AUSTRALIAN PRODUCT INFORMATION
MAXIGESIC® (PARACETAMOL / IBUPROFEN) TABLETS

1. NAME OF THE MEDICINE

Paracetamol
Ibuprofen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains paracetamol 500 mg and ibuprofen 150 mg.

Excipients with known effect:
Lactose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.
White, capsule shaped, film-coated tablets with a breakline on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Maxigesic® tablets are indicated for the temporary relief of pain, including pain where inflammation is present, associated with: headache, migraine headache, tension headache, sinus pain, toothache, dental procedures, backache, sore throat, arthritis, tennis elbow, period pain, muscular pain, rheumatic pain, aches and pains associated with colds and flu. Reduces fever.

4.2 Dose and method of administration

Adults and children over 12 years: The usual dosage is one to two tablets taken every six hours, as required, up to a maximum of eight tablets in 24 hours.

Adults should not use Maxigesic® for more than a few days at a time, unless advised to by a doctor. Children and adolescents aged 12-18 years should not use Maxigesic® for longer than 48 hours at a time, unless advised to by a doctor.

Children under 12 years: Maxigesic® is not recommended for children under 12 years.

4.3 Contraindications

Maxigesic® is contraindicated for use:

- in patients with known hypersensitivity to paracetamol, ibuprofen, aspirin, other NSAIDs or any other ingredients in the product;
- in patients with active alcoholism as chronic excessive alcohol ingestion may predispose patients to paracetamol hepatotoxicity (due to the paracetamol component);
- in patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin, ibuprofen or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients (see section 4.4, Pre-existing asthma).
- in patients with active gastrointestinal bleeding, peptic ulceration or other stomach disorders;
- during pregnancy or in patients trying to become pregnant;
- in patients with impaired kidney function, impaired liver function or heart problems;
- in patients with heart failure;
- in patients undergoing treatment of perioperative pain in the setting of coronary artery bypass surgery (CABG).

4.4 Special warnings and precautions for use

Maxigesic® should not be taken with other products containing ibuprofen, paracetamol, aspirin, salicylates or with any other anti-inflammatory medicines unless under a doctor's instruction. Refer to section 4.5 for additional information.

Gastrointestinal events

Upper gastrointestinal ulcers, gross bleeding or perforation have been described with NSAIDs. The risks increase with dose and duration of treatment, and are more common in patients over the age of 65 years. Some patients will experience dyspepsia, heartburn, nausea, stomach pain or diarrhoea. These risks are minimal when this product is used at the prescribed dose for a few days.

Maxigesic® should be used with caution, and at the lowest effective dose for the shortest duration, in patients with a history of gastrointestinal haemorrhage or a history of peptic ulcers since their condition may be exacerbated. It is contraindicated in patients with active gastrointestinal bleeding and in those with peptic ulcers or other stomach disorders.

This product should be discontinued if there is any evidence of gastrointestinal bleeding.

The concurrent use of aspirin and NSAIDs also increases the risk of serious gastrointestinal adverse events.

Cardiovascular thrombotic events

Observational studies have indicated that non-selective NSAIDs may be associated with an increased risk of serious cardiovascular events, including myocardial infarction and stroke, which may increase with dose or duration of use. Patients with cardiovascular disease, history of atherosclerotic

cardiovascular disease or cardiovascular risk factors may also be at greater risk. Maxigesic® is contraindicated in patients with heart problems.

Patients should be advised to remain alert for such cardiovascular events, even in the absence of previous cardiovascular symptoms. Patients should be informed about signs and/or symptoms of serious cardiovascular toxicity and the steps to take if they occur.

Hypertension

Fluid retention, hypertension and oedema have been reported in association with NSAID therapy. NSAIDs may lead to onset of new hypertension or worsening of pre-existing hypertension and patients taking antihypertensive medicines with NSAIDs may have an impaired anti-hypertensive response. Caution is advised when prescribing Maxigesic® to patients with hypertension (see also section 4.3). Blood pressure should be monitored closely during initiation of treatment with Maxigesic® and at regular intervals thereafter.

Hepatic effects

As with other NSAIDs elevations of one or more liver function tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may resolve with continued therapy. Meaningful elevations (three times the upper limit of normal) of ALT or AST occurred in controlled trials in less than 1% of patients.

