SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Naproxen 250 mg Gastro-resistant Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant tablet contains 250 mg of Naproxen.

Excipient(s) with known effect
One Naproxen 250 mg Gastro-resistant Tablet contains 74.24 mg of lactose monohydrate Ph. Eur.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gastro-resistant Tablets

White, round, biconvex gastro-resistant tablets, overprinted in black 3N3.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Naproxen is indicated for the treatment of juvenile rheumatoid arthritis, rheumatoid arthritis, ankylosing spondylitis, osteoarthrosis (degenerative arthritis), acute gout, acute musculoskeletal disorders (for example sprains and strains, tenosynovitis, fibrositis, lumbosacral pain, direct trauma, and cervical spondylitis), and dysmenorrhoea.

4.2 Posology and method of administration

Posology

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

Adults

Naproxen gastro-resistant tablets should be swallowed whole and not broken or crushed.

Therapy should be started at the lowest recommended dose, especially in the elderly.

Rheumatoid arthritis, osteoarthrosis and ankylosing spondylitis

The usual dose is 500 mg to 1 g per day taken in two divided doses at 12 hour intervals. Where 1 g per day is needed either one 500 mg tablet twice daily or two 500 mg tablets in a single administration (morning or evening) is recommended. In the following cases a loading dose of 750 mg or 1 g per day for the acute phase is recommended:

a) In patients reporting severe night-time pain/or morning stiffness.

b) In patients being switched to Naproxen from a high dose of another anti-rheumatic compound.

c) In osteoarthrosis where pain is the predominant symptom.

Acute gout

750 mg immediately, then 250 mg every 8 hours until the attack has passed.

Acute musculoskeletal disorders and dysmenorrhoea

500 mg initially, then 250 mg every 6 – 8 hours as needed. The maximum daily dose (after the first day) is 1250 mg.

Paediatric population

Juvenile rheumatoid arthritis:

Normally, dosage is 10 mg/kg bodyweight daily taken in 2 doses at 12 hour intervals.

The Elderly

Studies indicate that although total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly. The implication of this finding for Naproxen dosing is unknown.

The elderly are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective does should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

For the effect of reduced elimination in the elderly refer to Section 4.4.

Renal/hepatic impairment

A lower dose should be considered in patients with renal or hepatic impairment. Naproxen is contraindicated 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 (see section 4.3).

Treatment should be reviewed at regular intervals and discontinued if no benefit is seen or intolerance occurs.

Method of administration

For oral administration preferably with or after food.

4.3 Contraindications

Hypersensitivity to naproxen or to any of the excipients.

Active or history of peptic ulceration or active gastrointestinal haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

NSAIDS are contraindicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, nasal polyps, angioedema or urticaria) in response to ibuprofen, aspirin, or other non-steroidal anti-inflammatory drugs (NSAIDs)/analgesic drugs as the potential exists for cross-sensitivity reactions. These reactions have the potential of being fatal. Severe anaphylactic-like reactions to naproxen have been reported in such patients.

Severe heart failure, hepatic failure and renal failure (See section 4.4).

During the last trimester of pregnancy (See section 4.6 – Pregnancy and lactation)

History of upper gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

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

4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI and cardiovascular risks below). Patients treated with NSAIDs long-term should undergo regular medical supervision to monitor for adverse events.

The antipyretic and anti-inflammatory activities of Naproxen may reduce fever and inflammation, thereby diminishing their utility as diagnostic signs.

As with other non-steroidal anti-inflammatory drugs, elevations of one or more liver function tests may occur. Hepatic abnormalities may be the result of hypersensitivity rather than direct toxicity. Severe hepatic reactions, including jaundice and hepatitis (some cases of hepatitis have been fatal) have been reported with this drug as with other nonsteroidal anti-inflammatory drugs. Cross reactivity has been reported.

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

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 Naproxen.

Combination with other NSAIDs

The use of naproxen with concomitant NSAIDs including cyclooxygenase-2-selective inhibitors should be avoided because of the cumulative risks of inducing serious NSAID-related adverse events (see section 4.5).

Elderly

The elderly and/or debilitated patients have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2). Prolonged use of NSAIDs in these patients is not recommended. Where prolonged therapy is required, patients should be reviewed regularly.

Respiratory disorders

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

Cardiovascular, Hepatic Impairment and Renal failure linked to reduced prostaglandin production

The administration of an NSAID may cause a dose dependant reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. Renal function should be monitored in these patients (see also section 4.3).

