Scroll down to view Clinical Summary

Essential Information:

Nuromol Dual Action Pain Relief 200 mg/500 mg tablets

PL 00063/0649 **Active Ingredient (s):** Each tablet contains ibuprofen 200 mg and paracetamol 500 mg. **Indications:** For the temporary relief of mild to moderate pain which has not been relieved by ibuprofen or paracetamol individually such as migraine, headache, backache, period pain, dental pain, rheumatic and muscular pain, cold and flu symptoms, sore throat and fever. **Dosage & Administration:** *Posology:* For short term-use only. For short term-use only. Before Nuromol Dual Action is taken, the patient should first try ibuprofen or paracetamol for pain relief in accordance with the product instructions, for the first day of treatment. If the pain has not been relieved by ibuprofen or paracetamol during the first day of treatment, then the next day Nuromol Dual Action can be taken. 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. **Adults:** One tablet to be taken up to three times per day with water. Leave at least six hours between doses. 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 of Nuromol Dual Action Pain Relief (3000mg Paracetamol, 1200mg Ibuprofen) in any 24 hour period. To minimise side effects, it is recommended that patients take Nuromol Dual Action Pain Relief 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. Not for use by children under 18 years. Method of Administration: For oral administration **Contraindications:** This product is contraindicated: • In patients with a known hypersensitivity to ibuprofen, paracetamol or any other excipients in the product. • In concomitant use with other Paracetamol-containing products – increased risk of serious adverse effects (see Section 4.5). • 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 Active, or a history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding). • 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). • 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:** Do not exceed the recommended dose. Do not use until first trying ibuprofen or paracetamol individually to relieve your pain according to the pack instructions. Consult a doctor if the symptoms persist or worsen or if the product is required for more than 3 days. Keep out of the sight and reach of children. **Paracetamol:** The hazards of paracetamol overdose are greater in patients with non-cirrhotic alcoholic liver disease. 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. Do not take with any other paracetamol containing products. Immediate medical advice should be sought if this occurs, even if you feel well as this can result in an overdose (see section 4.9). **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. • **SLE and mixed connective tissue disease:** In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disease disorders there may be an increased risk of aseptic meningitis (see Section 4.8). • **Cardiovascular and cerebrovascular effects** Appropriate monitoring and medical advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention, hypertension and oedema have been reported in association with NSAID therapy. Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) may be associated 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/day) is associated with an increased risk of arterial thrombotic events.Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided. Careful consideration should 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. • **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 (see Section 4.3). • **Gastrointestinal effects:** NSAIDS should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8). 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. • **Severe skin reactions:** Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported 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. • **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. • **Impaired female fertility:** There is limited evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may impair female fertility by an effect on ovulation and is not recommended in women attempting to conceive. This is reversible on withdrawal of treatment. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of the product should be considered. • **Excipients** This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'. Fertility, **Pregnancy and Lactation:** *Pregnancy:* There is no experience of use of this product in humans during pregnancy. A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency. Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern. In view of the known effects of NSAIDs on the foetal cardiovascular system (risk of closure of ductus arteriosus), use in the last trimester is contraindicated. The onset of labour may be delayed, and duration increased with an increased bleeding tendency in both mother and child (see Section 4.3). NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the foetus. Therefore if possible, the use of this product should be avoided in the first six months of pregnancy and contraindicated in the last three months of pregnancy (see Section 4.3). Lactation: Ibuprofen and its metabolites can pass in very small amounts (0.0008% of the maternal dose) into the breast milk. No harmful effects to infants are known. Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breastfeeding. Therefore it is not necessary to interrupt breastfeeding for short-term treatment with the recommended dose of this product. See Section 4.4 regarding female fertility.

