Medicines and Healthcare Products Regulatory Agency

Dear Sir/Madam

CONSULTATION DOCUMENT: ARM 86; NUROFEN EXPRESS 400MG ORAL POWDER

REQUEST TO RECLASSIFY A PRODUCT FROM P TO GSL

I am writing to inform you that consultation document ARM **86** which includes the applicant's Reclassification Summary and Patient Information Leaflet, has been posted on the MHRA website today (www.mhra.gov.uk). The consultation seeks your views on the reclassification from P to GSL of **Nurofen Express 400mg Oral Powder**.

You are invited to comment on the proposal, a copy of which is attached. A form for your reply is also attached.

Comments should be sent to me either by post to room 3-M, 151 Buckingham Palace Road, London SW1W 9SZ or by email (reclassification@mhra.gsi.gov.uk) to arrive by **31 January 2014.** Contributions received after that date cannot be included in the exercise.

To help informed debate on the issues raised by this consultation exercise, and within the terms of the Freedom of Information Act, the Agency intends to make copies of comments received publicly available. Unless you state otherwise we will assume that you have no objections to your comments being publicly available on the Agency's website.

Yours faithfully

Abiodun Aderogba
Reclassification Unit

Medicines and Healthcare Products Regulatory Agency

To: Abiodun Aderogba

From: _____

MHRA
Room 3-M
151 Buckingham Palace Road
LONDON SW1W 9SZ

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_____

CONSULTATION DOCUMENT: ARM 86; NUROFEN EXPRESS 400mg oral powder

REQUEST TO RECLASSIFY A PRODUCT FROM P TO GSL

ALL RESPONDENTS MUST TICK ONE OF THE FOLLOWING BOXES

- **My reply may be made freely available** ☐
- **I wish parts of my reply to remain confidential*** ☐
- **I wish my reply to remain confidential*** ☐

*Please use the space below to explain why you feel the information in your reply should be treated as confidential. In line with the Freedom of Information Act 2000, if we receive a request for disclosure of the information we will take full account of your explanation, but we cannot give an assurance that confidentiality can be maintained in all circumstances. Responses to consultation will not normally be released under FOI until the regulatory process is complete

Explanation regarding why your response should remain confidential

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Name: **Signature**

Date:

CPRD NIBSC MHRA

ARM 86 CONSULTATION PERIOD: 6 JANUARY TO 31 JANUARY 2014

RECLASSIFICATION SUMMARY FOR P TO GSL APPLICATION NUROFEN EXPRESS 400MG ORAL POWDER

1. APPLICANT DETAILS

1.1. Name of the Applicant

Reckitt Benckiser Healthcare (UK) Limited
Wellcroft House
Wellcroft Road
Slough
SL1 4AQ

1.2. Name & Address of Contact for Provision of Statements of Support

UK Regulatory and Medical Director
Reckitt Benckiser Healthcare (UK) Limited
Wellcroft House
Wellcroft Road
Slough
SL1 4AQ

2. PRODUCT DETAILS

2.1. Name and MA Number

Nurofen Express 400 mg oral powder
PL 00063/0616

2.2. Active Ingredients

683.34 mg ibuprofen lysine, which is equivalent to 400 mg of ibuprofen.

2.3. Indications

For the relief of mild to moderate pain associated with headache, migraine, backache, period pain, dental pain, rheumatic and muscular pain, cold and flu symptoms such as sore throat and fever.

2.4. Dosage Including Age-Limits and Restrictions on Length of Treatment

For oral administration and short-term use only.
The lowest effective dose should be used for the shortest duration necessary to relieve symptoms. The patient should consult a doctor if symptoms persist or worsen, or if the product is required for more than 5 days when treating pain and 3 days when treating fever.

Adults, the elderly and children aged over 12 years

Initial dose - one sachet. Then, if necessary, one sachet up to three times a day as required.
Dissolve the contents of the sachet in a glass of water, stir, and then drink immediately.
Leave at least six hours between doses. Do not exceed more than 3 sachets (1200 mg) in any 24 hour period.
Special patient groups:

Elderly:
No special dose adjustment is required. Because of the possible undesirable effect profile (see section 4.4), it is recommended to monitor the elderly particularly carefully.
Renal insufficiency:
No dose reduction is required in patients with mild to moderate impairment to renal function (patients with severe renal insufficiency, see section 4.3).
Hepatic insufficiency (see section 5.2):
No dose reduction is required in patients with mild to moderate impairment to hepatic function (patients with severe hepatic dysfunction, see section 4.3).
Children and adolescents:
Not to be given to children under 12 years of age.

2.5. Pack Size
The product is available in a single-dose sachet containing 683.34 mg ibuprofen lysine, equivalent to 400 mg ibuprofen. A maximum of 8 sachets will be available per consumer unit, providing a maximum of 2.7 days treatment.

