Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nurofen Long Lasting 300 mg Prolonged Release Hard Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged release hard capsule contains 300 mg ibuprofen.

Excipients with known effect:
Each prolonged release hard capsule contains 34.5mg sucrose per capsule.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged release hard capsule.

Capsules with colourless transparent cap and body printed with "N 300" in red ink containing white granules.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Nurofen Long Lasting 300mg Prolonged Release Hard Capsules is indicated in adults and children over 12 years old.

For the short term management of backache and muscular pains and dysmenorrhoea.

4.2 Posology and method of administration

For Oral administration and short-term use only.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4).

The patient should consult a doctor if symptoms persist or worsen, or if the product is required for more than 3 days. If in adolescents this medicinal product is required for more than 3 days, of if symptoms worsen a doctor should be consulted.

Adults, the elderly and children over 12 years of age (weighing over 40kg):
300mg - 600mg up to twice a day as required.

Leave at least 8 hours between doses. Do not take more than 1200mg in any 24 hour period.

Oral use: the capsules should be swallowed whole with a sufficient quantity of liquid on an empty stomach or during a meal.

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

Nurofen Long Lasting 300mg Prolonged Release Hard Capsules is contraindicated in children under 12 years of age.

Elderly:
Non-steroidal anti-inflammatory drugs 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

This product should not be given to patients with/who have/are:

- Severe heart failure (NYHA Class IV), renal failure or hepatic failure (see section 4.4)
- 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 disorders.
- hypersensitive (eg. bronchospasm, asthma, rhinitis, angioedema, urticaria) to aspirin or other non-steroidal anti-inflammatory agents
- hypersensitivity to ibuprofen or any of the excipients listed in section 6.1
- Last trimester of pregnancy (see section 4.6)
- Under 12 years of age
- cerebrovascular or other active bleeding.
- coagulation disorders or bleeding diathesis.
- severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake).

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 relieve symptoms.

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

Other NSAIDs: The use of this product with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.

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

Renal and Hepatic Impairment: In patients with renal or hepatic impairment, caution is required since the use of NSAIDs may result in deterioration of renal and/or hepatic function. Assessment of renal function should occur prior to the initiation of therapy and regularly thereafter (see section 4.3 and 4.8).

SLE and mixed connective tissue disease: Ibuprofen should be used with caution in patients with Systemic lupus erythematosus and mixed connective tissue disease, due to increased risk of aseptic meningitis (see section 4.8).

Gastrointestinal Effects: 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).

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 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 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 Nurofen Long Lasting 300mg Capsules, the treatment should be withdrawn.

Cardiovascular and Cerebrovascular 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, hypertension and oedema have been reported in association with NSAID therapy.

Clinical studies suggest that use of ibuprofen, particularly at high doses (2400mg daily) 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/day) is associated with an increased risk of arterial thrombotic events.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided.

Careful consideration should also be exercised before initiating longer-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400mg/day) are required.

Blood effects: As NSAIDs can interfere with platelet function, they should be used with caution in patients with idiopathic thrombocytopenic purpura (ITP), intracranial haemorrhage and bleeding diathesis.

Severe Skin Reactions: Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported 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. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Ibuprofen should be discontinued at the first appearance of signs and symptoms of severe skin reactions such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

Masking of symptoms of underlying infections:

Nurofen Long Lasting Tablets can mask symptoms of infection, which may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When Nurofen Long Lasting Tablets are administered for fever or pain relieve in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissue infectious complications. It is advisable to avoid the use of ibuprofen in cases of varicella.

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.

This medicinal product contains 34.5mg of sucrose per capsule. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

There is a risk of renal impairment in dehydrated adolescents.

4.5 Interaction with other medicinal products and other forms of interaction

Simultaneous administration of ibuprofen with the products listed below requires rigorous monitoring of the clinical and biological condition of the patient.

Ibuprofen should be avoided in combination with:

Other NSAIDs including cycloxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects (see section 4.4).

Concomitant use of Acetylsalicylic acid (aspirin) and ibuprofen may increase the risk of adverse reactions (see section 4.4).

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelets aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding the 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 use (see section 5.1).

Ibuprofen should be used with caution in combination with:

Oral hypoglycaemic agents: Ibuprofen may increase the hypoglycaemic effect of sulphonylureas (displacement of their binding to plasma proteins): this combination is not advisable.

Lithium: Ibuprofen raises blood lithium concentration, which may possible attack toxic levels: this combination is not advisable but, if it is used, lithium concentrations should be monitored in order to adjust the dosage during and after the period of combined treatment.

Methotrexate: An increase in the haematotoxicity of methotrexate has been reported in cases of combination with some NSAI drugs.

Ciclosporin: Increased risk of nephrotoxicity.

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

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 (positive) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

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.

Probenacid: Probenacid may reduce the metabolism and elimination of ibuprofen.

