## 1.3.1.1 PROFESSIONAL INFORMATION FOR NUROFEN PERIOD PAIN TABLETS

**SCHEDULING STATUS:** S1

### 1. NAME OF MEDICINE:

**NUROFEN PERIOD PAIN**

Ibuprofen 400 mg tablets

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

NUROFEN PERIOD PAIN

Each sugar-coated tablet contains ibuprofen 400 mg.

Contains sugar: sucrose 232,2 mg per tablet.

For the full list of excipients, see **section 6.1**.

### 3. PHARMACEUTICAL FORM

NUROFEN PERIOD PAIN: a white, polished sugar-coated tablet, printed NUROFEN 400 in red on one face.

### 4. CLINICAL PARTICULARS:

#### 4.1. Therapeutic indications

NUROFEN PERIOD PAIN is indicated for the relief of menstrual pain.

## 4.2. Posology and method of administration

**Polosogy:**

***NUROFEN PERIOD PAIN***

The recommended dosage of NUROFEN PERIOD PAIN is 1200 mg daily in divided doses, that is, one tablet three times a day.

Do not exceed 3 tablets in any 24 hours.

Not to be given to children under 12 years.

If symptoms persist for more than 7 days or worsen or new symptoms occur, consult your doctor.

Use the lowest effective dose for the shortest possible duration of treatment.

**Method of administration:**

For oral administration and short-term use only.

## 4.3. Contraindications

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

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 (NSAIDs).

Heart failure.

Severe renal failure or hepatic failure (see section 4.4).

History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including NUROFEN PAIN.

Active or history of recurrent ulcer, haemorrhage or perforations.

Last trimester of pregnancy (see **section 4.6**).

### 4.4. Special warnings and precautions for use

**General:**

NUROFEN PERIOD PAIN should not be given to patients with bleeding disorders, cardiovascular disease, peptic ulceration or a history of such ulceration. Asthma sufferers should only take NUROFEN PERIOD PAIN after consulting a doctor. Caution is advised in those patients who are receiving coumarin anticoagulants. Patients who are sensitive to aspirin should not be given NUROFEN PERIOD PAIN.

**DRESS:**

Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as NUROFEN PERIOD PAIN. Some of these events have been fatal or life threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophillia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue NUROFEN PERIOD PAIN and evaluate the patient immediately.

**Respiratory:**

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

**Other NSAIDs:**

Using NUROFEN PERIOD PAIN concomitantly with other NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

**SLE and mixed connective tissue disease:**

Systemic lupus erythematosus as well as those with mixed connective tissue disease increased risk of aseptic meningitis (see **section 4.8**). Clinical trial and epidemiological data suggest that the use of ibuprofen, particularly at high doses (2 400 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. ≤ 1 200 mg daily) is associated with an increased risk of myocardial infarction.

**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

**Hepatic:**

Hepatic dysfunction (see **sections 4.3 and 4.8**)

**Cardiovascular and cerebrovascular effects:**

Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with NUROFEN PERIOD PAIN therapy. In view of NUROFEN PERIOD PAIN's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

**Impaired female fertility:**

There is limited evidence that medicines which inhibit cyclo-oxygenase/ prostaglandin synthesis (such as NUROFEN PERIOD PAIN) 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 (GI) disease (ulcerative colitis, hiatus hernia, Crohn's disease, gastro-oesophageal reflux disease, angiodysplasia) 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 any time 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 ulcers and in the elderly.

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 medicines such as aspirin (see **section 4.5**).

When GI bleeding or ulceration occurs in patients receiving NUROFEN PERIOD PAIN, the treatment should be withdrawn.

**Severe skin reactions:**

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

**Masking of symptoms of underlying infections:**

NUROFEN PERIOD PAIN can mask symptoms of infection, which may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When NUROFEN PERIOD PAIN 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.

**Elderly:**

The elderly have an increased frequency of adverse reactions to NSAIDs including NUROFEN PERIOD PAIN, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.

**Excipients:**

NUROFEN PERIOD PAIN contains the sugar, sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take NUROFEN PERIOD PAIN.