Patients should be advised to remain alert for hepatotoxicity and be informed about the signs and/or symptoms of hepatotoxicity (e.g. nausea, fatigue, lethargy, pruritus, jaundice, abdominal tenderness in the right upper quadrant and "flu-like" symptoms). Excessive use can be harmful and increase the risk of liver damage.

Combination use of ACE inhibitors or angiotensin receptor antagonists, anti-inflammatory drugs and thiazide diuretics

The use of an ACE inhibiting drug (ACE-inhibitor or angiotensin receptor antagonist), an anti-inflammatory drug (NSAID or COX-2 inhibitor) and thiazide diuretic at the same time increases the risk of renal impairment (see also section 4.3). This includes use in fixed-combination products containing more than one class of drug. Combined use of these medications should be accompanied by increased monitoring of serum creatinine, particularly at the institution of the combination. The combination of drugs from these three classes should be used with caution particularly in elderly patients.

Severe skin reactions

NSAIDs may very rarely cause serious cutaneous adverse events such as exfoliative dermatitis, toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS), which can be fatal and occur without warning. These serious adverse events are idiosyncratic and are independent of dose or duration of use. Patients should be advised of the signs and symptoms of serious skin reactions and to consult their doctor at the first appearance of a skin rash or any other sign of hypersensitivity.

Pre-existing asthma

Products containing ibuprofen should not be administered to patients with aspirin-sensitive asthma and should be used with caution in patients with pre-existing asthma.

Ophthalmological effects

Adverse ophthalmological effects have been observed with NSAIDs; accordingly, patients who develop visual disturbances during treatment with products containing ibuprofen should have an ophthalmological examination.

Aseptic meningitis

For products containing ibuprofen, aseptic meningitis has been reported only rarely, usually, but not always, in patients with systemic lupus erythematosus (SLE) or other connective tissue disorders.

Masking signs of infection

As with other drugs of this class containing ibuprofen, by reducing fever this may mask the usual signs of infection.

Haematological effects

Blood dyscrasias have been rarely reported. Patients on long-term therapy with ibuprofen should have regular haematological monitoring.

Coagulation defects

Like other NSAIDs, ibuprofen can inhibit platelet aggregation. Ibuprofen has been shown to prolong bleeding time (but within the normal range), in normal subjects. Because this prolonged bleeding effect may be exaggerated in patients with underlying haemostatic defects, ibuprofen should be used with caution in persons with intrinsic coagulation defects and those on anti-coagulation therapy.

High Anion Gap Metabolic Acidosis

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or patients with malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Special precautions

In order to avoid exacerbation of disease or adrenal insufficiency, patients who have been on prolonged corticosteroid therapy should have their therapy tapered slowly rather than discontinued abruptly when ibuprofen is added to the treatment program.

Use in the elderly

No adjustment in labelled dosage is necessary for older patients who require paracetamol therapy. Those who require therapy for longer than a few days should consult their physician for condition monitoring; however, no reduction in recommended dosage is necessary. However, caution should be taken with regard to the use of ibuprofen as it should not be taken by adults over the age of 65 without consideration of co-morbidities and co-medications because of an increased risk of adverse effects, in particular heart failure, gastrointestinal ulceration and renal impairment (see also section 4.3).

Paediatric use

Maxigesic® is not recommended for children under 12 years (see also section 4.2).

Effects on laboratory tests

Using current analytical systems, paracetamol does not cause interference with laboratory assays. However, there are certain methods with which the possibility of laboratory interference exists, as described below:

Blood tests:

Paracetamol at recommended doses does not appear to interfere with glucose analysis using currently marketed blood glucose meters. For further detail, it may be advisable to contact the specific laboratory instrumentation manufacturer.

Urine tests:

Paracetamol in therapeutic doses may interfere with the determination of 5-hydroxyindoleacetic acid (5HIAA), causing false-positive results. False determinations may be eliminated by avoiding paracetamol ingestion several hours before and during the collection of the urine specimen.