Cardiovascular and cerebrovascular effects

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 oedema have been reported in association with NSAID therapy.

Clinical trial and epidemiological data suggest that use of coxibs and some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Although data suggest that the use of naproxen (1000 mg daily) may be associated with a lower risk, some risk cannot be excluded.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with naproxen after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

Renal Effects

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

Use in patients with impaired renal function

As naproxen is eliminated to a large extent (95%) by urinary excretion via glomerular filtration, it should be used with great caution in patients with impaired renal function and the monitoring of serum creatinine and/or creatinine clearance is advised in these patients. Naproxen is contraindicated in patients having a baseline creatinine clearance of less than 30ml/minute.

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

Certain patients, specifically those whose renal blood flow is compromised, such 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 Naproxen therapy. Some elderly patients in whom impaired renal function may be expected, as well as patients using diuretics, may 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 Naproxen dosing is unknown but it is prudent to use the lowest effective dose.

Gastrointestinal bleeding, ulceration and perforation

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime 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 (see section 4.3), and in the elderly. 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 (see below and section 4.5).

Patients with a history of GI toxicity, particularly when 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 the risk of ulceration or bleeding, such as oral corticosteroids, or anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (see section 4.5).

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 diseases (ulcerative colitis, Crohn’s disease) as these conditions may be exacerbated (see section 4.8).

Haematological

Patients who have coagulation disorders or are receiving drug therapy that interferes with haemostasis should be carefully observed if naproxen-containing products are administered.

Patients at high risk of bleeding or those on full anticoagulation therapy (e.g. dicoumarol derivatives) may be at increased risk of bleeding if given naproxen-containing products concurrently.

Anaphylactic (anaphylactoid) 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 non-steroidal anti-inflammatory drugs or naproxen-containing products. They may also occur in individuals with a history of angio-oedema, bronchospastic reactivity (e.g. asthma), rhinitis and nasal polyps.

Anaphylactoid reactions, like anaphylaxis, may have a fatal outcome.

Steroids

If steroid dosage is reduced or eliminated during 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 arthritis.

Ocular effects

Studies have not shown changes in the eye attributable to naproxen administration. 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-containing products should have an ophthalmological examination.

SLE and mixed connective tissue disease:

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).

Dermatological:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk for these reactions early in the course of the therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Naproxen should be discontinued at the first appearance of skin risk, mucosal lesions, or any other sign of hypersensitivity.

Precautions related to female fertility:

The use of naproxen, as with any drug known to inhibit cyclooxygenase/prostaglandin synthesis, may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of fertility, withdrawal of naproxen should be considered.

4.5 Interaction with other medicinal products and other forms of interaction

Other analgesics: including cyclooxygenase-2 selective inhibitors

Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects (See section 4. 4).

Concomitant administration of antacid, colestyramine or food may delay the absorption of naproxen but does not affect its extent.

*Anti-hypertensive*s: reduced anti-hypertensive effect.

Naproxen and other non-steroidal anti-inflammatory drugs may increase the risk of renal impairment associated with the use of ACE-inhibitors.

Diuretics: can decrease diuretic effect. The natriuretic effect of furosemide has been reported to be inhibited by some drugs of this class. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Lithium: Decreased renal elimination of lithium leading to increases in plasma lithium concentrations.

Methotrexate: Possible enhancement of methotrexate toxicity due to decreased elimination of methotrexate.

Ciclosporin: Increased risk of nephrotoxicity.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding (See section 4.4).

Anti-coagulants and sulphonylureas: NSAIDs may enhance the effects of anti-coagulants, such as warfarin and heparin (See section 4.4).

Naproxen is highly bound to plasma proteins and if anti-coagulants, hydantoins, other NSAIDs, aspirin or highly protein-bound sulphonamides are given simultaneously, overdosage of these drugs may result.

Patients simultaneously receiving Naproxen and a hydantoin, sulphonamide or sulphonylurea should be observed for adjustment of dose if required.

No interactions have been observed in clinical studies with naproxen and anticoagulants or sulphonylureas, but caution is nevertheless advised since interaction has been seen with other non-steroidal agents of this class.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs); Increase risk of gastrointestinal bleeding (see section 4.4)

Quinolone antibiotics: Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

Co-administration of probenecid inhibits the renal tubule secretion of naproxen, so raising its plasma concentration and prolonging its half-life.

It is suggested that naproxen is withdrawn 48 hours before adrenal function tests as it may interfere with some tests for 17-ketogenic steroids. Naproxen may interfere with some assays of urinary 5-hydroxy-indoleacetic acid.

