Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Strepsils Intensive Mint 8.75 mg Granules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One sachet with 850 mg granules contains 8.75 mg of flurbiprofen

Excipient: 4.25 mg of aspartame/sachet

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Granule
White to cream-coloured, free-flowing granule with a characteristic mint odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Strepsils Intensive Mint 8.75mg Granules are indicated for the short term symptomatic relief of sore throat.

Strepsils Intensive Mint 8.75mg Granules are indicated in adults and children over the age 12 years

4.2 Posology and method of administration

Method of Administration: For oral use only.

Indicated for adults and children over the age of 12 years:
One sachet of granules to be dissolved in the mouth, then swallowed. Strepsils Intensive Mint 8.75mg Granules can be taken every 3-6 hours as required, up to a maximum of 5 sachets of granules in a 24 hour period.

The product should not be used for more than 3 days. Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

There are no specific requirements in relation to food and drink.

Paediatric population
The safety and efficacy of Strepsils Intensive Mint 8.75mg Granules in children under 12 years has not been established.

Elderly population
A general dose recommendation cannot be given, since to date clinical experience is limited. The elderly are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

4.3 Contraindications

Hypersensitivity to flurbiprofen or any of the excipients in the product.

Patients who have previously shown hypersensitivity reactions (e.g. asthma, bronchospasm, rhinitis, angiodema or urticaria) in response to aspirin (acetylsalicylic acid) or other NSAIDs.

Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration) and intestinal ulceration.

History of gastrointestinal bleeding or perforation, severe colitis, haemorrhagic or haematopoietic disorders related to previous NSAIDs therapy.

Last trimester of pregnancy (See section 4.6)

Severe heart failure, renal failure or hepatic failure (see section 4.4).

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).

Phenylketonuria
Strepsils Intensive Mint 8.75mg Granules contains aspartame which is a source of phenylalanine and this may be harmful for people with phenylketonuria.

Elderly population
The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.

Respiratory
Bronchospasm may be precipitated in 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. Strepsils Intensive Mint 8.75mg Granules should be used with caution in these patients.

Other NSAIDs
The use of Strepsils Intensive Mint 8.75mg Granules with concomitant NSAIDs including cyclo-oxygenase-2 selective inhibitors should be avoided (see section 4.5).

Systemic lupus erythematosus (SLE) and mixed connective tissue disease
Patients with SLE and mixed connective tissue disease may have an increased risk of aseptic meningitis (see section 4.8).

Renal Impairment
NSAIDs have been reported to cause nephrotoxicity in various forms including interstitial nephritis, nephrotic syndrome and renal failure. 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 and the elderly. Renal function should be monitored in these patients (see also section 4.3). The habitual administration of analgesics may lead to persistent kidney damage with the risk of renal failure, particularly in combination of several analgesic substances, but this is not usually seen with short term, limited use products such as Strepsils Intensive Mint 8.75mg Granules.

Hepatic Impairment
Flurbiprofen is hydrolysed in the liver and impaired hepatic function may reduce the rate at which the drug is removed from the body. At the short term, low doses of Strepsils Intensive Mint 8.75mg Granules this is not believed to be of significant concern.

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 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). There are insufficient data to exclude such a risk for flurbiprofen.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with flurbiprofen 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).

Effects on the Nervous System
In the event of prolonged use of analgesics or use beyond the regulations cephalea may occur, which must not be treated with increased doses of the medicinal product.

Impaired female fertility
There is some evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

It is recommended to discontinue the use of flurbiprofen treatment in women attempting to conceive, in women who have difficulties conceiving and women who are undergoing investigation of infertility.

Gastrointestinal
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).

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 acetylsalicylic acid, or other drugs likely to increase gastrointestinal risk (see below and 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, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as acetylsalicylic acid (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving flurbiprofen, the treatment should be withdrawn.

Haematological effects
Flurbiprofen, like other NSAIDs, may inhibit platelet aggregation and prolong bleeding time. Strepsils Intensive Mint 8.75mg Granules should be used with caution in patients with a potential for abnormal bleeding.

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 therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Strepsils Intensive Mint 8.75mg Granules should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Infections
Since in isolated cases an exacerbation of infective inflammations (e.g. development of necrotising fasciitis) has been described in temporal association with the use of systemic NSAIDs as a class, the patient is advised to consult a physician immediately if signs of a bacterial infection occur or worsen during the Strepsils Intensive Mint 8.75mg Granules therapy. It should be considered whether initiation of an anti-infective antibiotic therapy is indicated. In cases of purulent bacterial pharyngitis/tonsillitis, Strepsils Intensive Mint 8.75mg Granules should be used with antibiotic therapy.

