References: 1. Daniels SE, *et al*. A randomised, five-parallel-group, placebo-controlled trial comparing the efficacy and tolerability of analgesic combinations including a novel single-tablet combination of ibuprofen/paracetamol for postoperative dental pain. *Pain*. 2011;152:632–642.

Essential Information:

Nuromol Pain Relief 200mg/500mg Film Coated Tablets

Active Ingredient (s): Each tablet contains ibuprofen 200 mg and paracetamol 500 mg. **Indications**: For the temporary relief of mild to moderate pain associated with migraine, headache, backache, period pain, dental pain, rheumatic and muscular pain, pain of non-serious arthritis, cold and flu symptoms, sore throat and fever. This product is especially suitable for pain which has not been relieved by ibuprofen or paracetamol alone. Nuromol Pain Relief 200mg/500mg Film Coated Tablets is indicated in adults aged 18 years. **Dosage & Administration:** For oral administration and short term-use only (not more than 3 days). The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4). The patient should consult a doctor if the symptoms persist or worsen or if the product is required for more than 3 days. This medicine is for short-term use and it is not recommended for use beyond 3 days. *Adults:* One tablet to be taken up to three times per day with water. The interval between single doses should be at least six hours. If the one tablet dose does not control symptoms, a maximum of two tablets may be taken up to three times a day. Leave at least six hours between doses. Do not take more than six tablets (1200mg Ibuprofen, 3000mg Paracetamol) in any 24 hours period. To minimise side effects, it is recommended that patients take this medicine with food. *Elderly:* No special dosage modifications are required (see section 4.4). The elderly are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used for the shortest possible duration. The patient should be monitored regularly for gastrointestinal bleeding during NSAID therapy. *Paediatric population* Not for use by children and adolescents under 18 years. *Method of administration* Oral use. **Contraindications:** This product is contraindicated: • In patients with a known hypersensitivity to active substances - ibuprofen, paracetamol or to any of the excipients listed in section 6.1. • In patients with a history of hypersensitivity reactions (e.g. bronchospasm, angioedema, asthma, rhinitis, or urticaria) associated with acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs). • In patients with a history of, or an existing gastrointestinal ulceration/perforation or bleeding, including that associated with NSAIDs (see Section 4.4). • Patients with defects in coagulation. • In patients with severe hepatic failure, severe renal failure or severe heart failure (NYHA Class IV) (see Section 4.4). • In concomitant use with other NSAID containing products, including cyclo-oxygenase-2 (COX-2) specific inhibitors and doses of acetylsalicylic acid above 75 mg daily – increased risk of adverse reactions (see Section 4.5). • In concomitant use with other paracetamol-containing products – increased risk of serious adverse effects (see Section 4.5). • During the last trimester of pregnancy due to risk of premature closure of the foetal ductus arteriosus with possible pulmonary hypertension (see Section 4.6) **Special warnings and precautions for use:** This medicine is for short-term use and is not recommended for use beyond 3 days. **Paracetamol:** Care is advised in the administration of Paracetamol to patients with severe renal or severe hepatic impairment. The hazard of paracetamol overdose is greater in patients with non-cirrhotic alcoholic liver disease. Do not take with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if the patient feels well, because of the risk of delayed, serious liver damage (see section 4.9). Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended. **Ibuprofen:** Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see Section 4.2, and gastrointestinal and cardiovascular risks below) and by patients taking the dose with food (see Section 4.2). *Elderly:* The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see Section 4.2). Caution is required in patients with certain conditions: • *Respiratory disorders:* In patients suffering from, or with a history of, bronchial asthma or allergic disease NSAIDs have been reported to precipitate bronchospasm. • *Cardiovascular, renal and hepatic impairment:* The administration of NSAIDs may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. Renal function should be monitored in these patients. Treatment should be stopped in those patients who develop severe renal failure (see Section 4.3). Dose reduction is recommended in patients showing signs of worsening hepatic function. Treatment should be stopped in those patients who develop severe liver failure (see section 4.3). • *Cardiovascular and cerebrovascular effects* Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy. Clinical studies suggest that use of ibuprofen, particularly at high doses (2400 mg daily) with a small increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤1200mg daily) 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 be exercised before initiating long-term treatment for 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. • *Gastrointestinal bleeding, ulceration and perforation:* Gastrointestinal (GI) bleeding, ulceration and 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 serious GI events. The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see Section 4.3) and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose acetylsalicylic acid, or other drugs likely to increase gastrointestinal risk (see below and 4.5). 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 antiplatelet agents such as acetylsalicylic acid (see Section 4.5). When GI bleeding or ulceration occurs in patients receiving ibuprofen containing products, the treatment should be withdrawn. NSAIDs should be given with care to patients with a history of GI disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see Section 4.8). • *SLE and mixed connective tissue disease:* In patient with systemic lupus erythematosus (SLE) and mixed connective tissue disease disorders there may be an increased risk of aseptic meningitis (see Section 4.8). • *Severe 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 NSAIDs (see Section 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Use of this product 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. • *Impaired female fertility:* The use of the product may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of the product should be considered. 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 fever or pain relief in relation to infection, monitoring of infection is advised. In non- hospital settings, the patient should consult a doctor if symptoms persist or worsen.

