapy. The ALT test is probably the most sensitive indicator of liver dysfunction.

Meaningful elevations (three times the upper limit of normal) of ALT or AST occurred in controlled clinical trials in less than 1% of patients. Physicians and patients should remain alert for hepatotoxicity. Patients should be informed about the signs and/or symptoms of hepatotoxicity. A patient with symptoms and/or signs suggesting hepatic dysfunction (e.g. nausea, fatigue, lethargy, pruritis, jaundice, abdominal tenderness in the right upper quadrant and 'flu-like' symptoms), or in whom an abnormal hepatic test has occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with naproxen.

Hepatic abnormalities may be the result of hypersensitivity or direct toxicity.

Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with naproxen as with other NSAIDs. Cross reactivity has been reported. Although such reactions are rare, if abnormal hepatic tests persist or worsen, if clinical signs and symptoms consistent with hepatic disease develop, or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), naproxen should be discontinued.

Chronic alcoholic hepatic disease and potentially other forms of cirrhosis reduce the total plasma concentration of naproxen; however the plasma concentration of unbound naproxen is increased. The implication of this finding for naproxen dosing is unknown.

In patients with impaired hepatic function, the lowest effective dose is recommended.

Infection

The antipyretic, anti-inflammatory and analgesic effects of naproxen may mask the usual signs or symptoms of infection.

Ocular effects

Adverse ophthalmological effects have been observed with NSAIDs. In rare cases, adverse ocular disorders including papillitis, retrobulbar optic neuritis and papilloedema, have been reported in users of NSAIDs including naproxen, although a cause-and-effect relationship cannot be established; accordingly, patients who develop visual disturbances during treatment with naproxen should have an ophthalmological examination.

Fluid retention and oedema

Peripheral oedema has been observed in some patients taking naproxen or other NSAIDs. Although sodium retention has not been reported in metabolic studies, it is possible that patients with compromised cardiac function may be at greater risk when taking naproxen. For this reason, naproxen should be used with caution in patients with fluid retention, hypertension or heart failure.

Paediatric use

Naproxen is not recommended in children under 5 years of age as the safety and efficacy in this population has not been established.

Use in the elderly

The lowest effective dose is recommended in elderly patients.

Studies indicate that although the total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly.

Effects on laboratory tests

Naproxen decreases platelet aggregation and prolongs bleeding time. This effect should be considered when bleeding times are determined.

Naproxen may result in artefactual interference with some tests for 17-ketogenic steroid and may interfere with some urinary assays for 5-hydroxy-indoleacetic acid (5HIAA). 17-hydroxycorticosteroid measurements (Porter/Silber test) do not appear to be altered.

Naproxen therapy should be temporarily discontinued for at least 72 hours before testing adrenal function.

4.5 Interaction with other medicines and other forms of interaction

Concomitant administration of sucralfate or cholestyramine can delay the absorption of naproxen, but does not affect its extent. Antacids have a variable effect on absorption.

Other NSAIDs

Combination of naproxen and other NSAIDs, including cyclooxygenase-2 (COX-2) selective inhibitors, is not recommended, because of the cumulative risks of inducing serious NSAID-related adverse events.

Protein binding

Naproxen is highly bound to plasma albumin; thus naproxen has a theoretical potential for interaction with other albumin-bound medicines, for example, warfarin or bishydroxycoumarin may be displaced and induce excessively prolonged prothrombin times. Similarly, patients receiving hydantoins, sulfonamides or sulfonylureas should be observed for increased effect or toxicity (see section 4.4).

Warfarin

The concurrent use of NSAIDs and warfarin has been associated with severe, sometimes fatal, haemorrhage. The exact mechanism of the interaction between NSAIDs and warfarin is unknown, but may involve enhanced bleeding from NSAID-induced gastrointestinal ulceration, or an additive effect of anticoagulation by warfarin and inhibition of platelet function by NSAIDs. Naproxen should be used in combination with warfarin only if absolutely necessary, and patients taking this combination of drugs should be closely monitored.

Anticoagulants/ antiplatelets

Patients who have coagulation disorders or are receiving drug therapy that interferes with haemostasis should be carefully observed if naproxen is administered. Patients on full anticoagulation therapy (e.g., heparin or dicoumarol derivatives) may be at increased risk of bleeding if given naproxen concurrently. Thus, the benefits should be weighed against these risks.

There is an increased risk of gastrointestinal bleeding when anti-platelet agents are combined with NSAIDs.

Selective serotonin reuptake inhibitors (SSRIs)

There is an increased risk of gastrointestinal bleeding when SSRIs are combined with NSAIDs.

Steroids

If steroid dosage is reduced or eliminated during naproxen therapy, the steroid dosage should be reduced slowly and the patients must be observed closely for any evidence of adverse effects, including adrenal insufficiency and exacerbation of symptoms of underlying disease.