Antihypertensives (ACE inhibitors and Angiotensin II Antagonists) and diuretics: NSAIDs may diminish the effects of these drugs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor or Angiotensin II antagonist and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. These interactions should be considered in patients taking a coxib concomitantly with ACE inhibitors or angiotensin II antagonists. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter. Diuretics can increase the risk of nephrotoxicity of non-steroidal anti-inflammatory drugs.

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) and heparin (the risk of haemorrhage is increased through the inhibition of platelet aggregation and irritation of the digestive mucosa): this combination is not advisable. However, if combination with oral anticoagulants is necessary, prothrombin levels should be monitored, as the effects of such treatments may be potentiated.

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

It may produce an additive effect with:

* Ticlopidine (a greater inhibitory effect on platelet aggregation); this combination is not advisable, but if used, calls for monitoring of bleeding time;

* Other NSAI agents (increased risk of ulceration and haemorrhage); this combination is not advisable.

Concomitant use of Clopidrogrel and NSAIDs may increase the risk of gastrointestinal bleeding.

Cardiac glycosides: Ibuprofen may exacerbate cardiac failure reduce GFR and increase plasma glycosides levels. Administration of ibuprofen considerably increases plasma digoxin levels (0.9 ng/ml before administration, against 3.5 ng/ml with a dose of 400 mg 4 times daily), due to reduction of the renal clearance of digoxin.

Aminoglycosides: Ibuprofen may decrease the elimination of aminoglycosides and result in increased concentrations. Nephrotoxicity may result.

4.6 Fertility, pregnancy and lactation

Pregnancy:
Inhibition of prostaglandin in 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 has been shown to result in increased pre-and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

From the 20th week of pregnancy onward, ibuprofen use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus construction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, ibuprofen should not be given, unless clearly necessary. If ibuprofen is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Anti-natal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure for several days from gestational week 20 onward. Treatment should be discontinued if oligohydramnios or ductus arteriosus constriction are found.
During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- Cardiopulmonary toxicity (with premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- Renal dysfunction (see above)

The mother and the neonate, at the end of the pregnancy to:

- Possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- Inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, ibuprofen is contraindicated during the third trimester of pregnancy (see section 4.3).
Lactation/Breastfeeding:
In limited studies, ibuprofen and its metabolites appear in the breast milk in very low concentration (0.0008% of the maternal dose) and is unlikely to affect the breast-fed infant adversely.
Fertility:
There is some evidence that medicinal products which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment (see Section 4.4 regarding female fertility).

4.7 Effects on ability to drive and use machines

None expected at recommended doses and duration of therapy.

4.8 Undesirable effects

Possible side effects are those experienced with ibuprofen acid (maximum 1200mg Ibuprofen per day), in short-term use. In the treatment of chronic conditions, under long-term treatment, additional adverse events may occur.

Adverse events which have been associated with Ibuprofen are given below, tabulated by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10,000 and < 1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data).

Within each frequency grouping adverse events are presented in order of decreasing seriousness.

System Organ Class	**Frequency**	**Adverse Events**
Blood and Lymphatic System Disorders	Very rare	Haematopoietic disorders1
Immune System Disorders	Uncommon	Hypersensitivity with urticaria and pruritus2
	Very rare	Swelling face, swollen tongue, pharyngeal oedema, dyspnoea, tachycardia, and hypotension (anaphylaxis, angioedema or severe shock)2
Nervous System Disorders	Uncommon	Headache
	Very rare	Aseptic meningitis3
Ear and Labyrinth Disorders	Not Known	Hearing Impaired
Cardiac Disorders	Not known	Cardiac failure andoedema4
Vascular Disorders	Not known	Hypertension4
Respiratory, Thoracic and Mediastinal Disorders	Not known	Respiratory tract reactivity comprising asthma, bronchospasmordyspnoea2
Gastrointestinal Disorders	Uncommon	Abdominal pain, nausea and dyspepsia5
	Rare	Diarrhoea, flatulence, constipation and vomiting
	Very rare	Peptic ulcer, gastrointestinal perforation or gastrointestinal haemorrhage, melaena, and haematemesis6. Mouth ulceration and gastritis
	Not known	Exacerbation of colitis and Crohn'sdisease7
Hepatobiliary Disorders	Very rare	Liver disorder
	Not Known	Hepatic function abnormal
Skin and Subcutaneous Tissue Disorders	Uncommon	Skinrash2
	Very rare	Bullous reactions, including Stevens-Johnson syndrome, erythema multiforme and toxic epidermal necrolysis2
	Not Known	Rash maculo-papular, erythema. Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome). Acute generalised exanthematous pustulosis (AGEP) Photosensitivity reactions
Renal and Urinary Disorders	Very rare	Acute renal failure8
Investigations	Very rare	Haemoglobin decreased
Infections and infestations	Very rare	Exacerbation of infections related inflammation (e.g. development of necrotizing fasciitis), in exceptional cases, severe skin infections and soft-tissue complication may occur during a varicella infection.