Side effects:

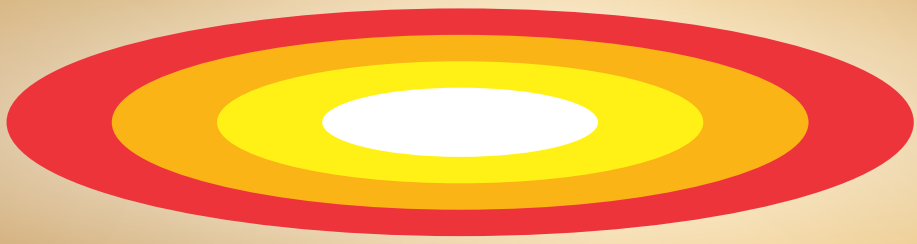
SYSTEM ORGAN CLASS	FREQUENCY	ADVERSE EVENT
Blood and Lymphatic System Disorders	Very rare	Haematopoictic disorders[1]
Immune System Disorders	Uncommon	Hypersensitivity with urticaria and pruritus[2]
	Very rare	Severe hypersensitivity reactions. Symptoms can include facial, tongue and throat swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock)[2]
Psychiatric Disorders	Very rare	Confusion, depression and hallucinations
Nervous System Disorders	Uncommon	Headache and dizziness
	Very rare	Aseptic meningitis[3], paraesthesia, optic neuritis and somnolence
Eye Disorders	Very rare	Visual disturbance
Ear and Labyrinth Disorders	Very rare	Tinnitus and vertigo
Cardiac Disorders	Very rare	Cardiac failure and oedema[4]
Vascular Disorders	Very rare	Hypertension[4]
Respiratory and thoracic and mediastinal disorders	Very rare	Respiratory reactivity including: asthma, exacerbation of asthma, bronchospasm and dyspnoea[2]
Gastrointestinal Disorders	Common	Abdominal pain, vomiting, diarrhoea, nausea, dyspepsia and abdominal discomfort[5]
	Uncommon	Peptic ulcer, gastrointestinal perforation or gastrointestinal haemorrhage, melaena, haematemesis[6], mouth ulceration, exacerbation of colitis and Crohn's disease[7] gastritis, pancreatitis, flatulence and constipation
Hepatobiliary Disorders	Very rare	1)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	Nephrotoxicity in various forms, including interstitial nephritis, nephrotic syndrome, and acute and chronic renal failure[9]
General Disorders and Administration Site Conditions	Very rare	Fatigue and malaise
Investigations	Common	Alanine aminotransferase increased, gamma-glutamyltransferase increased and liver function tests abnormal with paracetamol. Blood creatinine increased, blood urea increased.
	Uncommon	Aspartate aminotransferase increased, blood alkaline phosphatase increased, blood creatine phosphokinease increased, haemoglobin decreased and platelet count increased

Legal Classification: GSL **Licence Holder:** Reckitt Benckiser Healthcare (UK) Limited, Slough, SL1 3UH **Licence Number:** PL 00063/0649 **Price (ex VAT):** £3.99 for 12 tablets **Last Revised:** 16/08/2021

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

NUROMOL DUAL ACTION PAIN RELIEF CLINICAL SUMMARY

IBUPROFEN + PARACETAMOL



RB-M-87378 February 2022

Essential information on back page

FROM THE MAKERS OF NUROFEN

NUROMOL DUAL ACTION PAIN RELIEF EFFICACY VS. OTC CODEINE COMBINATIONS

Nuromol Dual Action Pain Relief is a fixed-dose combination analgesic

- Each Nuromol Dual Action Pain Relief tablet contains:[1]
  - 200 mg ibuprofen
  - 500 mg paracetamol

- Nuromol Dual Action Pain Relief's technology[2] simultaneously releases paracetamol and ibuprofen, delivering a combination effect[1]

Nuromol Dual Action Pain Relief is more effective in relieving pain over 12 hours than fixed dose combinations of ibuprofen (200 mg) + codeine (12.8 mg) or paracetamol (500 mg) + codeine (15 mg)[3]

- The Daniels study, a 2011 head-to-head, double-blind, parallel group, placebo-controlled, randomised single dose study, compared Nuromol Dual Action Pain Relief with a fixed-dose combination of ibuprofen 200 mg + codeine 12.8 mg and paracetamol 500 mg + codeine 15 mg in patients with post-operative dental pain following third molar extraction[3]