3. RATIONALE FOR RECLASSIFICATION
Reckitt Benckiser Healthcare (UK) Ltd markets Nurofen and Nurofen Express (ibuprofen and salts of ibuprofen). These products are well established and recognised by Healthcare Professionals and consumers as effective painkiller with a strong benefit/risk ratio.
Nurofen® products have been available in the UK with OTC status for almost 30 years for adults and children over 12 years and include:
- Nurofen Express 400 mg liquid capsules and Nurofen Express Extra Strength Migraine 684 mg caplets (single dose 400 mg, maximum daily dose 1,200 mg) as Pharmacy only (P)
- Nurofen 200 mg tablets, Nurofen Express 256 mg caplets or Nurofen Express 200 mg liquid capsules (single dose 200-400 mg, maximum daily dose 1,200 mg) as General Sales List (GSL)
Recently, Reckitt Benckiser obtained a marketing authorisation with a P status for an ibuprofen lysine (equivalent to 400 mg ibuprofen) oral powder. This is a new pharmaceutical form of ibuprofen in the UK. One sachet of the product is dissolved in water to create an easy to take liquid dose of 400 mg ibuprofen. The indications are limited to the short-term symptomatic relief of a number of easily self-diagnosed, self-limiting conditions of short duration (e.g., headache, migraine, backache, period pain, dental pain, rheumatic and muscular pain and cold and flu symptoms such as sore throat).

There is no reason to suggest that 1 x 400 mg sachet of ibuprofen presents a higher risk to consumers than a 2x200 mg dose of ibuprofen in a tablet presentation, since consumer studies have shown that the majority of ibuprofen users dose with 2 X 200 mg tablets when pain relief is required. Also, the presentation of this product is so different from a tablet that it would be difficult to confuse it with the tablet dosing instructions. The risk of confusion is further minimised by clear pack labelling. Moreover, it is conventional for most sachet medicines to be taken as 1 single sachet and so it is unlikely that the patient would take more than the dose instructed on pack.

In addition, as the pharmaceutical form is new to the UK market and no other strength is available, there is no risk of a patient being confused by ibuprofen sachets of different strengths.

Sachet products containing a unit dose of 1000 mg of paracetamol are currently available GSL in the UK and have been available for more than 10 years despite the maximum allowable tablet size being 500 mg. Examples include: Lemsip Max Cold and Flu Lemon; Resolve; Resolve Extra; and, Beechams Flu-Plus Hot Berry Fruits. These paracetamol products have a long history of safe use in the short-term treatment of self-diagnosed, mild-moderate pain conditions. It has been demonstrated that soluble sachet forms of ibuprofen have been associated with fewer cases of poisoning than tablets or capsules (Volans, et al., 2003).
Available GSL, Nurofen Express 400 mg oral powder would be an appropriate alternative to paracetamol sachets which are already available in general sales stores at the maximum strength of 1000 mg.
Nurofen Express 400 mg oral powder is presented in a new pharmaceutical form and offers a simple and easy-to-swallow therapeutic dose with appropriate indications and duration of treatment. The product has a posology comparable to the posology of 2x200 mg tablets already available GSL and it is proposed that this presentation should be made available GSL to self-selecting patients and that it can be safely administered without the requirement for pharmacist intervention.

3.1. Hazard to Health

Ibuprofen lysine 683.34 mg tablets are currently marketed in the UK as a P product.
Following oral administration, ibuprofen lysine dissociates to lysine and ibuprofen, and the mechanism of action of the dissociated ibuprofen will be identical to that of ibuprofen ingested as ibuprofen acid which, at OTC doses, is recognised to have a very good safety profile.
PSUR data indicates that poisoning, procedural complications and overdose by Nurofen 400 mg tablets have been reported, and that all of them have been resolved. It is estimated that overdose is generally well tolerated when no other drugs are involved. The 400 mg sachets would be expected to have a safety profile that is at least as good as standard tablets and this is based on historical data (tablets versus effervescent forms) and currently marketed products containing maximal single unit doses of paracetamol (1000 mg) in a sachet format. Single unit doses of 200 mg and 400 mg ibuprofen are not dissimilar in terms of safety, with the majority of ADRs relating to gastrointestinal complaints. Any risk (i.e., cardiovascular and gastrointestinal) can also be potentially increased by long-term cumulative exposure.
However, the maximum daily dose of 1 sachet of 400 mg 3 times per day still results in a maximum daily dose of 1200 mg (equivalent to 6 tablets of 200 mg). Moreover, this product is only intended for short-term use (up to 5 days compared with 10 days for the 200 mg tablets), after which time medical support is recommended.
This, together with the proposed pack sizes and the accepted inherent safety of ibuprofen, makes this sachet presentation of ibuprofen an appropriate proposition for GSL classification.

3.2. Risk of Misuse

The risk of misuse of this product is negligible.

UK consumers are accustomed to self-treatment using products containing ibuprofen for the relief of minor self-limiting conditions. The proposed indications are suitably descriptive to allow self-diagnosis and self-treatment, and are consistent with the indications of other ibuprofen-containing products currently available GSL and in line with MHRA list C guidance information on ibuprofen lysine GSL products. Ibuprofen lysine products (200 mg dose) have been available GSL in the UK since 2001 (eg. Nurofen Migraine Pain) and consumers are now familiar with these “Express” products.
The pack information directs the user to seek medical attention if there is no improvement in the condition within 3 or 5 days depending on the symptoms.

The information on pack and in the leaflet is similar to other GSL presentations of ibuprofen and is clearly laid out to provide concise information about the product. This information is in line with that on other Nurofen products available GSL and provides a familiar environment for those seeking information in the PIL or label, although it is sufficiently different (picture of the sachet and strength written in red instead of green) for the user to be able to differentiate it from 200 mg Nurofen Tablet products.

