# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Nurofen Meltlets Lemon

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ibuprofen 200 mg

Excipient(s) with known effect:

Aspartame

For the full list of excipients, section see 6.1.

## 3 PHARMACEUTICAL FORM

Orodispersible tablet
White to off-white tablets.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

For the relief of mild to moderate pain, such as headache, backache, period pain, dental pain, neuralgia, rheumatic and muscular pain, migraine, cold and flu symptoms and feverishness.

### 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).
*Adults, the elderly and children and adolescents between 12 and 18 years:*
If in children and adolescents this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted.

Adults should consult a doctor if symptoms persist or worsen, or if the product is required for more than 10 days.

**Children and Adolescents between 12 and 18 years:** Take 1 or 2 tablets up to three times a day as required.
**Adults:** Take 1 or 2 tablets up to three times a day as required.

Place a tablet on the tongue, allow it to dissolve and then swallow; no water is required.

Leave at least 4 hours between doses.

Do not exceed six tablets in any 24 hours.

Not for use by children under 12 years.

## 4.3 Contraindications

Hypersensitivity to ibuprofen or any of the excipients in the product.

Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema, or urticaria) in response to aspirin or other non-steroidal anti-inflammatory drugs.

Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

Severe heart failure (NYHA Class IV), renal failure or hepatic failure (see section 4.4)

Last trimester of pregnancy

## 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 control symptoms (see GI and cardiovascular risks below).

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

*Respiratory:*

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

*Other NSAIDs:*

The use of ibuprofen with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

*SLE and mixed connective tissue disease:*

Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8).

*Renal:*

Renal impairment as renal function may further deteriorate (see sections 4.3 and 4.8).

There is a risk of renal impairment in dehydrated children and adolescents

Renal tubular acidosis and hypokalaemia may occur following acute overdose and in patients taking ibuprofen products over long periods at high doses (typically greater than 4 weeks), including doses exceeding the recommended daily dose.

*Hepatic:*

Hepatic dysfunction (see sections 4.3 and 4.8)

*Cardiovascular and cerebrovascular effects:*

Cases of Kounis syndrome have been reported in patients treated with Nurofen Meltlets Lemon. Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to myocardial infarction.

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 dose (2400 mg/day) 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. ≤1200 mg/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 long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

*Impaired female fertility:*

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

*Gastrointestinal:*

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8).

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 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.

Patients with a history of GI toxicity, particularly the 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, the treatment should be withdrawn.

<u>Severe cutaneous adverse reactions (SCARs)</u>

Severe cutaneous adverse reactions (SCARs), including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome), and acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with the use of ibuprofen (see section 4.8). Most of these reactions occur within the first month.

If signs and symptoms suggestive of these reactions appear ibuprofen should be withdrawn immediately and an alternative treatment considered (as appropriate).

Masking of symptoms of underlying infections

This medicinal product 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 this medicine is administered for pain or fever in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

Caution is required in patients with phenylketonuria or who are intolerant to phenylalanine. The product contains aspartame which is a source of phenylalanine. Each orodispersible tablet contains a source equivalent to 14 mg of phenylalanine.

*The label will include:*

Read the enclosed leaflet before taking this product

Do not take if you:

- have (or have had two or more episodes of ) a stomach ulcer, perforation or bleeding
- are allergic to ibuprofen, to any of the ingredients, or to aspirin or other painkillers
- are taking other NSAID pain killers or aspirin with a daily dose above 75 mg

Speak to a pharmacist or your doctor before taking if you:

- have or have had asthma, diabetes, high cholesterol, high blood pressure, a stroke, heart, liver, kidney or bowel problems or are dehydrated
- Are a smoker
- Are pregnant

If symptoms persist or worsen, consult your doctor or pharmacist.

## 4.5 Interaction with other medicinal products and other forms of interaction

**Ibuprofen should be avoided in combination with:**

*Aspirin (Acetylsalicylic acid)*: concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects, unless low-dose aspirin (not above 75mg daily) has been advised by a doctor as this may increase the risk of adverse reactions (see section 4.4).

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin (acetylsalicylic acid) on platelet aggregation when they are dosed concomitantly. 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 5.1).

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

**Ibuprofen should be used with caution in combination with:**

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

*Antihypertensives 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 NSAIDs.

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

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

*Cardiac glycosides:* NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

*Lithium:* There is evidence for potential increases in plasma levels of lithium.

*Methotrexate*: There is a potential for an increase in plasma methotrexate.

*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 haemarthroses and haematoma in HIV (+) 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.

## 4.6 Pregnancy and lactation

**Pregnancy:**

Inhibition of prostaglandin 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 embryfoetal 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, Nurofen 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 constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, Nurofen should not be given unless clearly necessary. If Nurofen 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. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to Nurofen for several days from gestational week 20 onward. Nurofen 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 (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction (see above), which may progress to renal failure with oligohydroamniosis;

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, Nurofen is contraindicated during the third trimester of pregnancy.

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

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

Adverse events which have been associated with Ibuprofen are given below, listed by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <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.

The list of the following adverse events relates to those experienced with ibuprofen at OTC doses, for short-term use. In the treatment of chronic conditions, under long-term treatment, additional adverse events may occur.