Probenecid

Probenecid significantly prolongs the half-life of naproxen (from 14 to 37 hrs). This is associated with a decrease in conjugated metabolites and an increase in 6-0 desmethyl naproxen.

Methotrexate

Concomitant administration of naproxen and methotrexate should be administered with caution, because naproxen has been reported among other NSAIDs to reduce the tubular secretion of methotrexate in animal models, and have been reported to reduce the clearance of methotrexate; and thus possibly increasing the toxicity of methotrexate.

Beta-blockers

Naproxen and other NSAIDs can reduce the anti-hypertensive effect of beta-blockers, angiotensin converting enzyme inhibitors (ACE inhibitors), and angiotensin receptor blockers (ARBs).

Diuretics

As with other NSAIDs, naproxen may inhibit the natriuretic effect of furosemide.

Lithium

Inhibition of renal lithium clearance leading to increases in plasma lithium concentrations has been reported.

Sodium bicarbonate

Sodium bicarbonate may enhance the rate of naproxen absorption.

Zidovudine

In vitro studies have shown that naproxen may interfere with the metabolism of zidovudine, resulting in higher zidovudine plasma levels. Therefore, to avoid the

potential side effects associated with increased zidovudine plasma levels, dose reduction should be considered.

ACE-inhibitors

Concomitant use of NSAIDs with ACE inhibitors or angiotensin receptor blockers may increase the risk of renal dysfunction, especially in patients with pre-existing poor renal function (see section 4.4).

Combination use of ACE inhibitors or angiotensin receptor antagonists, anti-inflammatory drugs and thiazide diuretics

The use of an ACE inhibiting drug (ACE-inhibitor or angiotensin receptor antagonist), an anti-inflammatory drug (NSAID or COX-2 inhibitor) and a thiazide diuretic at the same time (triple whammy) increases the risk of renal impairment. This includes use in fixed-combination products containing more than one class of drug. Combined use of these medications should be accompanied by increased monitoring of serum creatinine, particularly at the initiation of the combination. The combination of drugs from these three classes should be used with caution particularly in elderly patients or those with pre-existing renal impairment.

4.6 Fertility, pregnancy and lactation

Fertility

No data available.

Pregnancy

Category C

Naproxen sodium is contraindicated in 3rd trimester of pregnancy.

Naproxen sodium should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the fetus. If there is a compelling need for NSAID treatment during the first or second trimester, limit use to the lowest effective dose and shortest duration possible.

Data from epidemiological studies suggest an increased risk of miscarriage and congenital malformation associated with NSAID use in early pregnancy.

Use of NSAIDs in the second or third trimester may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Oligohydramnios is generally seen after days to weeks of treatment, although it has been reported as soon as 48 hours after NSAID initiation. Oligohydramnios is usually, but not always, reversible after treatment discontinuation. Consider ultrasound monitoring of amniotic fluid if treatment extends beyond 48 hours. Discontinue treatment with naproxen sodium if oligohydramnios occurs.

NSAID use during the 3rd trimester may cause premature closure of the fetal ductus arteriosus, fetal renal impairment, inhibition of platelet aggregation, and may delay labour and birth. NSAID use in the 3rd trimester of pregnancy is therefore contraindicated.

Use in lactation

Naproxen has been found in the milk of lactating women at a concentration of approximately 1% of that found in plasma. As the effect of naproxen in the newborn is not known, the use of naproxen in lactating mothers is not recommended.

4.7 Effects on ability to drive and use machines

Some patients may experience drowsiness, dizziness, vertigo, insomnia or depression with the use of naproxen sodium. If patients experience these or similar undesirable effects, they should exercise caution in carrying out activities that require alertness.

4.8 Undesirable effects

Adverse effects reported in controlled clinical trials in patients treated for rheumatoid arthritis and osteoarthritis are listed below. In general, these effects were reported 2 to 10 times more frequently than they were in studies of 962 patients treated for mild to moderate pain.

Incidence between 3% and 9%

Gastrointestinal: The most frequently reported adverse events were related to the gastrointestinal tract. These were: constipation, heartburn, abdominal pain, nausea.

Central nervous system: headache, dizziness, drowsiness.

Dermatologic: itching (pruritis), skin eruption, ecchymoses.

Special senses: tinnitus.

Cardiovascular: oedema, dyspnoea.

Incidence between 1% and less than 3%

Gastrointestinal: dyspepsia, diarrhoea, stomatitis.

Central nervous system: light-headedness, vertigo.

Dermatologic: sweating, purpura.

Special senses: hearing disturbances, visual disturbances.

Cardiovascular: palpitations.

General: thirst.

Incidence less than 1%

Probable causal relationship

The following adverse effects were reported less frequently than 1% during controlled clinical trials and in post marketing reports. The probability of a causal relationship exists between naproxen and these adverse effects.