The posology for the relief of mild to moderate pain is a single maximum dose of 400 mg of ibuprofen, with at least 6 hours between doses and a maximum daily dose of 1200 mg in adults. This posology is similar to that of the current Nurofen 200 mg tablets (2 tablet dose) and other ibuprofen based products. Consumers are familiar with ibuprofen use and the prominently displayed instructions for use will give reassuring advice that this product has a 3-times-per-day treatment regime.

The powder in a sachet format is a new format for ibuprofen in the UK. Sachets are an inherently safe delivery system as they discourage inadvertent or deliberate overdose because of the need in such circumstances to access the contents of each sachet individually. It is generally recognised that larger pack sizes could increase the potential for any misuse. However, the maximum pack size in this application limits the intake to 3200 mg which is significantly less than the estimated 7000 mg toxic dose in humans. Ibuprofen has no known misuse / abuse issues and there is no anticipated increased risk associated with this product.

Accidental ingestion in children is a concern. However, the product is indicated for use from 12 years of age and will carry clear warnings to keep the medicine out of reach and sight of children and to only use the product for short periods of time and at the recommended dose.

Overall, given the low number of documented cases of accidental use, poisoning and overdose, relative to the total number of Nurofen packs sold, we consider the risk of incorrect use is limited. This risk is further reduced by the clear indications for use, the prominent warnings on pack, the limited pack size, a specific design making this product clearly different from other ibuprofen GSL products and the further emphasis of the 400 mg dosage strength in red type compared with the green type on the 200 mg dose products.

3.3. Special Precautions in Handling

There are no special precautions required.

3.4. Role of the Pharmacist

The pharmacist provides valuable assistance to patients choosing combination products or modified released forms containing ibuprofen. However, limited help is needed when standard forms of ibuprofen are concerned and where treatment for easily self-diagnosed mild -moderate pain is needed. This product will not require the type of advice seen in some formulations on risk of overdose in relation to big pack sizes or confusion between strength of tablets or capsules.
Considering the licensed indications of the product, its uniqueness in the range (the only powder form for ibuprofen) and its pack size availability, the risk to the consumer is minimal. Clear label and leaflet instructions will help to ensure safe use without the supervision of a pharmacist and will follow those already used for products containing ibuprofen and ibuprofen lysine. Indeed, the packaging will follow the same standardised guidelines for the use of NSAIDs and will make it clear that consumers should refer to healthcare professionals for further information and advice in the event of accidental overdose, use of contra-indicated medications, persistence of symptoms and development of possible side effects.

3.5. Convenience to the Purchaser

Nurofen Express 400 mg oral powder is the only ibuprofen powder available on the UK market. This format presents a convenient alternative to tablets for people who dislike or have difficulties swallowing tablets and also an alternative to paracetamol oral powder already available GSL at a maximum strength of 1000 mg.

Where the safety profile is suitable, it is more convenient to self-select a product from general sales outlets rather than from pharmacy only supply, particularly if a pharmacy is not locally available.

GSL availability of Nurofen® Express 400 mg oral Powder would therefore be a considerable advantage to the consumer.

4. SPECIFIC GSL REQUIREMENTS

For adults and children over 12 years of age, the indications and maximum daily dose of Nurofen Express 400mg oral Powder are in line with GSL ibuprofen lysine products authorised in the UK and list C guidance.
The only differences are:
The pharmaceutical form (oral powder compared to tablets on list C)
The unit dose: 400 mg instead of 200 mg

The following requirements have been incorporated in line with the Committee on Safety of Medicines (CSM) advice: (Medicines and Healthcare products Regulatory Agency, Committee on Safety of Medicines, 2005, revised 2007).

The pack and Patient Information Leaflet carry full advice and information to advise the individual on the correct and safe use of the product without the advice from a pharmacist.

The maximum proposed pack size is 8 sachets, which is sufficient for 2.7 days continuous treatment at the recommended dosage. This will not encourage overuse or inappropriate extended use. Advice on the need to seek further medical advice if the symptoms persist or worsen will be displayed prominently on the pack. The packaging also carries guidance relating to seeking healthcare advice, as well as a customer free phone number (helpline) and Reckitt Benckiser Healthcare (UK) Ltd monitors safety signals on all its products.

The patient information will address the disposition for identified population at risk (section 4.2 of the SmPC) as follow:
Patient with renal impairment – Patient with kidney problem are advices to speak to their pharmacist or doctor prior to taking this product (pack and leaflet section 2)
Elderly – Elderly are highlighted in section 4 of the leaflet that they are at increased risk to suffer from the side effects.
The proposed carton design, with a drawing of a sachet on front of pack, makes Nurofen Express 400 mg oral powder clearly distinctive from other GSL Nurofen products.

5. SAFETY PROFILE

Ibuprofen lysine containing products have been sold as GSL products in the UK since 2001. There is no reason to suppose that the safety profile of 683.34 mg ibuprofen lysine will be different from 2x342 mg of ibuprofen lysine and safety is not expected to be adversely affected by its availability in a sachet.
Once ibuprofen lysine enters the stomach, it dissociates to release ibuprofen. Thus, it can be assumed it will have the same clinical actions and risk-benefit profile as ibuprofen, which has

a well-established safety profile and post-marketing experience has given rise to very few adverse event reports.