- Subjects were randomised to one of 5 treatment arms and instructed to take treatment once pain was ranked as moderate-to-severe on the ordinal scale and at least 50 mm on the pain intensity Visual Analogue Scale (VAS):[3*]
  - 1 x Nuromol Dual Action Pain Relief tablet: ibuprofen 200 mg/paracetamol 500 mg (plus a placebo tablet); n=173
  - 2 x Nuromol Dual Action Pain Relief tablets: ibuprofen 400 mg/paracetamol 1000 mg; n=168
  - 2 x ibuprofen 200 mg/codeine 12.8 mg tablets; n=169
  - 2 x paracetamol 500 mg/codeine 15 mg tablets; n=113
  - 2 x placebo tablets; n=55

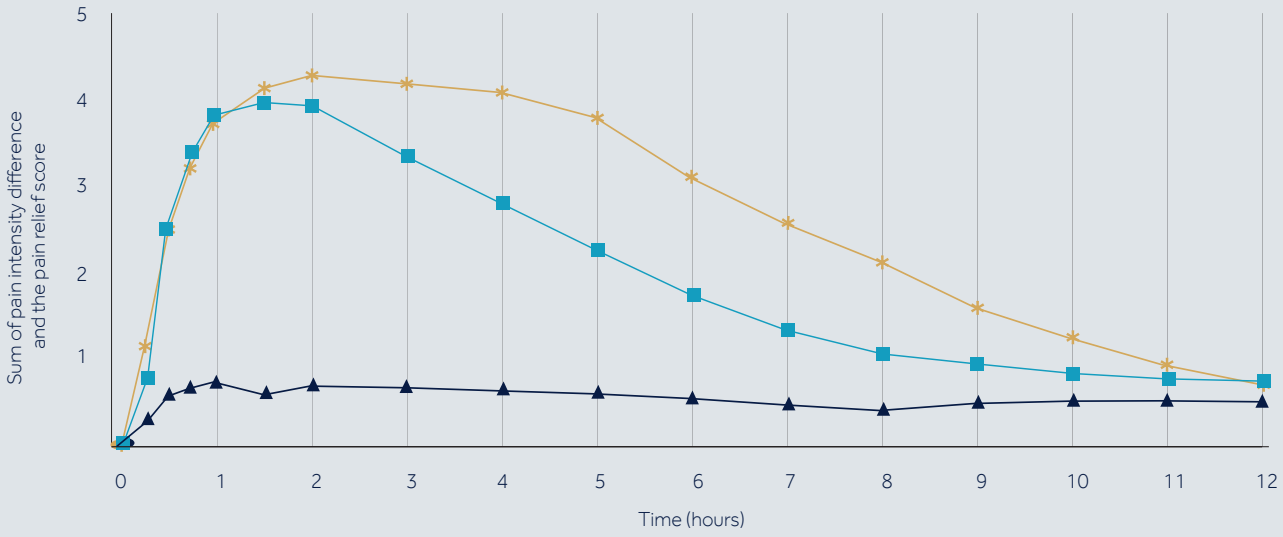
- The primary outcome was the sum of the mean scores of pain relief (PR*) combined with pain intensity (PI†) differences over 12 hours (SPRID 0–12 hours). Pain assessments were conducted at 0.25, 0.5, 0.75, 1.0, 1.5, 2.0 hours and hourly there after up to 12 hours post-dose[3]

- 2 x Nuromol Dual Action Pain Relief tablets were significantly more effective than (see Figure 1):[3]
  - 2 x ibuprofen 200 mg/codeine 12.8 mg tablets (P = 0.0001)
  - 2 x paracetamol 500 mg/codeine 15 mg tablets (P = 0.0001)
  - 2 x placebo tablets (P < 0.0001)

- 1 x Nuromol Dual Action Pain Relief tablet was:[3]
  - Superior for pain relief up to 12 hours to 2 x paracetamol 500 mg/codeine 15 mg tablets (P = 0.0001)
  - Non-inferior to 2 x tablets of ibuprofen 200 mg/codeine 12.8 mg tablets