## 4.5. Interaction with other medicines and other forms of interaction

**NUROFEN PERIOD PAIN (like other NSAIDs) should be avoided in combination with:**

**Aspirin (acetylsalicylic acid):**

Unless low-dose aspirin (not above 75 mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (see **section 4.4**). Experimental data suggest that NUROFEN PERIOD PAIN may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of *ex vivo* data to the clinical situation imply that no firm conclusions can be made for regular NUROFEN PERIOD PAIN use and no clinically relevant effect is considered to be likely for occasional NUROFEN PERIOD PAIN use.

**NSAIDs:**

Use of two or more NSAIDs concomitantly could result in an increase in side effects.

**NUROFEN PERIOD PAIN should be used with caution in combination with:**

**Corticosteroids:**

Increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs)

**Antihypertensives and diuretics:**

NSAIDs may diminish the effects of these medicines. 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 medicines 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.

**Anti-coagulants:**

NUROFEN PERIOD PAIN may enhance the effects of anti-coagulants such as warfarin.

**Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs):**

Increased risk of gastrointestinal bleeding.

**Cardiac glycosides:**

NUROFEN PERIOD PAIN may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

**Lithium:**

There is evidence for potential increase in plasma levels of lithium.

**Methotrexate:**

There is evidence for the potential increase in plasma levels of methotrexate.

**Ciclosporin:**

Increased risk of nephrotoxicity.

**Mifepristone:**

NUROFEN PERIOD PAIN 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 NUROFEN PERIOD PAIN is 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-positive haemophiliacs receiving concurrent treatment with zidovudine and NUROFEN PERIOD PAIN.

**Quinolone antibiotics:**

NUROFEN PERIOD PAIN can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NUROFEN PERIOD PAIN and quinolones may have an increased risk of developing convulsions.

## 4.6. Fertility, pregnancy and lactation

**Women of childbearing potential**

NUROFEN PERIOD PAIN may cause impairment of female fertility by an effect of ovulation. This is reversible upon withdrawal of treatment.

**Pregnancy**

NUROFEN PERIOD PAIN is contraindicated during the third trimester of pregnancy.
NUROFEN PERIOD PAIN is not recommended for use by pregnant women.

First trimester

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies raise concern about 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 %. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

Second and third trimester:

During the third trimester of pregnancy, prostaglandin synthesis inhibitors, may expose the foetus to: cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension); renal dysfunction, which may progress to renal failure with oligo hydroamniosis.

At the end of pregnancy, the mother and the neonate may be exposed 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.

**Lactation**

Patients using NUROFEN PERIOD PAIN should not breastfeed their infants.

### 4.7. Effects on ability to drive and use machines

NUROFEN has negligible influence on driving or operating machinery.

### 4.8. Undesirable effects

Adverse events which have been associated with NUROFEN PERIOD PAIN 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 NUROFEN PERIOD PAIN 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.

**Table 1: Report side effects for NUROFEN PERIOD PAIN**

| System organ class | Frequencies | Adverse event |
|---|---|---|
| **Blood and lymphatic system disorders** | Very rare | Haemopoietic disorders including anaemia, thrombocytopenia, neutropenia, eosinophilia, agranulocytosis. |
| **Immune system disorders** | Uncommon | Hypersensitivity reactions consisting of urticaria and pruritus[1,2] |
| | Very rare | Severe hypersensitivity reactions, including facial, tongue and throat swelling, dyspnoea, tachycardia, and hypotension (anaphylaxis, angioedema or severe shock)[2]. |
| **Nervous system disorders** | Uncommon | Headache |
| | Very rare | Aseptic meningitis[3] |
| **Cardiac disorders** | Not known | Cardiac failure and oedema[4] |
| **Vascular disorders** | Not known | Hypertension |
| **Respiratory, thoracic and mediastinal** | Not known | Provocation of bronchospasm in patients with asthma |