If the symptoms get worse or if new symptoms occur the treatment should be re-evaluated.

If mouth irritation occurs, treatment should be withdrawn.

4.5 Interaction with other medicinal products and other forms of interaction

Flurbiprofen should be avoided in combination with:

Other NSAIDS including cyclooxygenase-2 selective inhibitors
Avoid concomitant use of two or more NSAIDs, unless advised by a doctor, as this may increase the risk of adverse effects (esp. gastrointestinal adverse events as ulcers and bleeding), (see section 4.4).

Acetylsalicylic acid (low dose)
As with other products containing NSAIDs, concomitant administration of flurbiprofen and aspirin is not generally recommended because of the potential for adverse events. Unless low-dose aspirin (not above 75mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (see section 4.4).

Flurbiprofen should be used with caution (not recommended) in combination with:

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

Anti-platelet Agents
Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

Antihypertensive drugs (Diuretics, ACE inhibitors, angiotensin-II-antagonists)
NSAIDs may reduce the effect of diuretics and other antihypertensive drugs may enhance nephrotoxicity caused by inhibition of cyclooxygenase, especially in patients with compromised renal function (Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter).

Alcohol
May increase the risk of adverse reactions, especially of bleeding in the gastrointestinal tract.

Cardiac glycosides
NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels - adequate control and, if necessary, dose adjustment is recommended.

Ciclosporin
Increased risk of nephrotoxicity.

Corticosteroids
May increase the risk of adverse reactions, especially of the gastrointestinal tract (see section 4.3).

Lithium
May increase serum levels of glycosides – adequate control and, if necessary, dose adjustment is recommended.

Methotrexate
The administration of NSAIDs within 24 hours before or after administration of methotrexate may lead to elevated concentrations of methotrexate and an increase in its toxic effect.

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

Oral antidiabetics
Alteration of blood glucose levels reported (increased check rate recommended).

Phenytoin
May increase serum levels of phenytoin – adequate control and, if necessary, dose adjustment is recommended.

Potassium sparing diuretics
Concomitant use may cause hyperkaliaemia (check of serum potassium is recommended).

Probenecid Sulfinpyrazone
Medicinal products that contain probenecid or sulfinpyrazone may delay the excretion of flurbiprofen.

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.

Selective serotonin reuptake inhibitors (SSRI's)
Increased risk of gastrointestinal ulceration or 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.

No studies so far have revealed any interactions between flurbiprofen and tolbutamide or antacids.

4.6 Fertility, pregnancy and lactation

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor had been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increase incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, flurbiprofen should not be given unless clearly necessary. If flurbiprofen is used by a women attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low as possible and duration of treatment as short as possible,

During the third trimester of pregnancy, all prostaglandin synthesis inhitibitors may expose the foetus to:
- Cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension)
- Renal dysfunction, which may progress to renal failure with olgio-hydroamniosis;
- The mother and the neonate, at the end of pregnancy, to:
- Possible prolongation of bleeding time, an anti-aggregation effect which may occur even at very low doses.

- Inhibitions of uterine contractions resulting in delayed or prolonged labour.

Consequently, flurbiprofen is contraindicated during the third trimester of pregnancy.

Breastfeeding
In limited studies, flurbiprofen appears in the breast milk in very low concentration. However, because of possible adverse effects of NSAIDs on breast-fed infants, Strepsils Intensive Mint 8.75mg Granules are not recommended for use in nursing mothers.

Female fertility
There is some evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

Dizziness and visual disturbances are possible undesirable effects after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

a) Summary of safety profile

Low dose Flurbiprofen indicated for the short term treatment of sore throats exhibits primarily gastrointestinal adverse events. These are non-serious and transient in nature. Other non-serious, transient events noted during clinical assessment are typical of the patient group likely to be seeking alleviation of sore throat and similar symptoms associated with colds and influenza-type illness.

Common undesirable effects include a burning sensation or discomfort in the mouth, alteration of taste, headache and diarrhoea. All of these effects are transient and non-serious in nature.

b) Summary of adverse reactions

The following list of adverse effects relates to clinical assesment with flurbiprofen 8.75mg at OTC doses for short-term use.

(Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1000 to <1/100), Rare (≥1/10000 to <1/1000), Very rare (<1/10000), not known (cannot be estimated from the available data))

Blood and lymphatic system disorders
Uncommon: Lymphadenopathy
Rare: Anaemia
Very Rare: Haematopoietic disorders

Cardiac disorders
Rare: Palpitations

Ear and labyrinth disorders
Uncommon: Ear pain
Rare: Ear congestion, Deafness, Ear discomfort, Vertigo

Eye disorders
Rare: Conjunctivitis, Eye irritation, Photophobia, Lacrimation increased, Occular hyperaemia, Vision blurred

Gastrointestinal disorders
Common: Abdominal pain (general, upper or lower), Diarrhoea, Mouth ulceration, Nausea, Oral discomfort, Oral pain, Parasthesia oral,
Uncommon: Abdominal discomfort, Abdominal distension, Constipation, Dry mouth, Dyspepsia, Dysphagia, Glossodynia, Hypoaesthesia oral, Oral dysaethesia, Stomatitis, Tongue ulceration, Vomiting
Rare: Flatulence, Gastroesophageal reflux, Gingival bleeding, Gingival pain, Gingival ulceration, Malaena, Oral pruritis, Swollen tongue, Tongue coated, Tongue dry
Very Rare: Hepatitis and cholestactic icterus (jaundice)

General disorders and administration site conditions
Common: Influenza-like illness
Uncommon: Chest discomfort, Fatigue, Malaise, Pain, Pyrexia
Rare: Asthenia, Chest pain, Oedema peripheral, Thirst, Chills, Feeling hot, Sensation of a foreign body, Swelling, Ulcer

Immune system disorders
Rare: Seasonal allergy

Infections and infestations
Common: Upper respiratory tract infection
Uncommon: Ear infection, Eye infection, Gingival infection, Influenza, Laryngitis, Lower respiratory tract infection, Nasopharyngitis, Oral herpes, Pharyngitis, Rhinitis, Sinusitis, Tonsillitis, Viral infection
Rare: Bronchitis, Peritonsilar abcess, Urinary tract infection, Vulvovaginal candidiasis

Investigations
Rare: Blood glucose increased, Body temperature increased

Metabolism and nutrition disorders
Rare: Dehydration.

Musculoskeletal and connective tissue disorders
Uncommon: Arthralgia, Back pain
Rare: Joint swelling, Neck pain, Muscle spasms, Pain in extremity,

Nervous system disorders
Common: Dizziness, Dysgeusia, Headache, Parasthesia,
Uncommon: Aphonia, Burning sensation, Migraine, Somnolence
Rare: Hypoaesthesia, Lethergy, Ageusia,

Psychiatric disorders
Uncommon: Insomnia,
Rare: Confusional state, Sleep disorder, Abnormal dreams

Renal and urinary disorders
Rare: Pollakiuria, Urinary abnormality, Chromaturia, Interstitial nepritis, Nephritis syndrome

Reproductive system and breast disorders
Rare: Menorrhagia

Respiratory, thoracic and mediastinal disorders
Common: Cough, Oropharyngeal pain, Throat irritation, Wheezing
Uncommon: Asthma, Dry throat, Dysphonia, Dysponoea, Epistaxis, Increased upper airway secretion, Nasal congestion, Nasal discomfort, Pharyngeal erythema, Pharangeal hypoaesthesia, Productive cough, Rales, Rhinalgia, Rhinorrhoea, Sneezing,
Rare: Bronchospasm, Haemoptysis, Oropharangeal blistering, Pharangeal oedema, Sinus congestion, Aggravation of asthma

Skin and subcutaneous tissue disorders
Uncommon:Hyperhidrosis, Pruritus, Rash, Rash pruritic,
Rare: Acne, Dry skin, Eczema, Psoriasis, Skin nodule, Swelling face
Very Rare: Stevens-Johnson syndrome, Lyell syndrome

Vascular disorders
Rare: Hot flush

Adverse reactions reported with flurbiprofen, tablet form (i.e. at a higher dose and/or in the treatment of chronic conditions, under long-term treatment, not indicated for the Strepsils Intensive Mint 8.75mg Granules).

(Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1000 to <1/100), Rare (≥1/10000 to <1/1000), Very rare (<1/10000), not known (cannot be estimated from the available data))

Cardiac disorders
Very rare: Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment. Clinical trial 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).

Blood and lymphatic system disorders
Rare: haematological reactions (including anaemia, prolonged bleeding time)
Very rare: thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia).