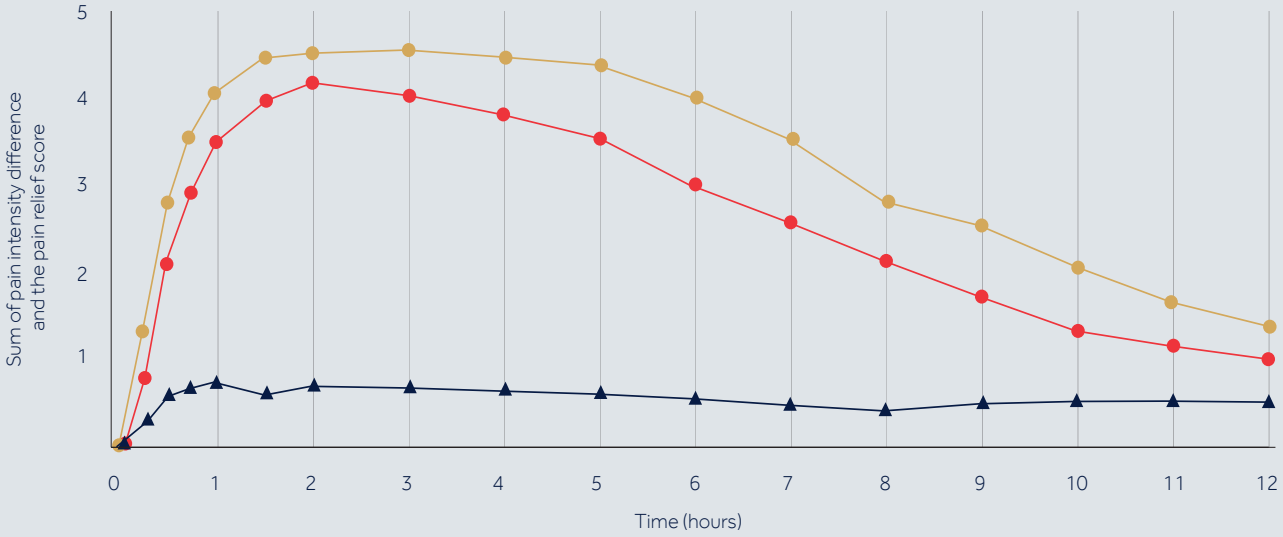
*Pain relief was rated on a 5-point ordinal scale (0=none, 1=a little, 2=some, 3=a lot, 4=complete).
†Pain Intensity was measured on a 4-point ordinal rating scale: 0=no pain, 1=mild pain, 2=moderate pain and 3=severe pain. PI VAS was rated on a horizontal 100-mm VAS labelled: No pain (0 mm) to worst pain (100 mm).

Figure 1: mean pain relief and intensity differences shown at each time point (intention-to-treat population)[3]



1 x Ibuprofen 200 mg/paracetamol 500 mg tablet (n=173) 2 x Paracetamol 500 mg/codeine 15 mg tablets (n=113) 2 x Placebo tablets (n=55)

Mean pain relief and intensity differences shown at each timepoint (intention-to-treat population). Sum of pain relief and intensity difference (SPRID) of 1 tablet of ibuprofen 200 mg/paracetamol 500 mg vs. 2 tablets paracetamol 500 mg/codeine 15 mg (P = 0.0001) and vs. 2 placebo tablets (P < 0.0001) based on area under the curve (AUC).[3]



2 x Ibuprofen 200 mg/paracetamol 500 mg tablets (n=168) 2 x Ibuprofen 200 mg/codeine 12.8 mg tablets (n=169) 2 x Placebo tablets (n=55)

Mean pain relief and intensity differences shown at each timepoint (intention-to-treat population). Sum of pain relief and intensity difference (SPRID) of 2 tablets of ibuprofen 200 mg/paracetamol 500 mg vs. 2 tablets ibuprofen 200 mg/codeine 12.8 mg (P = 0.0001) and vs. 2 placebo tablets (P < 0.0001) based on area under the curve (AUC).[3]

Graphs adapted from Daniels *et al.* 2011.[3]

The secondary endpoints also confirmed Nuromol Dual Action Pain Relief was more effective in relieving pain up to 12 hours than fixed-dose OTC codeine combinations, see Table 1[3]

Table 1: Secondary endpoints confirm Nuromol Dual Action Pain Relief is more effective than fixed-dose codeine combinations[3]

