# Nurofen Express Liquid Capsules PIL

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## NUROFEN EXPRESS LIQUID CAPSULES

### Ibuprofen 200mg, 400mg

**Product description**
Red, oval shaped transparent soft gelatin capsule with a Nurofen logo printed in white.

**Pharmacodynamic**
Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids; propionic acid derivative. ATC Code: M01A E01
Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) that in the conventional animal-experiment inflammation models has proven to be effective via prostaglandin-synthesis inhibition. In humans, ibuprofen reduces inflammatory-related pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits ADP-and collagen-induced platelet aggregation. Experimental data suggests that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 h before or within 30 min after immediate release dosing (81 mg), a decreased effect of ASA on the formation of thromboxane of platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusion can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

**Pharmacokinetic**
On oral application, ibuprofen is partly absorbed in the stomach and then completely in the small intestine.
Following hepatic metabolisation (hydroxylation, carboxylation), the pharmacologically inactive metabolites are completely eliminated, mainly renally (90 %), but also with the bile. The elimination half-life in healthy individuals and those with liver and kidney diseases is 1.8 -3.5 hours, plasma-protein binding about 99 %.
Peak plasma levels following oral administration of a normal-release pharmaceutical form (tablet) are reached after 1-2 hours. However, ibuprofen is absorbed more rapidly from the gastrointestinal tract following oral administration of Nurofen Express Liquid Capsules. In 2 pharmacokinetic studies, the times to peak plasma levels (Tmax) for ibuprofen acid tablets were 60 and 90 min compared with 35 and 40 min respectively for Nurofen Express Liquid Capsules. An average Cmax is achieved in half the time taken for Nurofen Express Liquid Capsules compared with normal-release pharmaceutical form (tablet Nurofen). Ibuprofen is detected in the plasma for more than 8 hours after administration of Nurofen Express Liquid Capsules.

**Indications**
Nurofen Express Liquid Capsules are indicated for the relief of pain such as headache, dental pain, period pain, rheumatic pain, muscular pain and backache. Nurofen Express Liquid Capsules also relieve fever such as fever associated with cold & flu.

**Recommended Dosage**
For oral use and short-term use only.
Capsules should not be chewed.

**Adults and children over 12 years**
Single dose: 1-2 liquid capsules of 200mg respectively.
1 liquid capsule of 400mg

If necessary, take additional doses of 1 or 2 capsules (200mg ibuprofen) or 1 capsule (400mg ibuprofen) but do not exceed a total dose of 1200mg ibuprofen in any 24-hour period. The dosing interval should not be below 4 hours for the 200mg dose and not below 6 hours for the 400mg dose.

If this product is required for more than 3 days, or if the symptoms worsen the patient is advised to consult a doctor.
It is recommended that patients with sensitive stomachs take Nurofen Express Liquid Capsules with food.

If taken shortly after eating, the onset of action of Nurofen Express Liquid Capsules may be delayed. If this happens do not take more Nurofen Express Liquid Capsules than recommended or until the correct re-dosing interval has passed.

**Contraindications**
- Hypersensitivity to ibuprofen, ponceau 4R (E124) or to any of the excipients
- In patients with a history of hypersensitivity reactions (e.g. bronchospasm, asthma, rhinitis, angioedema or urticaria) associated with the intake of acetylsalicylic acid (ASA) or other non-steroidal anti-inflammatory drugs (NSAIDs)
- 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
- Patients with severe hepatic failure, severe renal failure, coronary heart disease or severe heart failure (see also section Warnings and Precautions)
- In patients with cerebrovascular or other active bleeding
- In patients with bleeding diathesis or coagulation disordersIn patients with unclarified blood-formation disturbances
- In patients with severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake)
- In patients who have recently undergone coronary artery bypass graft (CABG) surgery and re -vascularization procedures.
- The last trimester of pregnancy (see section Pregnancy and Lactation)
- Adolescents weighing less than 40 kg or children under 12 years of age.

**Warnings and precautions**
Undesirable effects may be minimized by using the lowest effective dose for the shortest possible duration necessary to control symptoms (see Gastrointestinal and cardiovascular risks below).