Gastrointestinal: abnormal liver function tests, gastrointestinal bleeding, haematemesis, jaundice, melaena, peptic ulceration with bleeding and/or

perforation, non-peptic gastrointestinal ulceration, vomiting, ulcerative stomatitis, colitis, fatal hepatitis.

Renal: glomerular nephritis, haematuria, interstitial nephritis, renal papillary necrosis, nephrotic syndrome, renal disease, hyperkalaemia, renal failure.

Haematologic: eosinophilia, granulocytopenia, leukopenia, thrombocytopenia.

Central nervous system: depression, dream abnormalities, inability to concentrate, insomnia, malaise, myalgia, muscle weakness, aseptic meningitis.

Dermatologic: porphyria cutanea tarda, epidermolysis bullosa, alopecia, skin rashes, epidermal necrolysis, erythema multiforme, Stevens-Johnson syndrome (SJS), photosensitivity reactions including rare cases in which the skin resembles porphyria cutanea tarda (pseudoporphyria) or epidermolysis bullosa.

Special senses: hearing impairment.

Cardiovascular: vasculitis, congestive heart failure.

General: menstrual disorders, pyrexia (chills and fever), eosinophilic pneumonitis, anaphylactoid reactions (see section 4.4).

Causal relationship unknown

Other reactions have been reported in circumstances in which a causal relationship could not be established. Although rarely reported, the physician should be alerted to these.

Haematologic: agranulocytosis, aplastic anaemia, haemolytic anaemia.

Central and peripheral nervous system: cognitive dysfunction, convulsions, paraesthesia.

Dermatologic: urticaria, photosensitivity.

Mouth and throat: sore throat.

General: angioneurotic oedema, hyperglycaemia, hypoglycaemia, hyperkalaemia.

Reproductive: female infertility.

Post-marketing

The following are the adverse events that have been reported with NSAIDs and with naproxen:

Gastrointestinal*:* inflammation, peptic ulcers, ulceration, perforation and obstruction of the upper and lower gastrointestinal tract, gastrointestinal bleeding (sometimes fatal particularly in the elderly), heartburn, nausea, oesophagitis, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, non-peptic gastrointestinal ulceration, melaena, haematemesis, stomatitis, ulcerative stomatitis, exacerbation of ulcerative colitis and Crohn's disease, pancreatitis, gastritis.

Infections: aseptic meningitis.

Blood and lymphatic system disorders: agranulocytosis, aplastic anaemia, eosinophilia, haemolytic anaemia, leucopenia, thrombocytopenia.

Immune system disorders: anaphylactoid reactions.

Metabolic and nutrition disorders: hyperkalaemia.

Psychiatric disorders: depression, dream abnormalities, insomnia.

Nervous system disorders: dizziness, drowsiness, headache, light-headedness, retrobulbar optic neuritis, convulsions, cognitive dysfunction, inability to concentrate.

Eye disorders: visual disturbances, corneal opacity, papillitis, papilloedema.

Ear and labyrinth disorders: hearing impairment, hearing disturbances, tinnitus, vertigo.

Cardiac disorders: palpitations, cardiac failure, congestive heart failure.

Vascular disorders: hypertension, vasculitis.

Respiratory, thoracic and mediastinal disorders: dyspnoea, pulmonary oedema, asthma, eosinophilic pneumonitis.

Hepatobiliary disorders: hepatitis, jaundice.

Skin and subcutaneous tissue disorders: ecchymoses, itching (pruritus), purpura, skin eruptions, sweating, alopecia, epidermal necrolysis, very rarely toxic epidermal necrolysis (TEN), erythema multiforme, bullous reactions, (including SJS, Drug Reaction with Eosinophilia and Systemic

Symptoms (DRESS)), erythema nodosum, fixed drug eruption, lichen planus, pustular reaction, skin rashes, systemic lupus erythematosus (SLE), urticaria, photosensitivity reactions, including rare cases resembling porphyria cutanea tarda (pseudoporphyria), or epidermolysis bullosa, and angioneurotic oedema.

If skin fragility, blistering or other symptoms suggestive of pseudoporphyria occur, treatment should be discontinued and the patient monitored.

Musculoskeletal and connective tissue disorders: myalgia, muscle weakness.

Renal and urinary disorders: haematuria, interstitial nephritis, nephritic syndrome, renal disease, renal failure, renal papillary necrosis.

Pregnancy, puerperium and perinatal conditions: oligohydramnios, neonatal renal impairment.

Reproductive system: female infertility.

General disorders: oedema, thirst.

Investigations: abnormal liver function tests, raised serum creatinine.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

Symptoms

Significant naproxen overdosage may be characterised by dizziness, drowsiness, epigastric pain, abdominal discomfort, indigestion, nausea, transient alterations in liver function, hypoprothrombinaemia, renal dysfunction, metabolic acidosis, apnoea, disorientation 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 not clear if these were causally related to naproxen. It is not

known what dose of naproxen would be life threatening.