Secondary outcome	Result
SPRID at 0–4 hours, 0–6 hours and 0–8 hours	2 x Nuromol Dual Action Pain Relief tablets were statistically significantly more effective than fixed-dose codeine combinations (ibuprofen 200 mg/codeine 12.8 mg, P = 0.0001; paracetamol 500 mg/codeine 15 mg, P < 0.0001) 1 x Nuromol Dual Action Pain Relief tablet was significantly more effective than 2 x paracetamol 500 mg/codeine 15 mg tablets (P = 0.0001)
Sum of pain intensity difference (SPID) at 0–4 hours, 0–6 hours, 0–8 hours and 0–12 hours	2 x Nuromol Dual Action Pain Relief tablets were statistically significantly more effective than fixed-dose codeine combinations (0–4 hours: ibuprofen 200 mg/codeine 12.8 mg, P ≤ 0.007; paracetamol 500 mg/codeine 15 mg, P ≤ 0.007) 1 x Nuromol Dual Action Pain Relief tablet was significantly more effective than 2 x paracetamol 500 mg/codeine 15 mg tablets (0–4 hours: P ≤ 0.02)
Total pain relief (TOTPAR) at 0–4 hours, 0–6 hours, 0–8 hours and 0–12 hours	2 x Nuromol Dual Action Pain Relief tablets were statistically significantly more effective than fixed-dose codeine combinations (0–4 hours: ibuprofen 200 mg/codeine 12.8 mg, P ≤ 0.007; paracetamol 500 mg/codeine 15 mg, P ≤ 0.007) 1 x Nuromol Dual Action Pain Relief tablet was significantly more effective than 2 x paracetamol 500 mg/codeine 15 mg tablets (0–4 hours: P ≤ 0.02)
Patient global assessment*	- 84.8% of subjects rated 2 x Nuromol Dual Action Pain Relief tablets as good to excellent - 81.6% of subjects rated 1 x Nuromol Dual Action Pain Relief tablets as good to excellent - 77.9% of subjects rated 2 x ibuprofen 200 mg/codeine 12.8 mg tablets as good to excellent - 72.6% of subjects rated 2 x paracetamol 500 mg/codeine 15 mg tablets as good to excellent

*Patient Global Assessment was assessed on a 5-point ordinal scale (1=poor, 2=fair, 3=good, 4=very good, 5=excellent) in response to the question ''How effective do you think the study medication is as a treatment for pain?''

Nuromol Dual Action Pain Relief has fewer adverse events than fixed-dose codeine combinations of ibuprofen 200 mg/codeine 12.8 mg, paracetamol 500 mg/codeine 15 mg and placebo[3]

Table 2: Adverse events reported during study period[3]

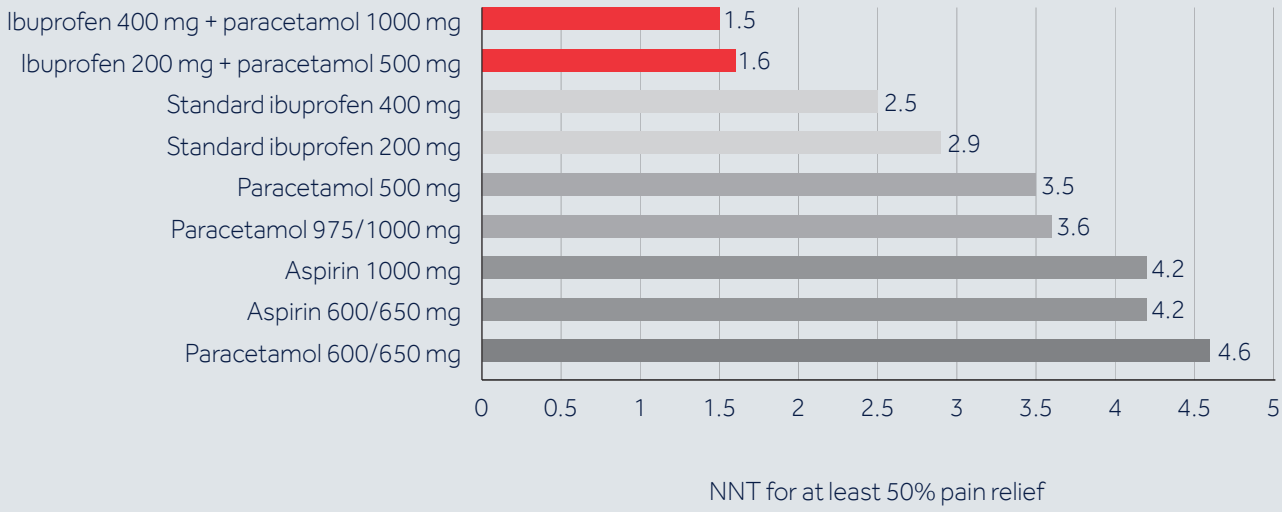
Treatment	Any adverse event (%)	Treatment-emergent adverse event (within 12 hours of dosing)
2 x Nuromol Dual Action Pain Relief tablets	51.8%	18.5%
1 x Nuromol Dual Action Pain Relief tablet	50.9%	24.9%
2 x Paracetamol 500 mg/codeine 15 mg tablets	63.7%	39.8%
2 x Ibuprofen 200 mg/codeine 12.8 mg tablets	57.4%	34.9%
Placebo	63.6%	38.2%

