IRISH MEDICINES BOARD ACTS 1995 AND 2006

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

(S.I. No.540 of 2007)

PA0417/017/001
Case No: 2067888

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

Seven Seas Ltd

Hedon Road, **Marfleet**, **Kingston-Upon-Hull HU9 5NJ**, **England**

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

Phensic 325mg/22mg Tablets

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 **15/03/2010**.

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

Phensic 325mg/22mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active constituents	mg/tablet
Acetysalcylic Acid (aspirin)	325.00
Caffeine	22.00

For excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet.

Smooth, white, capsule-shaped tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Indicated for the management of pain and fever such as may be associated with musculoskeletal disorders, headache, toothache, and for the relief of cold and flu symptoms.

4.2 Posology and method of administration

Directions for Use

Oral administration

Recommended Dose

Adults and Adolescents aged 16 years and over

Two tablets every 3 – 4 hours as required
Do not exceed 12 tablets in any period of 24 hours.

Do not give to children and adolescents aged under 16 years, except on medical advice, where the benefit outweighs the risk.

Elderly

The normal adult dose should be taken

NSAIDs 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

Known hypersensitivity reactions (e.g bronchospasm, rhinitis, urticaria) in response to aspirin, or to any of the other ingredients or to NSAIDs.

Active peptic ulceration, haemophilia, concurrent anti-coagulant therapy and gout.

History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy. Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

Severe heart failure.

4.4 Special warnings and precautions for use

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

Aspirin should only be given to children particularly those under the age of 16 on medical advice.

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

The use of Phensic 325mg/22mg Tablets with concomitant NSAIDs including cyclooxygenase-2-selective inhibitors should be avoided.

Undesirable effects may be reduced by using the minimum effective dose for the shortest duration possible. Patients treated with NSAIDs long-term should undergo regular medical supervision to monitor for adverse events.

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

Gastrointestinal bleeding, ulceration and 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 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 4.5).*

Prolonged use except under medical advice may be dangerous.

Take only when necessary. Consult your doctor if there is no improvement in 3 days.

Consult your doctor before taking this product if you are on any other medication.

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, anti-coagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents *(see section 4.5).*

When GI bleeding or ulceration occurs in patients receiving Phensic 325 mg/22mg Tablets, 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).*

Medical advice is required in patients suffering from asthma, allergic disease. 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 initiation of therapy and regularly thereafter.

There is possible association between aspirin and Reye's syndrome when given to children. Reye's syndrome is a very rare disease, which affects the brain and liver, and can be fatal. For this reason aspirin should not be given to children and adolescents aged under 16 years unless specifically indicated.

Elderly patients are particularly susceptible to the adverse effects of NSAIDs. Prolonged use of NSAIDas in the elderly is not recommended. Where prolonged therapy is required, patients should be reviewed regularly.

Phensic should be used with caution in patients with a history of peptic ulceration or inflammatory bowel disease.

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

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 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. Phensic 325mg/22mg Tablets should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

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 treatment.

Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention, hypertension and oedema have been reported in association with NSAID therapy.

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).*

Cardiovascular and cerebrovascular effects:

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 Phensic 325mg/22mgTablets when given at a daily dose of two tablets every 3 – 4 hours (not exceeding 12 tablets in any period of 24 hours) for 3 days.

4.5 Interaction with other medicinal products and other forms of interaction

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use *(see section 5.1).*

Aspirin may enhance the effects of phenytoin and may inhibit the action of uricosurics. Metopcloramide potentiates the effects of aspirin. Corticosteroids and large doses of antacids reduce plasma concentrations of aspirin.

It is considered unsafe to take aspirin 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-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 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 ulceration or bleeding *(see section 4.4)*

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

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

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

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

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

4.6 Pregnancy and lactation

Aspirin may prolong labour and contribute to maternal and neonatal bleeding, and should be avoided at term.

