Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Froben Tablets 25 mg.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 25 mg flurbiprofen.

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Coated tablets.
Yellow, circular, sugar-coated tablets, imprinted in black with an identifying motif (F25).

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Froben is indicated for the management of various arthroses such as rheumatoid arthritis and osteoarthritis, fibrositis, ankylosing spondylitis and other muscular syndromes such as low back pain. Froben is also used for the relief of acute and chronic pain.

4.2 Posology and method of administration

For oral administration.

Adults: The usual total daily dosage is 150 to 200 mg in divided doses. During the acute phase, the daily dose may be increased to 300 mg.

Elderly: NSAIDs should be used with particular caution in elderly patients. Dosage should be at the lowest level of the range. Prolonged use should be avoided. Those patients with impaired renal function may eliminate NSAIDs more slowly than normal. In these cases, Froben should be used with caution and dosage should be assessed individually.

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

4.3 Contraindications

Froben is contra-indicated in children and during lactation. It is also contra-indicated in patients with active peptic ulceration, gastrointestinal haemorrhage or ulcerative colitis.

Froben should not be used in patients with a history of asthma or in patients who have experienced bronchospasm, anaphylactic reactions, angioedema or other hypersensitivity-type reactions from the use of aspirin or other NSAIDs.

4.4 Special warnings and precautions for use

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

Froben should be used with caution in patients with a history of peptic or intestinal ulceration or bleeding.

NSAIDs have been reported to cause nephrotoxicity in various forms, including interstitial nephritis, nephrotic syndrome and renal failure. In patients with renal, cardiac or hepatic impairment, caution is required since the use of NSAIDs may result in deterioration of renal function. The dose should be kept as low as possible and renal function should be monitored in these patients prior to the initiation of treatment and regularly thereafter.

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

Caution is necessary if Froben is given to patients with a history of heart failure, hypertension or non-allergic asthma. As it has been shown that flurbiprofen may be used with caution in patients with a potential for abnormal bleeding or intracranial haemorrhage.

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:

Antihypertensives: 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 bleeding.

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

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

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

4.6 Pregnancy and lactation

Preclinical studies have not revealed any teratogenic effects. However, Froben should not be prescribed during pregnancy unless the benefits outweigh the possible risks. If Froben is used during early pregnancy, the lowest effective dosage should be employed. During the third trimester of pregnancy, regular use of NSAIDs has been associated with delayed and prolonged parturition and premature closure of the foetal ductus arteriosus *in utero* and possibly persistent pulmonary hypertension of the newborn.

The amount of flurbiprofen secreted into the breast milk during lactation is considered too small to be harmful. For this reason, breast feeding would not be contra-indicated.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Dyspepsia, nausea, vomiting, gastrointestinal haemorrhage, diarrhoea, mouth ulcers, fluid retention and oedema, as well as peptic ulceration and perforation, have been reported.

Urticaria, angioedema and rashes of varying description may occur. Very rarely, cholestatic jaundice and thrombocytopenia have been reported: these are usually reversible on withdrawal of the drug.

Very rarely, aplastic anaemia and agranulocytosis have been associated with the use of flurbiprofen but causality has not been established.

4.9 Overdose

Symptoms of overdosage may include nausea, vomiting and gastrointestinal irritation. Treatment should consist of gastric lavage and if necessary, correction of serum electrolytes. There is no specific antidote to flurbiprofen.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Flurbiprofen is a phenylpropionic acid-derived NSAID which has analgesic, anti-inflammatory and antipyretic properties. These are thought to result from the drug's ability to inhibit prostaglandin synthesis.

5.2 Pharmacokinetic properties

Flurbiprofen is well absorbed, reaching peak levels in the plasma 2-3 hours post-administration. Peak levels in the synovial fluid occur 6 hours post-administration. The drug is highly protein-bound and is slowly metabolised to inactive substances. The half-life is 4 hours with elimination mainly through the kidney.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose, lactose, talc, maize starch, titanium dioxide, povidone, liquid glucose, magnesium stearate, stearic acid, colloidal silicon dioxide, sandarac tablet varnish, carnauba wax, Opalux yellow AS-F-2230 and Opacode S-1-8152 black printing ink.

The colouring Opalux yellow AS-F-2230, contains sucrose, Quinoline Yellow Aluminium Lake (E104), titanium dioxide, FD& C Yellow No. 6 Aluminium Lake (sunset yellow E110), povidone and sodium benzoate.

The printing ink, Opacode S-1-8152 Black contains shellac, black iron oxide (E172), soya lecithin (E322) and dimeticone.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 months.

6.4 Special precautions for storage

Do not store above 25°C. Store in a dry place.

6.5 Nature and contents of container

PVC/Aluminium blister pack containing 10 tablets. The required number of blister packs are enclosed in printed cartons. Pack sizes: 100 tablets.

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

None.

7 MARKETING AUTHORISATION HOLDER

Abbott Laboratories Ireland Limited
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8 MARKETING AUTHORISATION NUMBER

PA0038/083/004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date if first authorisation: 10 November 1976

Date of last renewal: 10 November 2001