Description of Selected Adverse Reactions

[1]Examples include anaemia, leucopenia, thrombocytopenia, pancytopenia and agranulocytosis. First signs are fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.

[2]Hypersensitivity reactions: These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract reactivity, including asthma, aggravated asthma, bronchospasm, and dyspnoea or (c) various skin reactions, including pruritus, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses, including toxic epidermal necrolysis, Stevens-Johnson Syndrome and erythema multiforme.

[3]The pathogenic mechanism of drug-induced aseptic meningitis is not fully understood. However, the available data on

NSAID-related aseptic meningitis points to a hypersensitivity reaction (due to a temporal relationship with drug intake, and disappearance of symptoms after drug discontinuation). Of note, single cases of symptoms of aseptic meningitis (such as stiff neck, headache, nausea, vomiting, fever or disorientation) have been observed during treatment with ibuprofen in patients with existing auto-immune disorders (such as systemic lupus erythematosus and mixed connective tissue disease).
[4]Clinical trial and epidemiological studies 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 (e.g. myocardial infarction or stroke), (see section 4.4).
[5]The most commonly observed adverse events are gastrointestinal in nature.
[6]Sometimes fatal, particularly in the elderly.
[7]See Section 4.4.
[8] Especially in long term use, associated with increased serum urea and oedema. Also includes papillary necrosis.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance. Website: www.hpra.ie.

4.9 Overdose

In children ingestion of more than 400 mg/kg may cause symptoms. In adults the dose response effect is less clear cut.

The half-life in overdose is 1.5-3 hours.

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, toxicity is seen in the central nervous system, manifesting as vertigo, drowsiness, occasionally excitation and disorientation or coma.
Occasionally patients develop convulsions. In serious poisoning hyperkalaemia and 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, liver damage, hypotension, respiratory depression and cyanosis 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 emptying if the patient presents within 1 hour of ingestion of a potentially toxic amount. If ibuprofen has already been absorbed, alkaline substances may be administered to promote the excretion of acid ibuprofen in the urine. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: M01AE01

Ibuprofen is a non-steroidal anti-inflammatory agent (NSAI) which is a phenylpropionic acid derivative that has demonstrated its efficacy by inhibition of prostaglandin synthesis. In humans, ibuprofen reduces inflammatory pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).

Clinical evidence demonstrates that when a 2-tablet dose of Nurofen Long Lasting 300mg Prolonged Release Hard Capsules is taken the pain-relieving effects persist for up to 12 hours.

5.2 Pharmacokinetic properties

Ibuprofen is well absorbed from the gastrointestinal tract following administration and is rapidly distributed throughout the whole body. Ibuprofen is extensively bound to plasma proteins. Ibuprofen diffuses into the synovial fluid.

Ibuprofen is metabolised in the liver to two major metabolites with primary excretion via the kidneys, either as such or as major conjugates, together with a negligible amount of unchanged ibuprofen. Excretion by the kidney is both rapid and complete.

The half-life with this formulation is prolonged from 2 to 8 hours.

In limited studies, ibuprofen appears in the breast milk in very low concentrations.

Pharmacokinetic studies have shown that Nurofen Long Lasting 300mg Prolonged Release Hard Capsules provide a gradual release of the active substance, with a slower release compared to immediate-release formulations and with a lower peak serum concentration which occurs approximately 1-2 hours after administration.

The pharmacokinetic profile of 2 x 300mg Long Lasting 300mg Prolonged Release Hard Capsules, compared to 400mg immediate-release tablets taken three times daily, showed that the prolonged-release formulation reduced the difference between the peak and trough concentrations of the immediate release tablets. Compared with immediate-release tablets, the area under the plasma concentration-time curve (AUC) for prolonged-release tablets was similar.

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

5.3 Preclinical safety data

The subchronic and chronic toxicity of ibuprofen in animal experiments was observed principally as lesions and ulcerations in the gastro-intestinal tract. *In vitro* and *in vivo* studies gave no clinically relevant evidence of a mutagenic potential of ibuprofen. In studies in rats and mice no evidence of carcinogenic effects of ibuprofen was found. Ibuprofen led to inhibition of ovulation in rabbits as well as disturbance of implantation in various animal species (rabbit, rat, mouse). Experimental studies have demonstrated that ibuprofen crosses the placenta, for maternally toxic doses, an increased incidence of malformations (e.g. ventricular septal defects) was observed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sugar spheres
Povidone
Basic Butylated Methacrylate copolymer
Ammino Methacrylate Copolymer Type A
Talc
Colloidal anhydrous silica
Capsule shell (contains gelatin)
Printing ink (contains red iron oxide E172 and yellow iron oxide E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Blister packs composed of aluminium and PVC.

Boxes of 12, 24, 28, 30, 56 and 60 capsules.

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
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0979/032/015

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