IBUPROFEN + PARACETAMOL COMBINATION EFFICACY VS. OTHER OTC ANALGESICS[4]

Ibuprofen + paracetamol combinations have the lowest NNT values of OTC analgesics tested[4]

- A Cochrane review was conducted of existing Cochrane reviews of OTC analgesics for acute pain[4]
- This systematic review of 10 Cochrane reviews included 21 OTC analgesics and had as the primary outcome the number of participants with at least 50% pain relief over 4–6 hours, compared with placebo[4]
- From individual reviews, the Number-Needed-to-Treat (NNT) for each drug/dose combination was calculated and also the success rate to achieve at least 50% of maximum pain relief (see Box 1 for more information)[4]
- Ibuprofen 400 mg + paracetamol 1000 mg had the lowest NNT of all OTC analgesics analysed (see Figure 2)[4]

Figure 2: NNTs of OTC analgesics tested[4*]



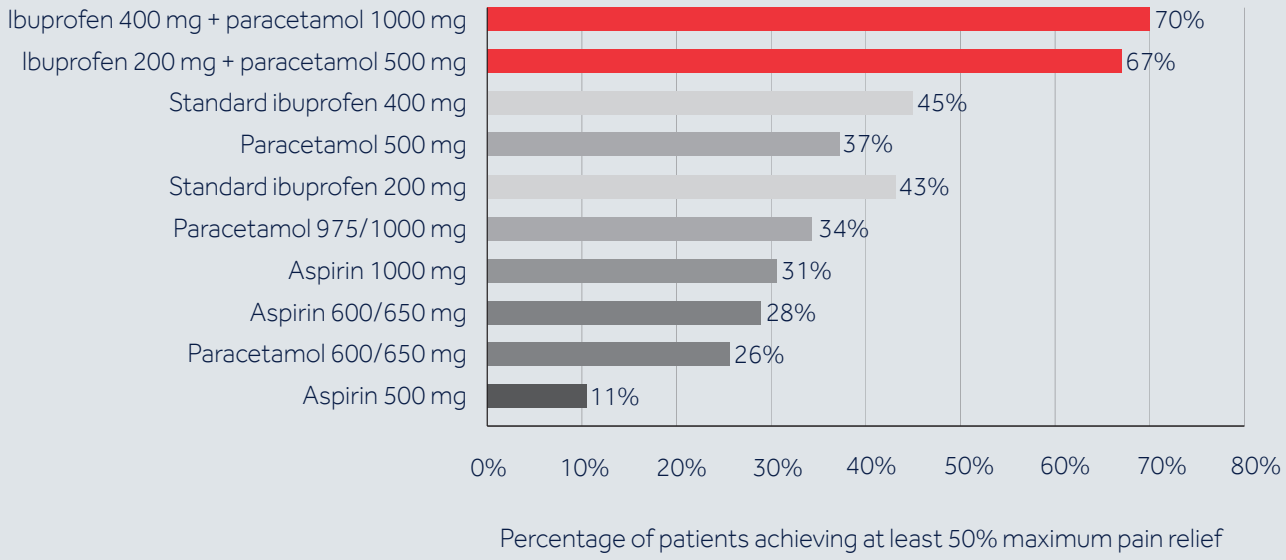
*NNT for aspirin 500 mg was no better than placebo.[4]
Adapted from Moore *et al.* 2015.[4]

Ibuprofen + paracetamol combinations have the highest success rate[†] of OTC analgesics analysed[4]

- Ibuprofen 400 mg + paracetamol 1000 mg had the highest success rate of OTC analgesics analysed in this Cochrane review – which means more people can get effective pain relief than with other OTC treatments analysed (see Figure 3).[4]

[†]See Box 1 for explanation of success rate.