Tacrolimus: Possible increase risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Zidovudine: Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Acetylsalicylic acid: Clinical pharmacodynamic data suggest that concomitant naproxen usage for more than one day consecutively may inhibit the effect of low-dose acetylsalicylic acid on platelet activity and this inhibition may persist for up to several days after stopping naproxen therapy. The clinical relevance of this interaction is not known.

4.6 Fertility, pregnancy and lactation

Pregnancy

Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern.

In view of the known effects of NSAIDs on the foetal cardiovascular system (risk of closure of the ductus arteriosus), use in the last trimester of pregnancy is contraindicated (See section 4.3 – Contraindications).

NSAIDs should not be used during the first two trimesters of the pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the foetus.

Labour and delivery

Naproxen containing products are not recommended in labour and delivery because, through its prostaglandin synthesis inhibitory effect, naproxen may adversely affect foetal circulation and inhibit contractions, with an increased bleeding tendency in both mother and child (See section 4.3 – Contraindications). The onset of labour may be delayed and the duration increased

Breast-feeding

NSAIDs can appear in the breast milk of lactating women. NSAIDs should be avoided when breastfeeding.

See section 4.4 – Special warning and precautions for use, regarding female fertility.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, vertigo, insomnia, fatigue, visual disturbances or depression are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

The following adverse events have been reported with NSAIDs and naproxen.

Gastro-intestinal: the most commonly-observed adverse events are gastrointestinal in nature. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, heartburn and epigastric distress. More serious reactions which may occur are gastro-intestinal ulceration, which is sometimes fatal, particularly in the elderly (see section 4.4), peptic ulceration, perforation, non-peptic gastro-intestinal ulceration, melaena, haematemesis, stomatitis, ulcerative stomatitis, exacerbation of ulcerative colitis and Crohn's disease (see section 4.4) and oesophagitis. Less frequently, gastritis has been observed. Pancreatitis has been reported very rarely.

Immune system disorders: hypersensitivity reactions have been reported following treatment with NSAIDs in patients with, or without, a history of previous

hypersensitivity reaction to NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis, erythema multiforme).

Metabolic and nutrition disorders: hyperkalaemia.

Psychiatric disorders: Insomnia, dream abnormalities, depression, confusion and hallucinations.

Cardiac disorders: Oedema, palpitations, cardiac failure and congestive heart failure have been reported in association with NSAID treatment.

Clinical trail and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Vascular disorders: Hypertension, vasculitis.

Renal and urinary disorders: Including, but not limited to, glomerular nephritis, interstitial nephritis, nephrotic syndrome, haematuria, raised serum creatinine, renal papillary necrosis and renal failure.

Hepatobiliary disorders: Abnormal liver function tests, fatal hepatitis and jaundice.

Nervous system disorders: Convulsions, dizziness, retrobulbar optic neuritis, headaches, light-headedness, drowsiness, paraesthesia, inability to concentrate and cognitive dysfunction have been reported. Reports of aseptic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (See section 4.4).

Eye disorders: Visual disturbances, corneal opacity, papillitis and papilloedema.

Ear and Labyrinth disorders: Tinnitus, hearing disturbances including impairment and vertigo.

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

Blood and lymphatic system disorders: Thrombocytopenia, neutropenia, granulocytopenia including agranulocytosis, eosinophilia, leucopenia, aplastic anaemia and haemolytic anaemia.

Skin and subcutaneous tissue disorders: Bullous reactions including Steven Johnson Syndrome and Toxic Epidermal necrosis (very rare). Skin rashes including fixed drug eruption, itching (pruritus), urticaria, ecchymoses, purpura, sweating. Also alopecia, erythema multiforme, erythema nodosum, lichen planus, pustular reaction, SLE, epidermal necrolysis, photosensitivity reactions (including cases in which skin resembles porphyria cutanea tarda "pseudoporphyria") or epidermolysis bullosa-like reactions which may occur rarely.

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 and muscle weakness.

Reproductive system and breast disorders: Female infertility.

General disorders and administration site conditions: Thirst, pyrexia, fatigue and malaise.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms

Symptoms include headache, heartburn, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, drowsiness, dizziness, tinnitus, fainting. In cases of significant poisoning acute renal failure and liver damage are possible.

Respiratory depression and coma may occur after the ingestion of NSAIDs but are rare.