Respiratory, thoracis and mediastinal disorders
Rare: bronchospasm, dyspnoea

Gastrointestinal disorders
Rare: GI bleeding, ulceration and perforation and ulcerative stomatitis

Renal and urinary disorders
Rare: renal dysfunction (including interstitial nephritis, nephritic syndrome and renal failure)

Skin and subcutaneous tissue disorders
Very rare: skin reactions (including Stevens Johnson syndrome and Lyell's syndrome)

General disorders and administration site conditions
Rare: Fever

Immune System disorders
Very rare: anaphylactic shock

Hepatobiliary disorders
Very rare: hepatic disorders (including hepatitis and cholestatic jaundice)

Adverse events associated with use of NSAIDs in general

(Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1000 to <1/100), Rare (≥1/10000 to <1/1000), Very rare (<1/10000), not known (cannot be estimated from the available data))

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

Clinical trial and epidemiological data suggest that use of NSAIDs (particularly at high doses 2400 mg daily) 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).

Blood and lymphatic system disorders
Very rare: Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.

Nervous System disorders
Uncommon: Headache
Very rare: Aseptic meningitis – single cases have been reported very rarely.

Respiratory, thoracis and mediastinal disorders
Exacerbation of asthma and bronchospasm.

Gastrointestinal disorders
The most commonly-observed adverse events are gastrointestinal in nature.
Uncommon: abdominal pain, nausea, dyspepsia.
Rare: diarrhea, flatulence, constipation and vomiting.
Very rare: peptic ulcer, perforation or gastrointestinal haemorrhage, melaena, haematemesis, sometimes fatal, particularly in the elderly. Ulcerative stomatitis, gastritis. Exacerbation of colitis and Crohn's disease (see section 4.4).

Renal and Urinary disorders
Very rare: Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema.

Skin and subcutaneous tissue disorders
Uncommon: Various skin rashes.
Very rare: Severe forms of skin reactions such as bullous reactions, including Stevens Johnson Syndrome, erythema multiforme and toxic epidermal necrolysis can occur.

Immune System disorders
Uncommon: Hypersensitivity reactions with urticaria and pruritus.
Very rare: severe hypersensitivity reactions. Symptoms could be facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension, (anaphylaxis, angioedema or severe shock).
In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with ibuprofen, single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed (see section 4.4).

Hepatobiliary disorders
Very rare: liver disorders.

c) Description of selected adverse events.

Consumers of low-dose flurbiprofen indicated for the treatment of sore throat may experience sensations described variously as burning, tingling or prickling in the mouth. The sense of taste may also be affected. These phenomenon are non-serious and transient in nature.

Headaches may also be experienced which are also transient and non-serious.

Some individuals may suffer minor, temporary gastrointestinal discomfort.

Flurbiprofen belongs to the pharmacological class of drugs known as non-steroidal anti-inflammatory drugs (NSAIDs) Hypersensitivity reactions to NSAIDs have occasionally been reported and these may consist of:

(a) Non-specific allergic reactions and anaphylaxis
(b) Respiratory tract reactivity, e.g. asthma, aggravated asthma, bronchospasm, dyspnoea
(c) Various skin reactions, e.g. pruritus, urticaria, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

4.9 Overdose

Symptoms
Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache, and gastrointestinal bleeding are also possible. In more serious poisoning with NSAIDs, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation, blurred vision and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning with NSAIDs metabolic acidosis may occur and the prothrombin time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

Management
Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal or gastric lavage and if necessary correction of serum electrolytes if the patient presents within one hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma. There is no specific antidote to flurbiprofen.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Other throat preparations, throat preparations

ATC Code: R02 AX01

Flurbiprofen is a propionic acid derivative NSAID which acts through inhibition of prostaglandins synthesis. In humans flurbiprofen has potent analgesic, antipyretic and anti-inflammatory properties. According to studies using the whole blood assay, flurbiprofen is a mixed COX-1/COX-2 inhibitor with some selectivity towards COX−1.

Pre-clinical studies suggest that the R (-) enantiomer of flurbiprofen and related NSAIDs may act on the central nervous system; the suggested mechanism is by inhibition of induced COX−2 at the level of the spinal cord.