Martindale notes a substantial increase in the number of cases of ibuprofen overdose reported to the National Poisons Information Service of the UK in the 2 years after its introduction as an OTC medicine. However, no concurrent increase in severity of poisoning was found and in only 1 of 203 (0.5%) cases was ibuprofen thought to have caused serious problems. Martindale then goes on to state that:
"Ibuprofen appears to be much less toxic in acute overdose than either aspirin or paracetamol. Adults who have ingested less than 100 mg per kilogram of body weight (the average body weight being roughly 70 kg and therefore 7000 mg of ibuprofen) are unlikely to require treatment." (Martindale: The Complete Drug Reference, 2011)

The above toxic dose (equivalent to 17.5 sachets x 400 mg) is much higher than the total ibuprofen dose in one pack (8 sachets x 400 mg = a total dose of 3200 mg).
Symptoms of overdose are generally mild and may include nausea, vomiting, abdominal pain, headache, dizziness, drowsiness, nystagmus, blurred vision, tinnitus and, rarely, hypotension, metabolic acidosis, renal failure and loss of consciousness. These symptoms of overdose are carried in the SmPC, together with detail of their management.

Ibuprofen products in sachets are available across Europe (15 products across 6 countries) and have been available OTC at a dose of 400 mg for almost 20 years (since 1992). Hence, a considerable number of patients will have been exposed to similar products, which are clearly now considered safe for use. This is not surprising owing to the long and well-documented use of ibuprofen.

Literature supports the safety of solubilised formats compared with tablets, capsules and modified release formats. This suggests that single unit 400 mg doses of ibuprofen in a sachet will have a similar safety to solid dose formats.

6. SUPPORT FOR RECLASSIFICATION

This is a company application and there is no additional support from other experts or organisations provided.
The motivation is to provide consumers with an alternative option to tablets for the treatment of minor ailments which are easily self-diagnosed.

7. REFERENCE LIST

Reference List
Martindale: The Complete Drug Reference (2011) Ibuprofen Monograph.
Medicines and Healthcare products Regulatory Agency.Committee on Safety of Medicines. Always Read the Leaflet - Getting the best information with every medicine. Report of the Committee on Safety of Medicines
Working Group on Patient Information. 2005. London: The Stationery Office, Published by TSO (The Stationery Office).
Ref Type: Online Source
Volans G, Monaghan J and Colbridge M (2003) Ibuprofen overdose. *Int J Clin Pract Suppl* **135**:54-60.

NUROFEN® EXPRESS 400mg Oral Powder

Contains Ibuprofen

INFORMATION FOR THE USER

Read all of this leaflet carefully because it contains important information for you.

- This medicine is available without prescription. However, you still need to take Nurofen® Express 400mg Oral Powder carefully to get the best results from it.
- This medicine is **not to be given to children under 12 years of age**
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- **You must contact a doctor if your symptoms worsen or do not improve after 5 days when treating pain or 3 days when treating fever.**
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT NUROFEN® EXPRESS 400mg ORAL POWDER IS AND WHAT IT IS USED FOR

Nurofen® Express 400mg Oral Powder contains ibuprofen 400mg as ibuprofen lysinate. Ibuprofen belongs to a group of medicines called Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). These medicines provide relief by changing the body's response to pain, swelling and high temperature.

Nurofen® Express 400mg Oral Powder is used to relieve:

- **symptoms of mild to moderate pain such as headache, toothache, period pains, rheumatic and muscular pain and migraine.**
- **cold and flu symptoms such as sore throat and fever.**

2. BEFORE YOU TAKE NUROFEN® EXPRESS 400mg ORAL POWDER

Do not take Nurofen® Express 400mg Oral Powder if you:

- have (or have had two or more episodes of) a stomach ulcer, perforation or bleeding of the stomach
- are allergic to ibuprofen, tartrazine (E102) or any of the other ingredients (see section 6) of Nurofen Express 400mg Oral Powder or to acetylsalicylic acid (aspirin) or other anti-inflammatory painkillers
- suffer from severe kidney, liver or heart problems
- have had gastrointestinal bleeding or perforation when previously taking NSAIDs (Non-Steroidal Anti-inflammatory drugs)
- have ever suffered from shortness of breath, have had a worsening of asthma, skin rash, itchy runny nose or facial swelling when previously taking ibuprofen, acetylsalicylic acid (aspirin) or other similar painkillers (NSAIDs)
- are suffering from severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake)
- are suffering from cerebrovascular or other active bleeding
- are suffering from blood cell production or clotting disorders
- are in the last three months of pregnancy (see below).

Please do not give to children under 12 years of age.

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

- have or have had asthma
- have kidney, heart, liver or bowel problems
- have high blood pressure, diabetes, high cholesterol or are a smoker
- have been told by your doctor that you have an intolerance to some sugars
- have systemic lupus erythematosus (a condition of the immune system causing joint pain, skin changes and other organ disorders)
- have had a heart attack or stroke
- have a history of gastrointestinal disease (such as ulcerative colitis or Crohn's disease)
- are in the first 6 months of pregnancy
- have chicken pox (varicella).

