IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0678/061/001
Case No: 2034532

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

GlaxoSmithKline Consumer Healthcare (Ireland) LTD

Stonemasons Way, **Rathfarnham**, **Dublin 16**, **Ireland**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Solpaflex 300mg Prolonged Release Capsules

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **29/08/2007** until **28/10/2009**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Solpaflex 300mg Prolonged Release Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ibuprofen 300 mg.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release capsules, hard
Prolonged release capsule, transparent with a clear orange cap printed with a red logo ‘Solpaflex’.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the symptomatic relief of rheumatic and muscular pain, backache, headache, dental pain, dysmenorrhoea, fever, colds and influenza.

4.2 Posology and method of administration

Directions for use
Solpaflex Sustained Release Capsules should be swallowed with water. The capsule should not be chewed or sucked as this destroys the sustained release properties. For patients who experience difficulty in swallowing the capsule, the contents of a capsule may be sprinkled onto a spoonful of cold, soft food, yoghurt, or similar substance.
Treatment should be reviewed at regular intervals and discontinued if no benefit is seen or if intolerance occurs.

Recommended Dose

Adults and children aged 12 years and over:
Usual starting dose is two capsules (600 mg) twice daily, taken morning and night. Maintenance dose: One to two capsules twice daily.

Children:
Not recommended for children under 12 years.

Elderly:
Non-steroidals should be used with particular caution in elderly patients who are more prone to adverse events. The lowest dose compatible with adequate safe clinical control should be employed. See also section 4.4.

4.3 Contraindications

Solpaflex Capsules are contraindicated in patients with hypersensitivity to ibuprofen or any of the other ingredients of these capsules. Also contraindicated in patients with hypersensitivity to aspirin or any other non-steroidal anti-inflammatory (NSAID)(symptoms include asthma, rhinitis or urticaria).
History of gastrointestinal bleeding or perforation, related to previous NSAID therapy. Active or history of recurrent

peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding.
Patients with severe heart failure.

4.4 Special warnings and precautions for use

The use of Solpaflex Sustained Release Capsules with concomitant NSAIDs including cyclo-oxygenase-2 selective inhibitors should be avoided.

Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration necessary to control symptoms.

Elderly: the elderly 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 the elderly is not recommended. Where prolonged therapy is required, patients should be reviewed regularly.

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, 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 Solpaflex Sustained Release Capsules, the treatment should be withdrawn.

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn’s disease) as their condition may be exacerbated (see section 4.8-undesirable effects)

In patients with renal, cardiac or hepatic impairment, caution is required since the use of NSAIDs may result in deterioration of renal function. Assessment of renal function should occur prior to the initiation of therapy and regularly thereafter.

As NSAIDs can interfere with platelet function, they should be used with caution in patients with intracranial haemorrhage and bleeding diathesis.

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.

Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patient with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with NSAID therapy. Undesirable effects may be minimised using the lowest effective dose for the shortest duration necessary to control symptoms (see GI cardiovascular risks below).

Cardiovascular and cerebrovascular effects:
Clinical trial and epidemiological data suggests that use of some NSAIDs, particularly at high doses (2400mg daily) and in long term treatment may be associated with a small increased risk of aertial thrombotic events (for example

myocardial infarction or stroke). NSAID therapy. Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200mg daily) is associated with an increased risk of myocardial infarction.

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Steven-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 of 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. Solpaflex Sustained Release Capsules should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

4.5 Interaction with other medicinal products and other forms of interaction

It is considered unsafe to take NSAIDs in combination with warfarin or heparin unless under direct medical supervision.

Care should be taken in patients treated with any of the following drugs as interactions have been reported:

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

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

Anti-hypertensives: reduced anti-hypertensive effect.

Diuretics: reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce glomelural filtration rate (GFR) and increase plasma cardiac glycoside levels.

Lithium: decreased elimination of lithium.

Methotrexate: decreased elimination of methotrexate.

Cyclosporin: increased risk of nephrotoxicity with NSAIDs.

Other NSAIDs: avoid concomitant use of two or more NSAIDs..

Corticosteroids: increased risk of gastrointestinal bleeding or ulceration.

Aminoglycosides: reduction in renal function in susceptible individuals, decreased elimination of aminoglycoside and increased plasma concentrations.

Probenecid: reduction in metabolism and elimination of NSAIDs and metabolites.

Oral hypoglycemic agents: inhibition of metabolism of sulfonylurea drugs, prolonged half-life and increased risk of hypoglycaemia.

4.6 Pregnancy and lactation

Whilst no teratogenic effects have been demonstrated in animal experiments, the use of Solpaflex Sustained Release Capsules during pregnancy should be avoided. The onset of labour may be delayed and its duration increased**.** In the limited data available, ibuprofen appears in the breast milk in very low concentrations and is unlikely to affect the breast fed infant adversely.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The most common observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation, or GI bleeding, sometimes fatal in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4-Sepcial warnings and precautions for use) have been reported following administration. Less frequently, gastritis has been observed.

Bullous reactions including Steven-Johnson syndrome and toxic epidermal necrolysis (very rare).
Clinical trial epidemiological data suggests the use of ibuprofen (particularly at high doses 2400mg daily) and in long term treatment may be associated with a small increased or arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4). Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

Other side effects include headache, dizziness, hearing disturbance, renal or hepatic dysfunction. Also rashes, and very rarely, thrombocytopenia have been reported. Bronchospasm may be precipitated in patients with a history of aspirin sensitive asthma.

4.9 Overdose

The symptoms of overdose include headache, vomiting, drowsiness, and hypotension. The treatment of overdose is by gastric lavage and, if necessary, correction of serum electrolytes. There is no specific antidote to ibuprofen overdosage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ibuprofen is a non-steroidal anti-inflammatory agent with marked analgesic and antipyretic properties. Ibuprofen inhibits prostaglandin synthesis.

5.2 Pharmacokinetic properties

The product is a sustained release formulation of ibuprofen designed to give a longer elimination half-life compared with immediate release ibuprofen and a duration of action of approximately 12 hours. Ibuprofen is extensively bound to plasma proteins and has a half life of about 2 hours. Excretion is rapid and complete via the kidneys.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to those already included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule Contents:
Sugar spheres (sucrose and maize starch)
Stearic acid
Povidone

Capsule Shell Ingredients:
Sunset yellow (E110)

Gelatin

Printing Ink:
Shellac
Red iron oxide (E172)
Soya lecithin (food grade)
Dimeticone

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

Three years.

6.4 Special precautions for storage

Store in the original container.

6.5 Nature and contents of container

Blister strips made from PVC/PVdC (200 µm/60g/m^2) film with aluminium foil backing containing 12, 24, 36 or 48 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Consumer Healthcare (Ireland) Ltd
Stonemasons Way
Rathfarnham
Dublin 16

8 MARKETING AUTHORISATION NUMBER

PA 678/61/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29 October 1999

Date of last renewal: 29 October 2004

10 DATE OF REVISION OF THE TEXT

August 2007