Figure 3: Success rate* of OTC analgesics analysed[4]



Adapted from Moore *et al.* 2015.[4]

*See Box 1 for explanation of success rate.

Studies have shown that ibuprofen + paracetamol combinations had a lower adverse event rate than placebo[4]

	Ibuprofen 200 mg + paracetamol 500 mg	Ibuprofen 400 mg + paracetamol 1000 mg	Placebo
Percentage of participants experiencing at least 1 adverse event	30%	29%	48%

Adapted from Moore *et al.* 2015.[4]

Box 1: NNT and success rate explained

The NNT determines the magnitude of the effect of an intervention and describes the number of people who need to be treated with an analgesic for one more person to have good pain relief than if they had been treated with placebo. The ideal NNT is 1 and the closer an analgesic's NNT is to 1, the more effective it is.

The success rate determines the degrees of effectiveness between analgesics. It is calculated by taking the proportion of subjects who get good pain relief with placebo and expressing this as a percentage of the maximum possible success rate for the treatment, i.e. 100 minus the response rate with placebo. The higher the success rate, the more people in the population who will achieve pain relief.

NUROMOL DUAL ACTION PAIN RELIEF KEY BENEFITS

Simple, convenient dosing schedule

- Take 1 tablet, if 1 tablet dose does not control symptoms, a maximum of 2 tablets may be taken up to three times a day[1]
- Leave at least six hours between doses[1]
- To minimise side effects, it is recommended that patients take Nuromol Dual Action Pain Relief with food[1]
- Refer to GP if Nuromol Dual Action Pain Relief is required for more than 3 days[1]

Synergistic action

- The pharmacological actions of ibuprofen and paracetamol differ in their site and mode of action[1]
- Nuromol Dual Action Pain Relief's complementary modes of action are synergistic, which results in greater antinociception and antipyresis than the single actives alone[1]

Onset of action

Data from a randomised, controlled trial show:

- Nuromol Dual Action Pain Relief starts to absorb from 5 minutes[1]
- Onset of action with perceptible pain relief in a median of 18.3 minutes[1]
  - Faster than standard ibuprofen (23.8 minutes, P = 0.0015)[1]

Duration of action

- Nuromol Dual Action Pain Relief lasts for up to 9.1 hours[1]
  - Longer than standard paracetamol 500 mg (4 hours) or 1000 mg (5 hours)[1]

Patient satisfaction

- Nuromol Dual Action Pain Relief had high levels of patient satisfaction:[1]
  - 93.2% of patients rated Nuromol Dual Action Pain Relief as 'good,' 'very good' and 'excellent' in achieving pain relief[1]

FROM THE MAKERS OF NUROFEN

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1. Nuromol Dual Action Pain Relief 200 mg/500 mg Tablets. Summary of Product Characteristics. Updated December 2021. Accessed February 2022. https://www.medicines.org.uk/emc/product/4967
2. Patented technology. Composition comprising a NSAID and paracetamol. 2007. Data on File.
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4. Moore RA, *et al.* Non-prescription (OTC) oral analgesics for acute pain – an overview of Cochrane reviews (Review). Cochrane Database of Systematic Reviews. 2015, Issue 11. Art. No.: CD010794.