Consult a doctor before using Nurofen® Express 400mg Oral Powder if any above mentioned conditions concerns you.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. In particular, tell them if you are taking:

- blood thinning or anti-clotting medicines (anticoagulants) such as acetylsalicylic acid (aspirin), warfarin, triciopine,
- glucocorticoids (medicinal products containing cortisone or cortisone-like substances), aspirin, or other NSAIDs (anti-inflammatories and analgesics): since these may increase the risk of gastrointestinal ulcers or bleeding
- lithium (a medicine for manic depressive illness and depression) since the effect of lithium may be enhanced
- selective serotonin reuptake inhibitors (a medicine used for depression) as these may increase the risk of gastrointestinal side effects.
- methotrexate (a medicine for cancer or rheumatism) since the effect of methotrexate may be enhanced
- zidovudine: (a medicine for treating HIV infection) since the use of Nurofen Express 400mg Oral Powder may result in an increased risk of bleeding into a joint or a bleeding that leads to swelling.
- ciclosporin and tacrolimus (to prevent transplant rejection) as there could be an increased risk for the kidney.
- medicines for high blood pressure (ACE-inhibitors e.g.captopril, betareceptor blocking medicines, angiotensin II antagonists) and water tablets (diuretics), as NSAIDs may reduce the effects of these medicines and there could be a possible increased risk for the kidney (using potassium sparing diuretics with ibuprofen can lead to high blood
levels of potassium)
- sulfonylureas (antidiabetic medicine) as i nteractions may be possible
- phenytoin (for epilepsy) as the effect may be enhanced
- quinolone antibiotics as the risk of convulsions may be increased.
- cardiac glycosides such as digoxin
- mifepristone (used to terminate pregnancies) as the effect may be reduced
- probenecid and sulfinpyrazones (medicines for gout): it may take longer for ibuprofen to be broken down by the body.

Other warnings

- Medicines such as Nurofen Express 400mg Oral Powder may be associated with **a small increased risk of heart attack or stroke.** Any risk is more likely with high doses and prolonged treatment. **If you have heart problems, have had a stroke or think that you might be at risk of these conditions** (for example if you have high blood pressure, diabetes, high cholesterol or are a smoker), you should discuss your treatment with your doctor or pharmacist.
- Taking a painkiller for headaches for too long can make them worse.

Fertility, pregnancy and breast-feeding

Do not take in the last 3 months of pregnancy. Speak to your doctor or pharmacist before taking this product if you are in the first 6 months of pregnancy or are breast-feeding.

This medicine passes into breast milk but may be used during breast-feeding if it is used at the recommended dose and for the shortest possible time.

Nurofen Express 400mg Oral Powder belongs to a group of medicines which may **impair fertility in women.** This is reversible on stopping the medicine. It is unlikely that Nurofen Express 400mg Oral Powder, used occasionally will affect your chances of becoming pregnant. However, tell your doctor before taking this medicine if you have problems becoming pregnant.

Driving and using machines

For short-term use and at normal dosage this medicine has no or negligible influence on the ability to drive and use machines.
If side-effects such as tiredness or dizziness occur do not drive or operate machines. Alcohol consumption increases the risk of these side-effect.

Important information about some of the ingredients of Nurofen® Express 400mg Oral Powder.

Nurofen Express 400mg Oral Powder contains sucrose.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Nurofen Express 400mg Oral Powder contains tartrazine (E102). This may cause allergic reactions.

RB004517

3. HOW TO TAKE NUROFEN® EXPRESS 400mg ORAL POWDER

This product is for **short term use only**. You should take the lowest dose for the shortest time necessary to relieve your symptoms.

Not to be given to children under 12 years of age

Always take Nurofen® Express 400mg Oral Powder exactly as stated in this package leaflet. You should check with your doctor or pharmacist if you are not sure. The standard dose is:

Adults, the elderly and children aged 12 years and older:

For oral use after dissolving in water.

Dissolve the content of one sachet in a glass of water, stir, then drink immediately.

You can take 1 sachet up to 3 times a day as required.

Leave at least 6 hours between doses. Do not take more than 3 sachets in any 24 hour period.

You should not take Nurofen Express 400mg Oral Powder for longer than **5 days** when treating pain and **3 days** when treating fever unless your doctor tells you to. If symptoms persist or worsen consult your doctor.

Please speak to the doctor or pharmacist if you feel that the effect of this medicine is greater or less than you expected.

If you take more Nurofen® Express 400mg Oral Powder than you should

Consult a doctor immediately. The following signs may occur: nausea, vomiting, stomach pain, headache, dizziness, drowsiness, nystagmus, blurred vision, ringing in the ear. Rarely: low blood pressure and loss of consciousness.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Nurofen Express 400mg Oral Powder can cause side effects, although not everybody gets them. Side effects may be minimised by taking the lowest dose for the shortest time necessary to relieve the symptoms. Although side effects are uncommon, you may suffer one of the known side effects of NSAIDs. If you do, or if you have concerns, stop taking this medicine and talk to your doctor as soon as possible. Elderly people using this product are at increased risk of developing problems associated with side effects.

STOP TAKING this medicine and seek immediate medical help if you develop:

- **signs of intestinal bleeding** such as: severe pain in the abdomen, black tarry stools, blood in your faeces (stools/motions), vomiting blood or dark particles that look like coffee grounds.
- **signs of rare but serious allergic reaction** such as worsening of asthma, unexplained wheezing or shortness of breath, swelling of the face, tongue or throat, difficulty breathing, racing heart, drop in blood pressure leading to shock. These can happen even on first use of this medicine.
- **severe skin reactions** such as rashes covering the whole body, peeling, blistering or flaking skin.