Strepsils Intensive Mint 8.75mg Granules have been demonstrated to relieve sore throat through a reduction in severity of throat soreness from 1 minute (-0.95; SD=1.45) and over 6 hours (-2.25; SD=1.76), sore throat pain relief with significance from 1 minutes (2.58; SD=1.37) and over 6 hours (3.26; SD=1.52), relief from difficulty swallowing with significance from 5 minutes (-13.63; SD=16.15) and over 6 hours (-23.50; SD=15.96) and reduction in sore throat pain intensity from 5 minutes (-13.81; SD=15.96) and over 6 hours (-22.62; SD=18.63). Multiple dose efficacy has also been observed. Patients also recorded a significant improvement in wellbeing at 3 hours and after 3 days treatment.

The mint flavoured granule format dissolves quickly in the mouth and contains polymers for adherence and retention.

Paediatric Population
No specific studies in children have been undertaken, although efficacy and safety studies on Strepsils Intensive Mint 8.75mg Granules have included children 12 – 17 years, although small sample size means that no statistical conclusions can be drawn.

5.2 Pharmacokinetic properties

Absorption
Strepsils Intensive Mint 8.75mg Granules dissolve rapidly and the flurbiprofen is readily absorbed, with plasma concentrations peaking at 60 - 70 minutes. Absorption of flurbiprofen can occur from the buccal cavity by passive diffusion. Rate of absorption is dependent on pharmaceutical form with peak concentrations achieved more rapidly than, but of similar magnitude to, those achieved after an equivalent swallowed dose, but more slowly than an equivalent lozenge dose.

Distribution
Flurbiprofen is rapidly distributed throughout the body and is extensively bound to plasma proteins.

Metabolism / Excretion
Flurbiprofen is mainly metabolised by hydroxylation and excreted via the kidneys. It has an elimination half-life of 3 to 6 hours. Flurbiprofen is excreted in very small amounts in human milk (less than 0.05ug/ml). Approximately 20-25% of a flurbiprofen oral dose is excreted unchanged.

Special Groups
No difference in pharmacokinetic parameters between elderly and young adult volunteers has been reported following oral administration of flurbiprofen tablets. No pharmacokinetic data have been generated in children below 12 years of age following administration of flurbiprofen 8.75 mg however administration of both flurbiprofen syrup and suppository formulations indicate no significant differences in pharmacokinetic parameters compared with adults.

5.3 Preclinical safety data

Flurbiprofen displays dose dependent effects typical of NSAIDS, including gastrointestinal effects such as ulceration, bleeding and perforation in rats, delayed onset and duration of parturition in pregnant rats, especially when exposure occurs late in pregnancy.

Genotoxicity
In-vitro and in-vivo studies to assess the genotoxicity potential of flurbiprofen demonstrate that the drug is unlikely to pose a risk of genotoxicity among humans. The chemical structure of flurbiprofen does not contain structural alerts for genotoxicity and NSAIDS are not considered to be mutagenic.

Systemic Toxicity
The principle toxic reaction to flurbiprofen is gastrointestinal erosion and ulceration in all species studies, with death at high doses due to ulceration and associated peritonitis. Renal papillary necrosis, liver toxicity and anaemia have been documented in several species.

Carcinogenicity
Carcinogenicity studies in mice and rats revealed no evidence of treatment related carcinogenicity.

Reproductive and Developmental toxicology
Fertility, reproductive performance and foetal development have been studied in rats and mice. Dose-dependent effects on dams (female rats) and offspring observed in these studies included prolonged pregnancy and labour, increased numbers of stillbirths, gastrointestinal ulceration and reduction in number of pups born to rats. Transfer of flurbiprofen to foetus and transfer from mother’s milk to the neonate have been observed, but no evidence of teratogenic effects has been seen.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Xylitol
Mannitol
Carbomer
Sodium hydrogen carbonate
Cool Mix for Mint Flavour
Peppermint flavour
Aspartame
Citric Acid anhydrous
Silicon Dioxide
Sodium Chloride

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 25°C

6.5 Nature and contents of container

Each sachet is composed of:
12 micron Polyester (PET)12 micron Polyethylene (PE)/9 micron Aluminium/37 gsm Polyethylene (PE)
Or
12 micron Polyester (PET)12 micron Polyethylene (PE)/12 micron Aluminium/37 gsm Polyethylene (PE)

Pack sizes contain 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 sachets. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements

7 MARKETING AUTHORISATION HOLDER

Reckitt Benckiser Ireland Ltd
7 Riverwalk,
Citywest Business Campus,
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA979/041/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 15th March 2013

10 DATE OF REVISION OF THE TEXT

August 2013