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Not for use by children under 18 years. Method of Administration: For oral administration **Contraindications:** This product is contraindicated: • In patients with a known hypersensitivity to ibuprofen, paracetamol or any other excipients in the product. • In concomitant use with other Paracetamol-containing products – increased risk of serious adverse effects (see Section 4.5). • 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 Active, or a history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding). • 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). • 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:** Do not exceed the recommended dose. Do not use until first trying ibuprofen or paracetamol individually to relieve your pain according to the pack instructions. Consult a doctor if the symptoms persist or worsen or if the product is required for more than 3 days. Keep out of the sight and reach of children. **Paracetamol:** The hazards of paracetamol overdose are greater in patients with non-cirrhotic alcoholic liver disease. 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. Do not take with any other paracetamol containing products. Immediate medical advice should be sought if this occurs, even if you feel well as this can result in an overdose (see section 4.9). **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. **• SLE and mixed connective tissue disease:** In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disease disorders there may be an increased risk of aseptic meningitis (see Section 4.8). **• Cardiovascular and cerebrovascular effects** Appropriate monitoring and medical advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention, hypertension and oedema have been reported in association with NSAID therapy. Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) may be associated 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/day) is associated with an increased risk of arterial thrombotic events.Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided. Careful consideration should 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. **• 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 (see Section 4.3). **• Gastrointestinal effects:** NSAIDS should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8). 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. **• Severe skin reactions:** Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported 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. **• 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.

• **Impaired female fertility:** There is limited evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may impair female fertility by an effect on ovulation and is not recommended in women attempting to conceive. This is reversible on withdrawal of treatment. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of the product should be considered. **• Excipients** This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'. Fertility, **Pregnancy and Lactation:** *Pregnancy:* There is no experience of use of this product in humans during pregnancy. A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency. Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern. In view of the known effects of NSAIDs on the foetal cardiovascular system (risk of closure of ductus arteriosus), use in the last trimester is contraindicated. The onset of labour may be delayed, and duration increased with an increased bleeding tendency in both mother and child (see Section 4.3). NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the foetus. Therefore if possible, the use of this product should be avoided in the first six months of pregnancy and contraindicated in the last three months of pregnancy (see Section 4.3). Lactation: Ibuprofen and its metabolites can pass in very small amounts (0.0008% of the maternal dose) into the breast milk. No harmful effects to infants are known. Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breastfeeding. Therefore it is not necessary to interrupt breastfeeding for short-term treatment with the recommended dose of this product. See Section 4.4 regarding female fertility.

Side effects:

SYSTEM ORGAN CLASS	FREQUENCY	ADVERSE EVENT
Blood and Lymphatic System Disorders	Very rare	Haematopoictic disorders[1]
Immune System Disorders	Uncommon	Hypersensitivity with urticaria and pruritus[2]
	Very rare	Severe hypersensitivity reactions. Symptoms can include facial, tongue and throat swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock)[2]
Psychiatric Disorders	Very rare	Confusion, depression and hallucinations
Nervous System Disorders	Uncommon	Headache and dizziness
	Very rare	Aseptic meningitis[3], paraesthesia, optic neuritis and somnolence
Eye Disorders	Very rare	Visual disturbance
Ear and Labyrinth Disorders	Very rare	Tinnitus and vertigo
Cardiac Disorders	Very rare	Cardiac failure and oedema[4]
Vascular Disorders	Very rare	Hypertension[4]
Respiratory and thoracic and mediastinal disorders	Very rare	Respiratory reactivity including: asthma, exacerbation of asthma, bronchospasm and dyspnoea[2]
Gastrointestinal Disorders	Common	Abdominal pain, vomiting, diarrhoea, nausea, dyspepsia and abdominal discomfort[5]
	Uncommon	Peptic ulcer, gastrointestinal perforation or gastrointestinal haemorrhage, melaena, haematemesis[6], mouth ulceration, exacerbation of colitis and Crohn's disease[7] gastritis, pancreatitis, flatulence and constipation
Hepatobiliary Disorders	Very rare	1)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	Nephrotoxicity in various forms, including interstitial nephritis, nephrotic syndrome, and acute and chronic renal failure[9]
General Disorders and Administration Site Conditions	Very rare	Fatigue and malaise
Investigations	Common	Alanine aminotransferase increased, gamma-glutamyltransferase increased and liver function tests abnormal with paracetamol. Blood creatinine increased, blood urea increased.
	Uncommon	Aspartate aminotransferase increased, blood alkaline phosphatase increased, blood creatine phosphokinease 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