Tell your doctor if you have any of the following side effects, they become worse or you notice any effects not listed.

Common (affects 1 to 10 users in 100)

- heart burn, abdominal pain, feeling sick and indigestion

Uncommon (affects 1 to 10 users in 1,000)

- inflammation of the stomach, worsening of colitis and Crohn's disease
- headache, dizziness, sleeplessness, agitation, irritability or tiredness
- visual disturbances
- flatulence (wind), diarrhoea, constipation and vomiting
- allergic reactions , such as skin rashes, itching and asthma attacks

Rare (affects 1 to 10 users in 10,000)

- tinnitus (ringing in the ears)
- kidney damage and the development of gout

Very rare (affects less than 1 users in 10,000)

- inflammation of the oesophagus or pancreas, blockages in the gut
- serious infections of the skin have occurred during chicken pox
- kidney disorders that may be shown by passing less or more urine than normal, cloudy urine, blood in the urine, pain in the back and/or swelling (particularly of the legs). In general, the habitual use of (several sorts of) analgesics can lead in rare cases to lasting severe kidney problems.
- blood disorders resulting in unexplained or unusual bruising or bleeding, fever, sore throat, mouth ulcers, flu-like symptoms and severe exhaustion
- psychotic reactions and depression
- worsening of inflammation due to infection
- high blood pressure, arterial hypertension, palpitations, heart failure, heart attack
- liver problems or inflammation of the liver. Liver failure or damage, particularly in long-term term use, shown by yellowing of the skin and eyes or pale stools and dark urine.
- the symptoms of aseptic meningitis with neck stiffness, headache, feeling sick, being sick, fever or consciousness clouding have been observed when using ibuprofen. Patients with autoimmune disorders (SLE, mixed connective-tissue disease) may be more likely to be affected. Contact a doctor at once, if these occur.
- swelling of skin tissue such as hands, feet or face.

Medicines such as Nurofen Express 400mg Oral Powder may be associated with a small increased risk of heart attack ("myocardial infarction") or stroke.

If any of the side effects get serious, or if you notice any side effects not listed in the leaflet, please tell your doctor or pharmacist.

Also you can help to make sure that medicines remain as safe as possible by reporting any unwanted side effects via the internet at www.mhra.gov.uk/yellowcard. Alternatively you can call Freephone 0808 100 3352 (available from 10 a.m. to 2 p.m. Mondays to Fridays) or fill in a paper form available from your local pharmacy.

5. HOW TO STORE NUROFEN® EXPRESS 400mg ORAL POWDER

Keep out of the reach and sight of children.

This medicinal product does not require any special temperature storage conditions.

Do not use Nurofen® Express 400mg Oral Powder after the expiry date which is stated on the carton and sachet. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask the pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Nurofen® Express 400mg Oral Powder contains:

Each sachet contains 400mg of the active substance ibuprofen (as ibuprofen lysinate).

The other ingredients are:

Betadex

Lemon essence (containing natural flavouring substances and preparations, maltodextrin, modified maize starch and tartrazine E102)

Saccharin sodium (E954)

Sodium cyclamate (E952)

Sodium citrate (E331)

Sucrose

What Nurofen® Express 400mg Oral Powder looks like and contents of the pack:

This medicine is a white, lemon flavoured powder supplied in sachets.

Single-dose sachet made of a heat-sealable paper/aluminium sheet /polythene complex.

Outer carton containing 1, 2, 3, 4, 5, 6, 7 and 8 sachets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Reckitt Benckiser Healthcare (UK) Ltd, HU8 7DS.

PL 00063/0616

Manufacturer

Laboratorio de aplicaciones farmacodinámicas, s.a. (fardi)
Grassot, 16
08025 BARCELONA (SPAIN)

or

Reckitt Benckiser Healthcare International Limited,
Thane Road, Nottingham,
NG90 2DB, United Kingdom

This leaflet was last approved in July 2013.

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Minimum point: 9pt

CUSTOMER INFO:
Minimum Point Size = 9.00pt

RB130106

Code this way

NUROFEN® EXPRESS 400mg Oral Powder

Contains Ibuprofen

INFORMATION FOR THE USER

Read all of this leaflet carefully because it contains important information for you.

- This medicine is available without prescription. However, you still need to take Nurofen® Express 400mg Oral Powder carefully to get the best results from it.
- This medicine is **not to be given to children under 12 years of age**
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- **You must contact a doctor if your symptoms worsen or do not improve after 5 days when treating pain or 3 days when treating fever.**
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT NUROFEN® EXPRESS 400mg ORAL POWDER IS AND WHAT IT IS USED FOR

Nurofen® Express 400mg Oral Powder contains ibuprofen 400mg as ibuprofen lysinate. Ibuprofen belongs to a group of medicines called Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). These medicines provide relief by changing the body's response to pain, swelling and high temperature.

