Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Stirlescent 250mg Effervescent Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 250 mg Naproxen.

Excipients with known effect
Each effervescent tablet contains:
- 0.52 mg benzyl alcohol
- 342.01 mg sodium
- 0.097 mg sorbitol (E420)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Effervescent tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Stirlescent is indicated in adults for the treatment of rheumatoid arthritis, osteoarthritis (degenerative arthritis), ankylosing spondylitis, acute gout, acute musculoskeletal disorders (such as sprains and strains, direct trauma, lumbosacral pain, cervical spondylitis, tenosynovitis and fibrositis) and dysmenorrhoea.

4.2 Posology and method of administration

Posology
Use of the lowest effective dose for the shortest duration necessary to control symptoms is recommended in order to minimise undesirable effects (see section 4.4).

Rheumatoid arthritis, osteoarthritis and ankylosing spondylitis
The recommended dose is 250 mg, twice daily. Adjust to 500 mg to 1000 mg daily in two divided doses at 12-hour intervals.

Acute gout
The recommended dose is 750 mg initially, followed by 250 mg every 8 hours until the attack has passed.

Acute musculoskeletal disorders and dysmenorrhoea
The recommended dose is 500 mg initially, followed by 250 mg at 6 to 8 hours intervals as needed, with a maximum daily dose after the first day of 1250 mg.

Paediatric population
Stirlescent is not recommended for use in children and adolescents under 18 years of age, because the correct dose cannot be administered using this formulation.

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 Stirlescent is unknown. Reduced elimination in the elderly (see section 4.4). Increased risk of serious consequences of adverse reactions. If NSAID use is considered necessary, the lowest effective dose should be used for the shortest possible duration. Monitor regularly for GI bleeding during treatment.

Renal/hepatic impairment

Consider a lower dose in patients with renal or hepatic impairment. Contraindicated in patients with baseline creatinine clearance less than 30 ml/minute because accumulation of naproxen metabolites (see section 4.3) has been seen in patients with severe renal failure or those on dialysis.

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

Method of administration
For oral administration.
Doses of 1 to 2 tablets must be dissolved in at least 150 ml (a glass) of water, doses of 3 tablets must be dissolved in 300 ml. The glass should be rinsed with a small amount of water (10 ml) and the contents drunk.
To be taken preferably with or after food.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

Active or a history of recurrent peptic ulcer/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 or urticaria) in response to ibuprofen, aspirin, or other NSAIDs. These reactions have the potential of being fatal. Severe anaphylactic-like reactions to naproxen have been reported in such patients.

Severe hepatic, renal and cardiac failure (see section 4.4).

During the last trimester of pregnancy (see section 4.6).

Active or a history of gastrointestinal bleeding or perforation, related to previous NSAID therapy.

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 use of Stirlescent with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

Elderly:
The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal. In the elderly the clearance is reduced. Use of the lower end of the dosage range is recommended (see section 4.2).

Prolonged use of NSAIDs in the elderly is not recommended. Where prolonged therapy is required, patients should be reviewed regularly.

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 Stirlescent after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

Gastrointestinal bleeding, ulceration 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 (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).

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 (see section 4.8).
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. When GI bleeding or ulceration occurs in patients receiving Stirlescent, the treatment should be withdrawn. Episodes of gastrointestinal bleeding have been reported in patients with naproxen therapy. Stirlescent should be given under close supervision to patients with a history of gastrointestinal disease.

Studies to date have not identified any subset of patients not at risk of developing peptic ulcer and bleeding. However the elderly and debilitated patients tolerate gastrointestinal ulceration or bleeding less well than others. Most of the serious gastrointestinal events associated with non-steroidal anti-inflammatory drugs occurred in this patient population.

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or antiplatelet agents such as aspirin (see section 4.5).

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).

Skin reactions:
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 therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Stirlescent should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

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.

Renal failure linked to reduced prostaglandin production:
The administration of an NSAID may cause a dose dependent 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, angiotensin converting enzyme inhibitors, angiotensin-II receptor antagonists and the elderly. Renal function should be monitored in these patients (see also Section 4.3).

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 and patients should be adequately hydrated. Stirlescent 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 Stirlescent 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.

Hepatic effects:
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 non-steroidal anti-inflammatory drugs. Cross reactivity has been reported.

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 Stirlescent dosing is unknown but it is prudent to use the lowest effective dose.

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 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, bronchial asthma or allergic disease.