In one case of naproxen overdose, transient prolongation of the prothrombin time due to hypothrombinaemia may have been due to selective inhibition of the synthesis of vitamin-K dependent clotting factors.

A few patients have experienced seizures, but it is not known whether these were naproxen-related or not. It is not known what dose of the drug would be life-threatening.

Treatment

Patients should be treated symptomatically as required.

Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

Good urine output should be closely monitored.

Renal and liver functions should be closely monitored.

Patients should be observed for at least four hours after ingestion of potentially toxic amounts.

Frequently or prolonged convulsions should be treated with intravenous diazepam.

Other measures may be indicated by the patient's clinical condition.

Haemodialysis does not decrease the plasma concentration of naproxen because of the high degree of protein binding. However, haemodialysis may still be appropriate in a patient with renal failure who has taken naproxen.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, nonsteroids, propionic acid derivatives, ATC code: M01AE02

Naproxen is a propionic acid derivative. It acts as an anti-inflammatory agent, analgesic and has anti-pyretic activity in man. By its action on cyclo-oxygenase, naproxen inhibits prostaglandin synthesis (as do other NSAIDs). Naproxen exhibits its anti-inflammatory effect even in adrenalectomised animals, indicating that its action is not mediated through the pituitary-adrenal axis. As with other NSAIDs, however, the exact mechanism of its anti-inflammatory action is not known.

5.2 Pharmacokinetic properties

Animal studies suggest that prompt administration of activated charcoal would reduce the absorption of naproxen.

Following oral administration, naproxen is fully absorbed from the gastro-intestinal tract. Depending on food in-take, peak plasma concentrations are reached 2 to 4 hours after ingestion. Naproxen is present in the blood mainly as unchanged drug, extensively bound to plasma proteins. More than 99% is bound to plasma proteins. The plasma half-life is between 12 and 15 hours, enabling a steady state to be achieved within 3 days of initiation of therapy on a twice daily dose regimen. The degree of absorption is not significantly affected by either foods or most antacids. Excretion in urine accounts for approximately 95% of the dose. Naproxen crosses the placental barrier and is excreted in breast milk.

Metabolism in children is similar to that in adults. Chronic alcoholic liver disease reduces the total plasma concentration of naproxen but the concentration of unbound naproxen increases. In the elderly, the unbound plasma concentration of naproxen is increased although total plasma concentration is unchanged.

When naproxen is administered in the gastro-resistant form, the peak plasma levels are delayed when compared with the standard tablets. However, the mean areas under the plasma concentration time curves, and hence bioavailability, are equivalent. The tablets do not disintegrate until they reach the small intestine, where dissolution is rapid and complete. This delay in absorption makes Naproxen gastro-resistant tablets of value for patients in whom gastric dissolution is undesirable.

5.3 Preclinical safety data

Carcinogenicity

Naproxen was administered with food to Sprague-Dawley rats for 24 months at doses of 8, 16 and 24mg/kg/day. Naproxen was not carcinogenic in rats.

Mutagenicity

Mutagenicity was not seen in *Salmonella typhimurium* (5 cell lines), *Saccharomyces cerevisiae* (1 cell line), and mouse lymphoma tests.

Fertility

Naproxen did not affect the fertility of rats when administered orally at doses of 30mg/kg/day to males and 20mg/kg/day to females.

Teratogenicity

Naproxen was not teratogenic when administered orally at dose of 20mg/kg/day during organogenesis to rats and rabbits.

Perinatal/Postnatal Reproduction

Oral administration of naproxen to pregnant rats at doses of 2, 10 and 20mg/kg/day during the third trimester of pregnancy resulted in difficult labour. These are known effects of this class of compounds and were demonstrated in pregnant rats with aspirin and indometacin.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet contains:

Lactose Monohydrate,

Maize Starch,

Povidone,

Sodium Starch Glycolate (type A),

Magnesium Stearate (E572).

Coating contains:

Lactose Monohydrate,

Hydroxypropyl methylcellulose (E464),

Colloidal silicon dioxide,

Polyethylene glycol,

Polyvinyl acetate phthalate,

Purified stearic acid (E570),

Purified talc (E553(b)),

Sodium alginate (E401),

Sodium bicarbonate (E500),

Triethyl citrate,

Titanium Dioxide (E171),

Antifoam AF emulsion.

Printing Ink:

Shellac,

Black iron oxide (E172),

Propylene Glycol (E1520).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

Blister strips in packs of 10, 28, 56 or 100 tablets.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Teva UK Limited

Ridings Point

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WF10 5HX

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