Nurofen® Express 400mg Oral Powder is used to relieve:

- **symptoms of mild to moderate pain such as headache, toothache, period pains, rheumatic and muscular pain and migraine.**
- **cold and flu symptoms such as sore throat and fever.**

2. BEFORE YOU TAKE NUROFEN® EXPRESS 400mg ORAL POWDER

Do not take Nurofen® Express 400mg Oral Powder if you:

- have (or have had two or more episodes of) a stomach ulcer, perforation or bleeding of the stomach
- are allergic to ibuprofen, tartrazine (E102) or any of the other ingredients (see section 6) of Nurofen Express 400mg Oral Powder or to acetylsalicylic acid (aspirin) or other anti-inflammatory painkillers
- suffer from severe kidney, liver or heart problems
- have had gastrointestinal bleeding or perforation when previously taking NSAIDs (Non-Steroidal Anti-inflammatory drugs)
- have ever suffered from shortness of breath, have had a worsening of asthma, skin rash, itchy runny nose or facial swelling when previously taking ibuprofen, acetylsalicylic acid (aspirin) or other similar painkillers (NSAIDs)
- are suffering from severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake)
- are suffering from cerebrovascular or other active bleeding
- are suffering from blood cell production or clotting disorders
- are in the last three months of pregnancy (see below).

Please do not give to children under 12 years of age.

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

- have or have had asthma
- have kidney, heart, liver or bowel problems
- have high blood pressure, diabetes, high cholesterol or are a smoker
- have been told by your doctor that you have an intolerance to some sugars
- have systemic lupus erythematosus (a condition of the immune system causing joint pain, skin changes and other organ disorders)
- have had a heart attack or stroke
- have a history of gastrointestinal disease (such as ulcerative colitis or Crohn's disease)
- are in the first 6 months of pregnancy
- have chicken pox (varicella).

Consult a doctor before using Nurofen® Express 400mg Oral Powder if any above mentioned conditions concerns you.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. In particular, tell them if you are taking:

- blood thinning or anti-clotting medicines (anticoagulants) such as acetylsalicylic acid (aspirin), warfarin, triciopine,
- glucocorticoids (medicinal products containing cortisone or cortisone-like substances), aspirin, or other NSAIDs (anti-inflammatories and analgesics): since these may increase the risk of gastrointestinal ulcers or bleeding
- lithium (a medicine for manic depressive illness and depression) since the effect of lithium may be enhanced
- selective serotonin reuptake inhibitors (a medicine used for depression) as these may increase the risk of gastrointestinal side effects.
- methotrexate (a medicine for cancer or rheumatism) since the effect of methotrexate may be enhanced
- zidovudine: (a medicine for treating HIV infection) since the use of Nurofen Express 400mg Oral Powder may result in an increased risk of bleeding into a joint or a bleeding that leads to swelling.
- ciclosporin and tacrolimus (to prevent transplant rejection) as there could be an increased risk for the kidney.
- medicines for high blood pressure (ACE-inhibitors e.g.captopril, betareceptor blocking medicines, angiotensin II antagonists) and water tablets (diuretics), as NSAIDs may reduce the effects of these medicines and there could be a possible increased risk for the kidney (using potassium sparing diuretics with ibuprofen can lead to high blood levels of potassium)
- sulfonylureas (antidiabetic medicine) as i nteractions may be possible
- phenytoin (for epilepsy) as the effect may be enhanced
- quinolone antibiotics as the risk of convulsions may be increased.
- cardiac glycosides such as digoxin
- mifepristone (used to terminate pregnancies) as the effect may be reduced
- probenecid and sulfinpyrazones (medicines for gout): it may take longer for ibuprofen to be broken down by the body.

Other warnings

- Medicines such as Nurofen Express 400mg Oral Powder may be associated with **a small increased risk of heart attack or stroke.** Any risk is more likely with high doses and prolonged treatment. **If you have heart problems, have had a stroke or think that you might be at risk of these conditions** (for example if you have high blood pressure, diabetes, high cholesterol or are a smoker), you should discuss your treatment with your doctor or pharmacist.
- Taking a painkiller for headaches for too long can make them worse.

Fertility, pregnancy and breast-feeding

Do not take in the last 3 months of pregnancy. Speak to your doctor or pharmacist before taking this product if you are in the first 6 months of pregnancy or are breast-feeding.

This medicine passes into breast milk but may be used during breast-feeding if it is used at the recommended dose and for the shortest possible time.

Nurofen Express 400mg Oral Powder belongs to a group of medicines which may **impair fertility in women.** This is reversible on stopping the medicine. It is unlikely that Nurofen Express 400mg Oral Powder, used occasionally will affect your chances of becoming pregnant. However, tell your doctor before taking this medicine if you have problems becoming pregnant.

Driving and using machines

For short-term use and at normal dosage this medicine has no or negligible influence on the ability to drive and use machines. If side-effects such as tiredness or dizziness occur do not drive or operate machines. Alcohol consumption increases the risk of these side-effect.

Important information about some of the ingredients of Nurofen® Express 400mg Oral Powder.

Nurofen Express 400mg Oral Powder contains sucrose.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Nurofen Express 400mg Oral Powder contains tartrazine (E102). This may cause allergic reactions.

3. HOW TO TAKE NUROFEN® EXPRESS 400mg ORAL POWDER

This product is for **short term use only**. You should take the lowest dose for the shortest time necessary to relieve your symptoms.

Not to be given to children under 12 years of age

Always take Nurofen® Express 400mg Oral Powder exactly as stated in this package leaflet. You should check with your doctor or pharmacist if you are not sure. The standard dose is:

Adults, the elderly and children aged 12 years and older:

For oral use after dissolving in water.