Gastrointestinal bleeding may occur. Hypertension, acute renal failure, respiratory depression and coma may occur after the ingestion of NSAIDs, and may occur following an overdose.

Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an 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, alkalinisation of urine, haemodialysis, or haemoperfusion may not be useful due to high protein binding.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Propionic acid derivatives **ATC code**: MO1AE02

Naproxen sodium is a non-steroidal anti-inflammatory (NSAID) with analgesic, anti-inflammatory and antipyretic properties. The onset of pain relief is more rapid with naproxen sodium than with naproxen, therefore naproxen sodium is recommended for the management of acute painful conditions.

Naproxen is a propionic acid derivative related to the arylacetic acid class of medicines. The chemical name of naproxen is (+)-6-methoxy-alpha-methyl-2-naphthaleneacetic acid. It is an odourless, white to off-white crystalline substance. It is lipid soluble, practically insoluble in water at low pH and freely soluble in water at high pH. Naproxen sodium is a white to creamy white, crystalline solid, freely soluble in water at neutral pH.

Mechanism of action

Naproxen has been shown to have anti-inflammatory properties when tested in human clinical studies. In addition, it has analgesic and antipyretic actions. It exhibits its anti-inflammatory effects even in adrenalectomised animals, indicating that its action is not mediated through the pituitary axis. It inhibits prostaglandin synthetase, as do other NSAIDs, however, the exact mechanism of its anti-inflammatory action is not known.

5.2 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. Concomitant administration of food can delay the absorption of naproxen and naproxen sodium, but does not affect its extent.

Naproxen sodium tablets: After oral administration of naproxen sodium tablets, because of rapid and complete absorption, clinically significant plasma levels and pain relief are obtained in patients within 30 minutes of administration. Peak plasma levels are attained in 1 - 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 relatively small volume of distribution (0.09 ± 0.03 L/kg), which corresponds to about 10% of the body weight in humans. At therapeutic levels naproxen is greater than 99% albumin bound. The plasma concentration of naproxen increases proportionally with doses up to 500 mg twice daily. Larger doses result in a less than proportional increase due to accelerated renal clearance of disproportionately increased amounts of non-protein bound drug. However, whether

this effect increases or decreases the toxicity of naproxen has not been established.

Steady-state plasma levels of naproxen are reached after 4 to 5 doses.

Naproxen enters synovial fluid, crosses the placenta. It has been found in the milk of lactating mothers at a concentration approximately 1% of that found in plasma.

Biotransformation

Naproxen is metabolised in the liver to 6-0-desmethyl naproxen (approximately 28% of an IV dose).

Elimination

Approximately 95% of the naproxen is excreted in the urine, primarily as naproxen (10%), 6-0- desmethyl naproxen (5%), or their conjugates. The rate of excretion of metabolites and conjugates has been found to coincide closely with the rate of naproxen clearance from the plasma. Small amounts, 5% or less, are excreted in the faeces.

The elimination half-life of naproxen is approximately 14 hours.

Special populations

Children

The pharmacokinetic profile of naproxen in children aged 5 - 16 years is similar to that in adults.

Renal impairment

Given that naproxen and its metabolites are primarily excreted by the kidney, the potential exists for accumulation in the presence of renal insufficiency. Elimination of naproxen is decreased in patients with severe renal impairment (creatinine clearance <20 mL/min), in whom there is higher clearance of naproxen than estimated from the degree of renal impairment alone (see section 4.4).

5.3 Preclinical safety data

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Colloidal silicon dioxide
- Crospovidone
- Magnesium stearate
- Maize starch
- Povidone
- Purified talc
- Purified water
- Opadry blue 03B50961 (film-coat)

Contains 25mg sodium per tablet.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25°C.

6.5 Nature and contents of container

Sonaflam 275 mg film-coated tablets are available in blister packs sizes of 10, 12, 20, 24, 30 and 120. Not all pack sizes may be marketed.

7. MEDICINE SCHEDULE

Pharmacy Only Medicine:	12 and 24 tablet pack sizes.
Pharmacist Only (Restricted) Medicine:	10, 12, 20, 24, 30 tablet pack sizes.
Prescription Medicine:	120 tablet pack size.

Not all pack sizes may be marketed.

8. SPONSOR

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9. DATE OF FIRST APPROVAL

03 May 2007

10. DATE OF REVISION OF THE TEXT

02 Dec 2025

SUMMARY TABLE OF CHANGES

Section	CHANGE
4.2 - 4.9, 5.2, 5.3	Information aligned with source data sheet and MARC directives.
6.2, 6.3, 6.5	Editorial changes
7	Inclusion of Restricted Medicine classification details.