Caution is required in patients with certain conditions, which may be made worse:
- Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section Side Effects)
- Congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria) gastrointestinal disorders and chronic inflammatory intestinal disease (ulcerative colitis, Crohn's disease) (see section Side Effects)
- Hypertension and/or cardiac impairment as renal function may deteriorate. (see sections Contraindications and Side Effects)
- Renal impairment (see sections Contraindications and Side Effects)
- Hepatic dysfunction (see sections Contraindications and Side Effects)
- Directly after major surgery
- In patients who react allergically to other substances, as an increased risk of hypersensitivity reactions occurring also exists for them on use of Nurofen Express Liquid Capsules
- In patients who suffer from hayfever, nasal polyps or chronic obstructive respiratory disorders as an increased risk exists for them of allergic reactions occurring.
- These may present as asthma attacks (so-called analgesic asthma). Quincke's oedema or urticaria

Gastrointestinal (GI) safety
The use with concomitant NSAIDs, including cyclo-oxygenase-2 specific inhibitors, increases risk of adverse reactions (see section Interactions with other medicaments) and should be avoided.

Elderly:
The elderly has an increased frequency of adverse reactions to NSAIDs especially gastrointestinal (GI) bleeding and perforation which may be fatal (see section Recommended Dosage).

Gastrointestinal bleeding, ulceration and perforation:
Gastrointestinal 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. When GI bleeding or ulceration occurs in patients receiving ibuprofen, it is advised to withdraw the treatment. The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses and patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section Contraindications) 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 acetylsalicylic acid, or other active substances likely to increase gastrointestinal risk (see below and section Interactions with other Medicaments). Patients with a history of GI toxicity, particularly the elderly, are advised to 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 ASA (see section Interactions with other Medicaments). 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 Side Effects).

Skin reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDSs (see section Side Effects). 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. The patient is advised to discontinue the intake of Nurofen Express Liquid Capsules at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of Nurofen Express Liquid Capsules in case of varicella.

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. Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration. Similar considerations should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).
Clinical trial and epidemiological data suggest that the use of ibuprofen, particularly at high doses (2400 mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200 mg daily) is associated with an increased risk of myocardial infarction.

Other notes
Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of hypersensitivity reaction after taking/administering Nurofen Express Liquid Capsules therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by specialist personnel.
Ibuprofen, the active substance of Nurofen Express Liquid Capsules may temporarily inhibit the blood-platelet function (thrombocyte aggregation). Therefore, it is recommended to monitor patients with coagulation disturbances carefully.
In prolonged administration of Nurofen Express Liquid Capsules regular checking of the liver values, the kidney function, as well as of the blood count, is required.
On prolonged use of painkillers, headache may occur that must not be treated with increased doses of the medicinal product.
In general terms, the habitual intake of painkillers, particularly on combination of several pain-relieving active substances, may lead to permanent renal damage with the risk of renal failure (analgesic nephropathy). This risk may be increased under physical strain associated with loss of salt and dehydration. Therefore, it should be avoided.
Through concomitant consumption of alcohol, active substance-related undesirable effects, particularly those that concern the gastrointestinal tract or the central nervous system, may be increased on use of NSAIDs.
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 (see section Pregnancy and Lactation).
The medicinal product contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.
This medicinal product contains Ponceau 4R. It may cause allergic reactions.
Risk of GI Ulceration, Bleeding and Perforation with NSAID

Date of Text Revision: May 2019

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Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAID therapy. Although minor upper GI problems (e.g. dyspepsia) are common, usually developing early in therapy, prescribers should remain alert for ulceration and bleeding in patients treated with NSAIDs even in the absence of previous GI tract symptoms.
Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Patients with prior history of serious GI events and other risk factors associated with peptic ulcer disease (e.g. alcoholism, smoking, and corticosteroid therapy) are at increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less than other individuals and account for most spontaneous reports for fatal GI events.

**Interaction with other medicinal products and other forms of interactions**
Ibuprofen should be avoided in combination with:
Aspirin: unless low-dose aspirin (not above 75mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (see Warnings and precautions).
Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitation of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusion can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use (see Pharmacodynamics).
Other NSAIDs including cyclooxygenase-2 selective inhibitors: as concomitant administration of several NSAIDs may increase the risk of gastrointestinal ulcers and bleeding due to a synergistic effect. The concomitant use of ibuprofen with other NSAIDs should therefore be avoided (see Warnings and precautions).
Digoxin, phenytoin, lithium: as concomitant use with digoxin, phenytoin or lithium preparations may increase serum levels of these medicinal products. A check of serum-lithium, serum-digoxin and serum-phenytoin levels is not as a rule required on correct use (maximum over 4 days).
Corticosteroids: as these may increase the risk of adverse reactions, especially of the gastrointestinal tract (gastrointestinal ulceration or bleeding) (see Contraindications).
Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see Warnings and precautions).
Anticoagulants: NSAIDs may enhance the effect of anti-coagulants, such as warfarin (see Warnings and precautions).
Probenecid and sulfinpyrazone: as these may delay the excretion of ibuprofen.
Diuretics, ACE inhibitors, betareceptor-blocker and angiotensin-II antagonists: since NSAIDs may reduce the effects of these drugs.
Potassium sparing diuretics: as it may lead to hyperkalaemia.
Methotrexate: as it may lead to elevated concentrations of methotrexate and an increase in its toxic effect.
Ciclosporin: increased risk of nephrotoxicity.
Tacrolimus: increased risk of nephrotoxicity.
Zidovudine: increased risk of haematological toxicity when NSAIDs are given with zidovudine.
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.
Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