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

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 anti-coagulation therapy (e.g. dicoumarol derivatives) may be at increased risk of bleeding if given naproxen-containing products concurrently.

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.

Precautions related to fertility:
The use of Stirlescent 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 infertility, withdrawal of Stirlescent should be considered.

Sodium/fluid retention in cardiovascular conditions and peripheral oedema:
Mild peripheral oedema has been observed in a few patients receiving naproxen. 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 Stirlescent.

Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

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

Combinations with other NSAIDs:
The combination of naproxen-containing products and other NSAIDs is not recommended, because of the cumulative risks of inducting serious NSAID-related adverse events.

Benzyl alcohol:
This medicine contains 0.52 mg benzyl alcohol in each effervescent tablet. Benzyl alcohol may cause allergic reactions.

Sodium:
This medicinal product contains 342.01 mg sodium per effervescent tablet, equivalent to 17.1% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

For most indications, the maximum daily dose of this product (1000 mg) is equivalent to 68.4% of the WHO recommended maximum daily intake for sodium. For acute gout treatment, the maximum daily dose (1250 mg) is equivalent to 85.5% of the WHO recommended maximum daily intake for sodium.

Stirlescent is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

Sorbitol:
This medicine contains 0.097 mg sorbitol (E420) in each effervescent tablet.

4.5 Interaction with other medicinal products and other forms of interaction

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

Due to the high plasma protein binding of naproxen, patients simultaneously receiving hydantoins, anticoagulants, other NSAIDs, aspirin or a highly protein-bound sulphonamide should be observed for signs of overdosage of these drugs. Patients simultaneously receiving Stirlescent and a hydantoin, sulphonamide or sulphonylurea should be observed for adjustment of dose if required.

It is considered unsafe to take NSAIDs in combination with warfarin or heparin unless under direct medical supervision. 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. NSAIDs may enhance the effects of anti-coagulants such as warfarin.

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).

Anti-hypertensives: Reduced anti-hypertensive effect of propranolol and other beta-blockers and may increase the risk of renal impairment associated with the use of ACE-inhibitors.

Diuretics, ACE inhibitors and Angiotension II Antagonists: NSAIDs may reduce the effect ofdiuretics and other anti-hypertensive drugs. Diuretics can increase the risk of nephrotoxicity of NSAIDs. In some patients with compromised renal function (e.g. dehydrated patients or the elderly with compromised renal function) the co-administration of an ACE inhibitor or angiotensin II antagonist and agents that inhibit cyclooxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible.

These interactions should be considered in patients taking naproxen concomitantly with ACE inhibitors or angiotensin II antagonists. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated, and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter.

Probenecid: Probenecid given concurrently increases naproxen plasma levels and extends its half-life considerably.

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

Lithium: Decreased elimination of lithium, leading to increased lithium plasma concentrations.

Methotrexate: Caution is advised where methotrexate is administered concurrently because of possible enhancement of its toxicity, since naproxen, in common with other non-steroidal anti-inflammatory drugs, has been reported to reduce tubular secretion of methotrexate in an animal model.

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: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see section 4.4).

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.

Furosemide: 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.

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.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding (see section 4.4).

Tacrolimus: Possible increased 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.

It is suggested that Stirlescent therapy be temporarily discontinued 48 hours before adrenal function tests are performed, because naproxen may artifactually interfere with some tests for 17-ketogenic steroids. Similarly, naproxen may interfere with some assays of urinary 5-hydroxyindoleacetic acid.

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. As with other drugs of this type, naproxen produces a delay in parturition in animals and also affects the human foetal cardiovascular system (closure of the ductus arteriosus). Use of Stirlescent in the last trimester of pregnancy is contraindicated (see Section 4.3). NSAIDs should not be used during the first two trimesters of 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 their prostaglandin synthesis inhibitory effect, naproxen may adversely affect foetal circulation and inhibit uterine contractions thus increasing the risk of uterine haemorrhage.

Breast-feeding

Naproxen has been found in the milk of lactating mothers. Do not use in patients who are breast-feeding.

Fertility

The use of naproxen 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 infertility, withdrawal of naproxen should be considered (see section 4.4).

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue, vertigo, insomnia, depression and visual disturbances are possible after taking Stirlescent. If patients experience these or similar undesirable effects, they should not drive or operate machinery.