Side effects:

System Organ Class	Frequency	Adverse Events
Blood and lymphatic system disorders	Very rare (≤1/10,000)	Haematopoietic disorders[1]
Immune system disorders	Uncommon	Hypersensitivity with urticaria and pruritus[2]
	Very rare (≤1/10,000)	Severe hypersensitivity reactions. Symptoms can include facial, tongue and throat swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock)[2]
Psychiatric disorders	Very rare (≤1/10,000)	Confusion, depression and hallucinations.
Nervous system disorders	Uncommon (≥1/1,000 to ≤1/100):	Headache and dizziness.
	Rare	Paraesthesia
	Very rare (≤1/10,000)	Aseptic meningitis, optic neuritis and somnolence.
Eye disorders	Very rare (≤1/10,000)	Visual disturbance.
Ear and labyrinth disorders	Very rare (≤1/10,000)	Tinnitus and vertigo.
Cardiac disorders	Common	Oedema
	Very rare (≤1/10,000)	Cardiac failure
Vascular Disorders	Very Rare	Hypertension[4]
Respiratory and thoracic and mediastinal disorders	Very rare (≤1/10,000)	Respiratory tract reactivity including: asthma, exacerbation of asthma, bronchospasm and dyspnoea [2]
Gastrointestinal Disorders	Common (≥1/100 to ≤1/10)	Abdominal pain, vomiting, diarrhoea, dyspepsia, nausea andabdominal discomfort[5]
	Uncommon (≥1/1,000 to ≤1/100):	Peptic ulcer, gastrointestinal perforation or gastrointestinal haemorrhage, melaena haematemesis[6], mouth ulceration, exacerbation of ulcerative colitis and Crohn's disease[7], gastritis, pancreatitis, flatulence and constipation.
Hepatobiliary disorders	Very rare (≤1/10,000)	Abnormal liver function, hepatitis and jaundice[8]
Skin and subcutaneous tissue disorders	Common	Hyperhidrosis
	Uncommon	Various skin rashes[2]
	Very Rare	Bullous reactions including Stevens-Johnson syndrome, erythema multiforme and toxic epidermal necrolysis[2].Exfoliative dermatoses, purpura, photosensitivity
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) Acute generalised exanthematous pustulosis (AGEP) Photosensitivity reactions
Renal and urinary disorders	Very rare (≤1/10,000)	Nephrotoxicity in various forms, including interstitial nephritis, nephrotic syndrome, and acute and chronic renal failure[9]
General disorders and administration site conditions	Very rare (≤1/10,000)	Fatigue and malaise.
Investigations	Common (≥1/100 to ≤1/10)	Alanine aminotransferase increased, gamma-glutamyltransferase increased and liver function tests abnormal with paracetamol. Blood creatinine increased and blood urea increased.
	Uncommon (≥1/1,000 to ≤1/100)	Aspartate aminotransferase increased, blood alkaline phosphatase increased, blood creatine phosphokinase increased, blood creatinine increased, haemoglobin decreased and platelet count increased.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for the MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Reckitt Benckiser Healthcare (UK) ltd on: 0333 200 5345