Due to the possible risk of Reye's syndrome, this product is not to be taken during lactation unless recommended by a doctor.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Aspirin may induce bronchospasm and attacks of asthma in susceptible individuals; very rarely skin rashes may occur. Aspirin may cause gastrointestinal disturbances such as nausea, dyspepsia and vomiting. It may induce gastric irritancy and gastrointestinal haemorrhaging in susceptible individuals. Caffeine may cause headache, restlessness and gastrointestinal disturbances such as nausea and dyspepsia

Aspirin

Respiratory, thoracic and mediastinal disorders

Aspirin may induce bronchospasm and attacks of asthma in susceptible individuals

Skin and subcutaneous tissue disorders
Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare), Skin rashes (very rarely)

Gastrointestinal disorders
The most commonly observed effects are gastrointestinal in nature. Aspirin may induce gastric irritancy and gastrointestinal haemorrhaging in susceptible individuals as well as may cause gastrointestinal disturbances such as:

Nausea,
Vomiting
Diarrhoea
Flatulence
Constipation
Dyspepsia
Abdominal pain
Melaena
Haematemesis
Ulcerative stomatitis
Exacerbation of colitis
Crohn's disease *(see section 4.4 – Special warnings and precautions for use)* have been reported following administration. Less frequently, gastritis has been observed.
Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur *(see section 4.4).*

General disorders and administration site conditions
Oedema has been reported in association with NSAID treatment.

Vascular disorders
Hypertension and arterial thrombotic events (for example myocardial infarction or stroke) have been reported in association with NSAID treatment,

Cardiac disorders
Cardiac failure has been reported in association with NSAID treatment and myocardial infarction may be associated use of some NSAIDs (particularly at high doses and in long term treatment)

Nervous system disorders
Stroke

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)*

Caffeine

Nervous system disorders
Caffeine may cause headache

Psychiatric disorders
Caffeine may cause restlessness

Gastrointestinal disorders
gastrointestinal disturbances such as nausea and dyspepsia.

4.9 Overdose

Mild chronic aspirin overdosage gives rise to the symptoms of salicylism. When fully developed, they consist chiefly of headache, dizziness, tinnitus, dimness of vision, mental confusion, lassitude, drowsiness, thirst, hyperventilation, nausea, vomiting and, occasionally, diarrhoea.

In more severe chronic overdosage, the symptoms of central nervous system disturbance are more pronounced: there may also be skin eruptions and marked alterations in the acid-base balance.

In acute overdosage, there is over-breathing, low blood pressure, low blood sugar, tinnitus, deafness and skin rashes, but most particularly severe sweating leading to dehydration. Coma may result.

High doses of caffeine may produce headache, tremor, nervousness and irritability.

Treatment of Acute Overdosage

Irrespective of the time interval since ingestion, gastric aspiration and lavage should be performed. Blood must be taken for plasma salicylate estimation. Forced alkaline diuresis may be needed. Electrolyte and acid/base balance should be monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherpaeutic group: Paracetamol, combinations excluding psycholeptics

ATC Code: N02BE51

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release aspirin (81mg), a decreased effect of ASA on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

Aspirin provides the analgesic, the antipyretic and anti-inflammatory actions required for the recommended indications.

Caffeine is a mild stimulant of the CNS.

5.2 Pharmacokinetic properties

Aspirin is absorbed into the systemic circulation from the stomach and upper intestine. It is rapidly distributed to the body tissues and is extensively bound to plasma proteins. It is excreted as salicylic acid and its glucuronide conjugate and as salicyluric acid.

Caffeine is absorbed from the gastrointestinal tract and distributed into all body compartments. It is metabolised primarily in the liver and excreted via the urine.

5.3 Preclinical safety data

Preclinical safety data on these active ingredients in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use of the product and which have not already been mentioned elsewhere in this summary.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize starch
Talc
Stearic acid

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

Five years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The tablets may be packed in either of the following containers:

i) PVC blister strips with aluminium foil backing. Pack sizes will be 6, 12, 24 or 48 tablets as follows:

Content: Six tablets per strip. The strips are contained in a boxboard carton (one or two strips).

Content: Twelve tablets per strip. The strips are contained in a boxboard carton (two or four strips).

ii) Cylindrical, white polyethylene (HDPE) bottle with a white polyethylene, child-resistant, tamper-evident, lined closure. The bottle is fitted with a polyether wad.

Pack size: 50 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements

7 MARKETING AUTHORISATION HOLDER

Seven Seas Limited
T/A Merck Consumer Health
Hedon Road
Marfleet
Kingston-upon-Hull HU9 5NJ
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 417/17/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10 March 1986

Date of last renewal: 10 March 2006

10 DATE OF REVISION OF THE TEXT

March 2010