4.8 Undesirable effects

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

Gastrointestinal disorders:
The most commonly-observed adverse events are gastrointestinal in nature. Inflammation, bleeding (sometimes fatal, particularly in the elderly), ulceration, perforation and obstruction of the upper and lower GI tract (see section 4.4). Heartburn, nausea, oesophagitis vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, stomatitis, exacerbation of ulcerative colitis and Crohn's disease (see section 4.4), pancreatitis and gastritis have been reported following administration.

Immune system disorders:
Hypersensitivity reactions have been reported following treatment with NSAIDs in patients with or without a history of previous hypersensitivity reactions 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, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

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

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) (see section 4.4).

Renal and urinary disorders:
Nephrotoxicity in various forms, including glomerulonephritis, haematuria, raised serum creatinine, renal papillary necrosis, interstitial nephritis, nephrotic syndrome and renal failure.

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

Nervous system disorders:
Visual disturbances, retrobulbar optic neuritis, headaches, light-headedness paraesthesia, convulsions, cognitive dysfunction, inability to concentrate, 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), dizziness and drowsiness.

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

Skin and subcutaneous tissue disorders:
Skin rashes including fixed drug eruption, itching (pruritus), urticaria, ecchymoses, purpura, sweating, angioedema. Alopecia, erythema multiforme, bullous reactions including Stevens-Johnson syndrome, erythema nodosum, lichen planus, pustular reaction, SLE, epidermal necrolysis, very rarely toxic 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, mild peripheral oedema, fatigue and malaise.

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

Vascular disorders:
Hypertension, vasculitis.

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

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

Metabolic and nutrition disorders:
Hyperkalaemia.

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

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 HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

a) Symptoms
Symptoms include headache, nausea, heartburn, indigestion, metabolic acidosis, apnoea, vomiting, epigastric pain, gastrointestinal bleeding, diarrhoea, disorientation, excitation, drowsiness, dizziness, tinnitus, fainting, hypoprothrombinaemia. Hypertension, respiratory depression and coma may occur after ingestion of NSAIDs but are rare.

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

In cases of significant poisoning acute renal failure and liver damage are possible.

Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs (see section 4.4) and may occur following an overdose.

b) Therapeutic measure
Patients should be treated symptomatically as required.
There are no specific antidotes.
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. Forced diuresis, alkalinisation of urine, haemodialysis or haemoperfusion may not be useful due to high protein binding.

Good urine output should be ensured.

Renal and liver function should be closely monitored.

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

Frequent or prolonged convulsions should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition.

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, non-steroids, propionic acid derivatives, ATC code: M01AE02

Naproxen has been shown to have anti-inflammatory, analgesic and antipyretic properties when tested in classical animal test systems.

Naproxen exhibits its anti-inflammatory effect even in adrenalectomised animals, indicating that its action is not mediated through the pituitary-adrenal axis. Like other NSAIDs, naproxen inhibits prostaglandin synthetase. However, the exact mechanism of its anti-inflammatory action is not known.

5.2 Pharmacokinetic properties

Naproxen is completely absorbed from the gastrointestinal tract, and peak plasma levels are reached in 2 to 4 hours. Naproxen is present in the blood mainly as unchanged drug, extensively 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 is almost entirely via the urine, mainly as conjugated naproxen, with some unchanged drug. 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.

5.3 Preclinical safety data

Carcinogenicity:

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

Mutagenicity:

Mutagenicity was not seen in *Salmonellatyphimurium*(5 cell lines), *Saccharomycescerevisiae*(1 cell line) and mouse lymphoma tests.

Fertility:

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

Teratogenicity:

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

Perinatal/Postnatal Reproduction:

Oral administration of naproxen to pregnant rats at doses of 2, 10 and 20 mg/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

Citric acid
Sodium hydrogen carbonate
Sodium carbonate
Sodium cyclamate
Saccharin sodium
Sodium citrate
Povidone
Macrogol 6000
Mannitol (E421)
Simeticone
Docusate sodium
Blackcurrant Flavour*

*blackcurrant flavour contains benzyl alcohol and sorbitol (E420)

6.2 Incompatibilities

Not known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Polypropylene tube with polyethylene desiccant stopper or laminated aluminium paper foil.
Pack sizes: 10, 12, 15, 20, 24 and 30 effervescent tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Doses of 1 to 2 tablets must be dissolved in at least 150 ml (a glass) of water, doses of 3 tablets must be dissolved in 300 ml. The glass should be rinsed with a small amount of water (10 ml) and the contents drunk.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA23138/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 29th January 2016
Date of Last Renewal: 19th November 2020

10 DATE OF REVISION OF THE TEXT

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