| System organ class | Frequencies | Adverse event |
|---|---|---|
| **disorders** | | |
| **Gastrointestinal disorders** | Uncommon | Abdominal pain, nausea, dyspepsia |
| | Rare | Diarrhoea, flatulence, constipation and vomiting |
| | Very rare | Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal, melaena, haematemesis, ulcerative stomatitis, gastritis. |
| | Not known | Exacerbation of colitis and Crohn's disease. |
| Hepatobiliary disorders | Very rare | Hepatotoxicity, abnormalities in liver function tests. |
| Skin and subcutaneous tissue disorders | Uncommon | Skin rash |
| | Very rare | Bullous reactions, including Stevens-Johnson syndrome, erythema multiforme and toxic epidermal syndrome. |
| | Not known | DRESS syndrome (see **section 4**), acute generalised exanthematous pustulosis (AGEP), photosensitivity reactions |
| **Renal and urinary disorders** | Very rare | Cystitis, haematuria, acute renal failure, interstitial nephritis, nephrotic syndrome. |
| **Investigations** | Very rare | Haemoglobin |

**Description of Selected Adverse Reactions**

[1]Hypersensitivity reactions may occur less frequently and include fever and rashes.[2]Other side effects include nervousness, tinnitus, depression, drowsiness, insomnia, and blurred vision and other visual field defects.

[2]NUROFEN PERIOD PAIN can provoke bronchospasm in patients with asthma.

[3]Other side-effects include blurred vision, changes in visual colour perception, and toxic amblyopia.

[4]Cardiovascular side-effects include: dizziness, nervousness, tinnitus, depression,, drowsiness and insomnia.

**Reporting of suspected adverse reactions:**

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

## 4.9. Overdose

**Symptoms:**

In adult, the dose response effect is less clear cut than in children where ingestion of more than 500 mg/ kg may cause symptoms. The half-life in overdose is1,5 to 3 hours. Nausea, vomiting, epigastric pain, or more rarely diarrhoea may develop. 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.

**Management:**

If recently taken, gastric lavage will remove any unabsorbed ibuprofen. Electrolytes may be corrected by intravenous infusion, if necessary. There is no specific antidote to NUROFEN PERIOD PAIN.

Management should be symptomatic and supportive. 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 bronchospasm.

## 5. PHARMACOLOGICAL PROPERTIES:

### 5.1. Pharmacodynamic properties

**Pharmacological classification:** A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesic

**Pharmacotherapeutic group:** ATC Code: M01AE01

NUROFEN PERIOD PAIN is a non-steroidal compound, with analgesic, anti-inflammatory and antipyretic actives

### 5.2. Pharmacokinetic properties

When taken with food, peak levels are observed after 1 to 2 hours. The half-life of Ibuprofen is about 2 hours. Excretion is via the kidneys.

## 6. PHARMACETICAL PARTICULARS:

### 6.1. List of excipients

**Tablet Core**

- Colloidal anhydrous silica
- Croscarmellose Sodium
- Sodium citrate

- Sodium lauryl sulphate
- Stearic acid

**Sugar coat ingredients**

- Acacia spray dried
- Carmellose sodium
- Macrogol 6000
- Sucrose
- Talc
- Titanium dioxide

**Black printing ink (NUROFEN TABLETS)**

- Iron oxide black (E172)
- Propylene glycol
- Shellac

**Printing ink (NUROFEN PERIOD PAIN)**

- Ammonium hydroxide (E527)
- Iron oxide red (E172)
- Propylene glycol (E1520)
- Shellac
- Simethicone

## 6.2. Incompatibilities

Not applicable.

### 6.3. Shelf life

NUROFEN PERIOD PAIN: 36 months

### 6.4. Special precautions for storage

Store at or below 25 ºC.

KEEP OUT OF REACH OF CHILDREN.

### 6.5. Nature and contents of container

NUROFEN PERIOD PAIN: blister pack of 12 tablets.

### 6.6. Special precautions for disposal

Not applicable.

## 7. HOLDER OF CERTIFICATE OF REGISTRATION:

Reckitt Benckiser Pharmaceuticals (Pty) Ltd.

8 Jet Park Road

Elandsfontein

1601

## 8. REGISTRATION NUMBERS:

NUROFEN PERIOD PAIN: W/2.7/142

## 9. DATE OF FIRST AUTHORISATION:

NUROFEN PERIOD PAIN: 27 September 1988

## 10. DATE OF REVISION OF THE TEXT:

25 March 2022