**Pregnancy and Lactation**
During the first and second trimester of pregnancy, ibuprofen should not be given unless clearly necessary.
Ibuprofen is contraindicated during the third trimester of pregnancy
This medicine passes into breast milk in low concentrations but may be used during breast-feeding if it is used at the recommended dose and for the shortest possible time.
Ibuprofen may affect female fertility. This effect is reversible on withdrawal of treatment.

Use of NSAIDs at about 20 weeks gestation or later in pregnancy may cause foetal renal dysfunction leading to oligohydramnios and in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation.

**Effects on Ability to drive and to use Machines**
Single administration or short term use of ibuprofen does not usually warrant the adoption of any special precautions

**Side Effects**
Side effects may be minimized by taking the lowest dose for the shortest time necessary to relieve the symptoms.
*Infections*
Very rare: Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with use of NSAIDs has been described. The symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever or consciousness clouding have been observed under ibuprofen. Patients with autoimmune disorders (SLE, mixed connective-tissue disease) appear to be predisposed.
*Blood disorders*
Very rare: Problems in the blood cell production.
*Immune system disorders*
Uncommon: Hypersensitivity reactions with urticarial and pruritus, as well as asthma attacks.
Very rare: Severe general hypersensitivity reactions. Symptoms could be: facial, tongue and laryngeal swelling, dyspnea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock), exacerbation of asthma and bronchospasm.
*Psychiatric disorders*
Very rare: Psychotic reactions, depression.
*Nervous system disorders*
Uncommon: Headache, dizziness, sleeplessness, agitation, irritability or tiredness.
*Eye disorders*
Uncommon: Visual disturbances.
*Ear and balance disorders*
Rare: Tinnitus.
*Cardiac disorders*
Very rare: Palpitations, heart failure, myocardial infarction.
*Vascular disorders*
Very rare: Arterial hypertension.
*Gastrointestinal disorders*
Common: Stomach complaints, such as dyspepsia, pyrosis, abdominal pain and nausea, vomiting, flatulence, diarrhea, constipation and slight gastrointestinal blood losses that may cause anaemia in exceptional cases.
Uncommon: Gastrointestinal ulcers, potentially with bleeding and perforation, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see Warnings and precautions), gastritis.
Very rare: Oesophagitis, pancreatitis, formation of intestinal diaphragm-like strictures.
*Liver disorders*
Very rare: Hepatic dysfunction, hepatic damage, particularly in long-term therapy, hepatic failure, acute hepatitis.
*Skin disorders*
Very rare: Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis, alopecia. In exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection (see Infections).
*Kidney disorders*
Rare: Kidney-tissue damage (papillary necrosis) and elevated uric acid concentrations in the blood.
Very rare: Formation of oedemas, particularly in patients with arterial hypertension or renal insufficiency, nephrotic syndrome, interstitial nephritis that may be accompanied by acute renal insufficiency.

**Symptoms and treatment of overdose**
In adolescents and adults the dose response effect is not clear cut.
Symptoms: 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 dizziness, drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. Acute renal failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.
Management: A specific antidote does not exist. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount.

**List of Excipients**
Macrogol 600, Potassium hydroxide, Purified water, Sorbitol, Gelatin, Ponceau 4R, Opacode WB white NS-78-18011 (consisting of Purified Water, Titanium dioxide, Propylene glycol, Isopropyl Alcohol, Hypromellose), Nitrogen, Medium Chain Triglycerides, Isopropyl Alcohol, Lecithin

**Storage Conditions**
Do not store above 30°C; store in original package.

**Shelf Life**
24 months

**Nature and Contents of Container**
Blister, white opaque PVC/PVDC aluminium. The blisters are packed in cardboard cartons.

**Pack size**
A box of 10 capsules

**Manufactured by:**
Patheon Softgels B.V.
De Posthoornstraat 7,
Tilburg, 5048AS, Netherlands

**Product Registration Holder**
RB (Health) Malaysia Sdn. Bhd. (1297081-V)
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**Product Registrant**
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