Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen 200mg Liquid Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 200mg ibuprofen.

Excipient: Also contains 0.606mg ponceau 4R (E124)

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Capsule, soft

A 7.5 minim oval capsule with a translucent red gelatin shell, containing a clear liquid, printed with 'NUROFEN' in white.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As an anti-inflammatory, analgesic and antipyretic for short term management of mild to moderate pain such as is associated with headache, dental pain, backache, feverishness, period pain, muscular strain, neuralgia, rheumatic pain and migraine and for the management of the symptoms of head colds and influenza.

4.2 Posology and method of administration

For oral administration. Do not chew.

Adults and children over 12 years: Initial dose is 400mg taken with water and subsequently if necessary, 200 to 400mg every four hours with a maximum of 1200mg in any 24 hour period.

Not for use by children under 12 years of age.

Elderly: *See section 4.4 Special Warnings and Special Precautions for Use.*

4.3 Contraindications

Severe heart failure.

Hypersensitivity to any of the constituents, aspirin, or other NSAIDs.

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 or other gastrointestinal disorder.

Patients with a history of bronchospasm, asthma, rhinitis, or urticaria associated with aspirin or other anti-inflammatory drugs.

Use in children under 12 years of age.

4.4 Special warnings and precautions for use

The use of Ibuprofen Liquid Capsules with concomitant NSAIDs including cycloosygenase-2 selective inhibitors should be avoided.

Undesirable effects may be minimised by using the minimum effective dose for the shortest duration necessary to control symptoms *(See section 4.2, and GI and cardiovascular risks below).*

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: GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without any warning symptoms or a pervious 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 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 Ibuprofen Liquid 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).*

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 and oedema have been reported in association with NSAID therapy.

Cardiovascular and cerebrovascular effects: Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (2400mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke).

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, 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. Ibuprofen Liquid Capsules should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Bronchospasm may be precipitated in patients suffering from, or with a previous history of, bronchial asthma or allergic disease.

Caution is required in patients with renal, cardiac and hepatic impairment since renal function may deteriorate. The dose should be as low as possible and renal function should be monitored.

Asthma sufferers, anyone allergic to or taking any other pain killer, or receiving regular treatment, pregnant women, and persons who are on a restricted potassium intake should only take Ibuprofen Liquid Capsules after consulting their doctor.

If symptoms persist for more than 3 days, patients should be advised to consult their doctor.

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.

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.

4.5 Interaction with other medicinal products and other forms of interaction

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding *(see section 4.4).*

Anti-coagulants: NSAIDs may enhance the effects of anticoagulants, 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).*

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-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 glomerular filtration rate 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.

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

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).*

4.6 Fertility, pregnancy and lactation

Whilst no teratogenic effects have been demonstrated in animal experiments, the use of Nurofen Liquid Capsules during pregnancy should, if possible, be avoided. The onset of labour may be delayed and duration of labour increased.

In limited studies, ibuprofen appears in the breast milk in very low concentration and is unlikely to affect the breast-fed infant adversely.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Gastro-intestinal:	The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly 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 – Special warnings and precautions for use)* have been reported following administration. Less frequently, gastritis has been observed. Abdominal pain, nausea and dyspepsia. Occasionally peptic ulcer and gastro-intestinal bleeding.
Skin:	Pruritis, urticaria. Rarely exfoliative dermatitis and epidermal necrolysis have been reported with ibuprofen.
Renal:	Papillary necrosis which can lead to renal failure.
Cardiovascular:	Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment. Cardiovascular and cerebrovascular effects: Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (2400mg daily) and in long term treatment may be associated with a small increased risk or arterial thrombotic events (for example myocardial infarction or stroke) *(see section 4.4).*
Others:	Hepatic dysfunction, headache, dizziness, hearing disturbance. Rarely thrombocytopenia.

4.9 Overdose

Symptoms include nausea, vomiting, dizziness, hypotension, drowsiness and, rarely, loss of consciousness. Large overdoses are generally well tolerated when no other drugs are involved. No specific antidote is available and supportive therapy is indicated. Treatment consists of gastric lavage and, if necessary, correction of serum electrolytes.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ibuprofen is a propionic acid derivative, having analgesic, anti-inflammatory and antipyretic activity. The drug's therapeutic effects as a non-steroidal anti-inflammatory are thought to result from inhibitory activity on prostaglandin synthetase.

Experimental data suggests 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 h before or within 30 min after immediate release aspirin dosing 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.

5.2 Pharmacokinetic properties

The ibuprofen from Ibuprofen Liquid Capsules is absorbed to the same extent as ibuprofen from Nurofen tablets, the $AUC_{0-\infty}$ being equivalent.

Ibuprofen is rapidly absorbed from Ibuprofen Liquid Capsules with maximum plasma concentration achieved in 30 minutes. In comparison, the maximum plasma concentration of Nurofen tablets is achieved in 60 minutes. When taken with food, plasma peak levels may be delayed.

Ibuprofen is extensively bound to plasma proteins. Ibuprofen diffuses into the synovial fluid.

Ibuprofen is metabolised in the liver to two major inactive metabolites and these together with unchanged ibuprofen are excreted by the kidney either as such or as conjugates.

Excretion by the kidney is both rapid and complete.

Elimination half-life is approximately 2 hours.

No significant differences in pharmacokinetic profile are observed in the elderly.

5.3 Preclinical safety data

No relevant information additional to that contained elsewhere in the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Macrogol 600
Potassium hydroxide 50 % solution
Anidrisorb 85/70 (hydrogenated glucose syrup)
Gelatin 150 bloom
Ponceau 4R (E124)
Opacode NSP-78-18022 (titanium dioxide,
Propylene glycol, polyvinyl acetate phthalate,
Macrogol 400)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

Blister push-through pockets formed from white opaque 250µm PVC/30µmPE/90gsmPVdC laminate heat sealed to 20µm aluminium foil. Each blister tray contains 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, 30, 32, 36, 40, or 48 capsules. The blister trays are packed in a cardboard carton.

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

Reckitt Benckiser Ireland Ltd
7 Riverwalk
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8 MARKETING AUTHORISATION NUMBER

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