Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Gerinap 250mg Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 250mg naproxen.

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.
A yellow, flat, bevel-edged tablet approximately 11 mm in diameter and approximately 3.5 mm in thickness, with 'NP' breakline '250' on one side and 'G' on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the management of various arthritides, such as rheumatoid arthritis, osteoarthrosis, spondylitis, gout, etc., and of musculoskeletal disorders. For the management of rheumatoid arthritis in children over the age of five years.

4.2 Posology and method of adminstration

Adults
The usual dose is 250 mg twice daily, with a maximum daily dose of 1000 mg.

In the case of gout a dose of 750 mg may be required as an initial dose given once, with 250 mg every eight hours thereafter for a maximum of 72 hours. Subsequently use may be made of the usual regimen if necessary.

Elderly
The lowest effective dose should be administered to the elderly.

Children over the age of 5 years
Naproxen is effective in the treatment of juvenile rheumatoid arthritis in children over 5 years of age at a dose of 10mg/kg/day taken in two doses at 12 hour intervals. Naproxen tablets are not recommended for use for any other indication in children under 16 years of age.

Children under 5 years
The safety of Naproxen tablets in children under 5 years of age has not been established and therefore is not recommended.

4.3 Contraindications

a) Use in patients with peptic ulcer disease, active peptic ulceration or intestinal inflammatory disease.

b) Use in patients hypersensitive to Naproxen or other non-steroidal anti-inflammatory agents including aspirin.

4.4 Special warnings and precautions for use

a) Episodes of gastrointestinal bleeding have been reported in patients with naproxen therapy. Great caution should be exercised and close supervision should be given to patients with a history or existent gastro-intestinal disease.

b) The product should only be used with great caution in patients with a history of, or in those with impaired liver function.

c) As with other NSAIDs bronchospasm may be precipitated in patients suffering from, or with a history of, bronchial asthma or allergic disease.

d) The product will prolong bleeding time and decrease platelet aggregation.

e) Because of its occasional tendency to increase fluid retention, use of the drug requires careful observation for this feature in persons with incipient or existent congestive failure.

f) Naproxen is mainly excreted through the kidney by glomerular filtration. It should only be used with caution in patients with renal dysfunction particularly if long term dosage is under consideration. Such patients with pre-existent renal dysfunction should have regular monitoring of serum creatinine clearance. Use is not recommended in patients with a creatinine clearance of less than 20 ml/min.

g) Certain patients in whom renal blood flow is compromised such as in extra cellular fluid volume depletion, cirrhosis of the liver, sodium retention, congestive heart failure and renal disease should have renal function assessed before and during therapy. Elderly patients in whom renal function is often impaired would also be included in this group. Consideration should be given to a reduction in daily dosage.

h) Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

a) The excretion of methotrexate and lithium is reduced by co-administration of naproxen. Probenecid given with naproxen due to decreased excretion.

b) The product is highly bound to plasma protein so that caution should be exercised in use in patients concomitantly receiving other drugs strongly protein bound such as anticoagulants, sulphonamides and hydantoins.

c) Patients with established aspirin hypersensitivity may react similarly to naproxen. This is particularly of concern in those with asthma in whom bronchospasm may be precipitated.

d) Naproxen may interfere with some test of 17-ketogenic steroids and assays of urinary 5-hydroxyindoleacetic acid, it is advised that naproxen therapy be temporarily discontinued for 48 hours before adrenal function and other affected tests.

e) The natriuretic effect of frusemide has been reported to be inhibited by some drugs of this class. Also the anti-hypertensive effect of propranolol and other beta-blockers may be reduced.

4.6 Pregnancy and lactation

There is inadequate evidence of safety of the drug in human pregnancy. As with other drugs of this type naproxen delays parturition in animals but the relevance of this finding to human patients is not known. It also affects the human foetal cardiovascular system by causing closure of the ductus arteriosus.

Naproxen should not be used in pregnancy unless considered essential by the physician. Naproxen has been found in

the milk of lactating mothers. The use of naproxen should therefore be avoided in patients who are breast feeding.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Gastro-intestinal: Most commonly nausea, vomiting, epigastric distress and abdominal discomfort. Occasionally, but more serious, gastro-intestinal bleeding, colitis and peptic ulceration.

Hypersensitivity/skin reactions: Rashes, urticaria, anaphylaxis, angio-oedema and eosinophilic pneumonitis. Erythema multiforme, Stevens-Johnson syndrome, epidermal necrolysis, photosensitivity reactions and alopecia. Rarely epidermolysis bullosa and porphyria cutanea tarda have been reported.

CNS: Headache, insomnia, lack of concentration and cognitive dysfunction.

Haematological: Agranulocytosis, thrombocytopenia, aplastic and haemolytic anaemia may occur rarely.

Other side effects reported rarely include vertigo, hearing impairment, tinnitus and visual disturbances. Jaundice, hepatitis, mild peripheral oedema, nephropathy, haematuria, vasculitis, aseptic meningitis and ulcerative stomatitis.

4.9 Overdose

Overdosage can be characterised by drowsiness, heartburn, indigestion, nausea or vomiting. The stomach may be emptied and usual supportive measures employed. It is not known what dose is life-threatening.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Naproxen is a non steroidal anti-inflammatory agent and also has analgesic and antipyretic activity in man. Naproxen reduces the synthesis of prostaglandins by inhibiting the cyclo-oxygenase enzyme. The exact mechanism of its anti-inflammatory action is not known.

5.2 Pharmacokinetic properties

Naproxen is completely absorbed following oral administration. Peak plasma concentrations are seen after about 2 hours. Absorption rate, but not extent, is diminished by concomitant administration with food or antacids.

Naproxen is highly protein bound (>99%) resulting in a volume of distribution of $0.91kg^{-1}$.

Naproxen is extensively metabolised by the liver, and excretion is primarily by the kidneys. Less than 10% of a dose is excreted unchanged.

Plasma half-life is 12-15 hours.

5.3 Preclinical safety data

There is no potential mutagenicity of naproxen. There is no evidence of carcinogenicity in two year studies in rats. There is no evidence of teratogenicity in mice, rats or rabbits. Naproxen has been shown to delay parturition in animals and to effect the closure of the ductus arteriosus in the human foetal cardiovascular system.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Povidone
Sodium starch glycolate (type A)
Talc
Magnesium stearate
Polysorbate 80
Quinoline yellow (aluminium lake) (E104)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

4 years.

6.4 Special precautions for storage

Do not store above 25°C.

Store in the original package.

6.5 Nature and contents of container

Available in packs of 30 and 250 tablets in:

i. Polypropylene tablet container with tamper-evident polyethylene cap.

ii. Polyvinylchloride (PVC)/aluminium foil blister packs.

iii. High density polyethylene tablet container with polypropylene cap.

Not all pack sizes may be marketed.

6.6 Instructions for use and handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Generics [UK] Limited
Station Close
Potters Bar
Hertfordshire EN6 1TL
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 405/11/1

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