Dissolve the content of one sachet in a glass of water, stir, then drink immediately.

You can take 1 sachet up to 3 times a day as required.

Leave at least 6 hours between doses. Do not take more than 3 sachets in any 24 hour period.

You should not take Nurofen Express 400mg Oral Powder for longer than **5 days** when treating pain and **3 days** when treating fever unless your doctor tells you to. If symptoms persist or worsen consult your doctor.

Please speak to the doctor or pharmacist if you feel that the effect of this medicine is greater or less than you expected.

If you take more Nurofen® Express 400mg Oral Powder than you should
Consult a doctor immediately. The following signs may occur: nausea, vomiting, stomach pain, headache, dizziness, drowsiness, nystagmus, blurred vision, ringing in the ear.
Rarely: low blood pressure and loss of consciousness.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Nurofen Express 400mg Oral Powder can cause side effects, although not everybody gets them. Side effects may be minimised by taking the lowest dose for the shortest time necessary to relieve the symptoms. Although side effects are uncommon, you may suffer one of the known side effects of NSAIDs. If you do, or if you have concerns, stop taking this medicine and talk to your doctor as soon as possible. Elderly people using this product are at increased risk of developing problems associated with side effects.

STOP TAKING this medicine and seek immediate medical help if you develop:

- **signs of intestinal bleeding** such as: severe pain in the abdomen, black tarry stools, blood in your faeces (stools/motions), vomiting blood or dark particles that look like coffee grounds.
- **signs of rare but serious allergic reaction** such as worsening of asthma, unexplained wheezing or shortness of breath, swelling of the face, tongue or throat, difficulty breathing, racing heart, drop in blood pressure leading to shock. These can happen even on first use of this medicine.
- **severe skin reactions** such as rashes covering the whole body, peeling, blistering or flaking skin.

Tell your doctor if you have any of the following side effects, they become worse or you notice any effects not listed.

Common (affects 1 to 10 users in 100)

- heart burn, abdominal pain, feeling sick and indigestion

Uncommon (affects 1 to 10 users in 1,000)

- inflammation of the stomach, worsening of colitis and Crohn's disease
- headache, dizziness, sleeplessness, agitation, irritability or tiredness
- visual disturbances
- flatulence (wind), diarrhoea, constipation and vomiting
- allergic reactions , such as skin rashes, itching and asthma attacks

Rare (affects 1 to 10 users in 10,000)

- tinnitus (ringing in the ears)
- kidney damage and the development of gout

Very rare (affects less than 1 users in 10,000)

- inflammation of the oesophagus or pancreas, blockages in the gut
- serious infections of the skin have occurred during chicken pox
- kidney disorders that may be shown by passing less or more urine than normal, cloudy urine, blood in the urine, pain in the back and/or swelling (particularly of the legs). In general, the habitual use of (several sorts of) analgesics can lead in rare cases to lasting severe kidney problems.
- blood disorders resulting in unexplained or unusual bruising or bleeding, fever, sore throat, mouth ulcers, flu-like symptoms and severe exhaustion
- psychotic reactions and depression
- worsening of inflammation due to infection
- high blood pressure, arterial hypertension, palpitations, heart failure, heart attack
- liver problems or inflammation of the liver. Liver failure or damage, particularly in long-term term use, shown by yellowing of the skin and eyes or pale stools and dark urine.
- the symptoms of aseptic meningitis with neck stiffness, headache, feeling sick, being sick, fever or consciousness clouding have been observed when using ibuprofen. Patients with autoimmune disorders (SLE, mixed connective-tissue disease) may be more likely to be affected. Contact a doctor at once, if these occur.
- swelling of skin tissue such as hands, feet or face.

Medicines such as Nurofen Express 400mg Oral Powder may be associated with a small increased risk of heart attack ("myocardial infarction") or stroke.

If any of the side effects get serious, or if you notice any side effects not listed in the leaflet, please tell your doctor or pharmacist.

Also you can help to make sure that medicines remain as safe as possible by reporting any unwanted side effects via the internet at www.mhra.gov.uk/yellowcard. Alternatively you can call Freephone 0808 100 3352 (available from 10 a.m. to 2 p.m. Mondays to Fridays) or fill in a paper form available from your local pharmacy.

5. HOW TO STORE NUROFEN® EXPRESS 400mg ORAL POWDER

Keep out of the reach and sight of children.

This medicinal product does not require any special temperature storage conditions.

Do not use Nurofen® Express 400mg Oral Powder after the expiry date which is stated on the carton and sachet.
The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask the pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Nurofen® Express 400mg Oral Powder contains:

Each sachet contains 400mg of the active substance ibuprofen (as ibuprofen lysinate).

The other ingredients are:

Betadex

Lemon essence (containing natural flavouring substances and preparations, maltodextrin, modified maize starch and tartrazine E102)

Saccharin sodium (E954)

Sodium cyclamate (E952)

Sodium citrate (E331)

Sucrose

What Nurofen® Express 400mg Oral Powder looks like and contents of the pack:

This medicine is a white, lemon flavoured powder supplied in sachets.

Single-dose sachet made of a heat-sealable paper/aluminium sheet /polythene complex.

Outer carton containing 1, 2, 3, 4, 5, 6, 7 and 8 sachets.

Not all pack sizes may be marketed.

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CONSULTATION LIST: ARM 86

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