The adverse events observed most often are gastrointestinal in nature. Adverse events are mostly dose-dependent, in particular the risk of occurrence of gastrointestinal bleeding is dependent on the dosage range and duration of treatment.

Clinical studies suggest that use of ibuprofen (particularly at high doses 2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke), (see section 4.4).

| System Organ Class | Frequency | Adverse Event |
|---|---|---|
| Blood and Lymphatic System Disorders | Very rare: | Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis).<br>First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising. |
| Immune System Disorders | | Hypersensitivity reactions consisting of[1]: |
| | Uncommon | Urticaria and pruritus |
| | Very rare | Severe hypersensitivity reactions. Symptoms could be facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock). |
| | Not known | Respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea. |
| Nervous System Disorders | Uncommon | Headache |
| | Very rare | Aseptic meningitis[2] |
| Cardiac Disorders | Not known | Cardiac failure and oedema |
| | Not known | Kounis syndrome |
| Vascular Disorders | Not known | Hypertension |

| | | |
|---|---|---|
| Gastrointestinal Disorders | Uncommon | Abdominal pain, nausea, dyspepsia |
| | Rare | Diarrhoea, flatulence, constipation and vomiting |
| | Very rare | Peptic ulcer, perforation or gastrointestinal haemorrhage, sometimes fatal, particularly in the elderly. Melaena, haematemesis, ulcerative stomatitis, gastritis. |
| | Not known | Exacerbation of ulcerative colitis and Crohn's disease (section 4.4). |
| Hepatobiliary Disorders | Very rare | Liver disorders |
| Skin and Subcutaneous Tissue Disorders | Uncommon | Various skin rashes |
| | Very rare | Severe cutaneous adverse reactions (SCARs) (including Erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis) |
| | Not known | Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)<br>Acute generalised exanthematous pustulosis (AGEP)<br>Photosensitivity reactions |
| Metabolism and Nutrition Disorders | Not known | Decreased Appetite |
| | Not known | Hypokalaemia* |
| Renal and Urinary Disorders | Very rare | Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema. |
| | Not known | Renal insufficiency |
| | Not known | Ureteric colic, dysuria |
| | Not known | Renal tubular acidosis* |
| Investigations | Very rare | Decreased haemoglobin levels |

Description of Selected Adverse Reactions

[1] Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract activity comprising asthma, aggravated asthma, bronchospasm, dyspnoea or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

[2]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, mixed connective tissue disease).

*Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of the ibuprofen component at higher than recommended doses.

**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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 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 drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning 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 and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

In serious poisoning 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 and liver damage may occur.

Prolonged use at higher than recommended doses may result in severe hypokalaemia and renal tubular acidosis. Symptoms may include reduced level of consciousness and generalised weakness (see section 4.4 and section 4.8).

**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 if the patient presents within 1 hour of ingestion of a potentially toxic amount. 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 propionic acid derivative, having analgesic, anti-pyretic and anti-inflammatory activity. The drug's therapeutic effects as a non-steroidal anti-inflammatory drug are thought to result from inhibitory activity on prostaglandin synthesis. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose aspirin (acetylsalicylic acid) on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400mg were taken with 8 h before or within 30 min after immediate release aspirin 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 relevant effect is considered to be likely for occasional ibuprofen use.

## 5.2 Pharmacokinetic properties

Nurofen Meltlets Lemon consist of taste masked ibuprofen granules incorporated into a compressed tablet. When the tablet is placed on the tongue it rapidly dissolves to release the ibuprofen granules. The ibuprofen granules can then be swallowed without the need for water.

Ibuprofen is well absorbed from the gastrointestinal tract. Ibuprofen is extensively bound to plasma proteins. Ibuprofen diffuses into the synovial fluid.

Peak plasma concentrations from Nurofen Meltlets Lemon occur approximately 1 hour 50 minutes after administration. When taken with food, peak plasma levels may be delayed.

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 elsewhere in the Summary of Product Characteristics.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Ethylcellulose (E462),
Silicon Dioxide (E551),
Hypromellose (E464),
Mannitol (E420),
Aspartame (E951),
Croscarmellose Sodium (E468),
Magnesium Stearate (E572),
Flavour (lemon flavours, maltodextrin).

### 6.2 Incompatibilities

Not applicable

### 6.3 Shelf life

3 years

### 6.4 Special precautions for storage

Do not store above 25°C.

### 6.5 Nature and contents of container

The orodispersible tablets are packed in a cold formed blister pack. The blister pockets are formed from 60 µm PVC/ 45 µm aluminium / 25 µm polyamide film heat sealed to the 20µm aluminium foil blister lid .

The blister trays are packed into cardboard cartons containing 4, 6, 10, 12, 14, 16, 18, 20, 22, 24, 30, 36, 40 or 48 orodispersible tablets. Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

None

## 7 MARKETING AUTHORISATION HOLDER

Reckitt Benckiser Healthcare (UK) Ltd
Slough
SL1 4AQ

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 00063/0382

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

06/03/2009

## 10 DATE OF REVISION OF THE TEXT

15/08/2024