4.5 Interaction with other medicines and other forms of interaction

Paracetamol

The following interactions have been noted:

- anticoagulant drugs (e.g. warfarin): dosage may require reduction if paracetamol and anticoagulants are taken for a prolonged period of time;
- antiepileptic medications: the likelihood of toxicity may be increased by the concomitant use of enzyme inducing agents;
- paracetamol absorption is increased by substances that increase gastric emptying, e.g. metoclopramide;
- paracetamol absorption is decreased by substances that decrease gastric emptying, e.g. propantheline, antidepressants with anticholinergic properties, and narcotic analgesics;
- paracetamol may increase chloramphenicol plasma concentrations;
- hepatotoxic drugs or drugs that induce liver microsomal enzymes such as alcohol and anticonvulsant agents: the risk of paracetamol toxicity may be increased in patients receiving these drugs;
- probenecid: may affect paracetamol excretion and plasma concentrations;

- cholestyramine: reduces the absorption of paracetamol if given within 1 hour of paracetamol;
- isoniazid alone or combined with other drugs for tuberculosis: in patients receiving these drugs severe hepatotoxicity at therapeutic doses or moderate overdoses of paracetamol has been reported;
- zidovudine and co-trimoxazole: severe hepatotoxicity has occurred after use of paracetamol in a patients taking these drugs.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4).

Ibuprofen

The following interactions have been noted:

- anticoagulants, including warfarin: ibuprofen interferes with the stability of INR and may increase risk of severe bleeding and sometimes fatal haemorrhage, especially from the gastrointestinal tract. Ibuprofen should only be used in patients taking warfarin if absolutely necessary and they must be closely monitored.
- lithium: ibuprofen may decrease renal clearance and increase plasma concentration of lithium;
- ACE inhibitors, beta-blockers and diuretics: ibuprofen may reduce the anti- hypertensive effect of these drugs and may cause natriuresis and hyperkalaemia in patients under these treatments;
- methotrexate: ibuprofen reduces methotrexate clearance;
- cardiac glycosides: ibuprofen may increase the plasma levels of these drugs;
- corticosteroids: the risk of ibuprofen-induced gastrointestinal bleeding may be increased with concomitant use of oral corticosteroids;
- zidovudine: ibuprofen may prolong bleeding time in patients treated with this drug;
- probenecid, antidiabetic medicine and phenytoin: these medicines may interact with ibuprofen.

4.6 Fertility, pregnancy and lactation

Effects on fertility

Reversible infertility has been reported in women on long-term NSAIDs.

Use in pregnancy – Category C

There is inadequate information regarding the use of Maxigesic® in pregnancy. Therefore, Maxigesic® should not be used during pregnancy or in patients trying to become pregnant (see also section 4.3).

NSAIDs inhibit prostaglandin synthesis and, when given during the latter part of pregnancy, may cause closure of the foetal ductus arteriosus, foetal renal impairment, inhibition of platelet aggregation and delay labour and birth.

Paracetamol has been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

No information was found about the potential effects of ibuprofen on mating behavior, or early embryonic development in animals. Paracetamol reportedly does not affect reproductive performance in mice.

When administered to pregnant rats and rabbits during the period of organogenesis, ibuprofen reportedly does not affect foetal development in either species. When administered to pregnant mice throughout gestation, paracetamol reportedly results in reduced birth weights.

No information was found about the potential effects of ibuprofen on peri-/post-natal development in animals. When administered to mice throughout gestation and lactation, paracetamol reportedly resulted in reduced pup growth.

There is nothing in the available information on ibuprofen and paracetamol to suggest an increased or novel risk of reproductive or developmental toxicity with co-administration of the two drugs in the form of Maxigesic®.

Use in lactation

Paracetamol is excreted in small amounts (< 0.2%) in breast milk. Maternal ingestion of paracetamol in usual analgesic doses does not appear to present a risk to the breastfed infants.

Ibuprofen appears in breast milk in very low concentrations and is unlikely to affect the breastfed infant adversely.

As Maxigesic® has not been studied in nursing mothers, healthcare professionals should exercise caution and recommend the lowest effective dose for the shortest duration required.

4.7 Effects on ability to drive and use machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse effects (Undesirable effects)

Clinical trials with Maxigesic® have not indicated any other undesirable effects other than those for paracetamol alone or ibuprofen alone.

Side effects of paracetamol are rare and usually mild, although haematological reactions have been reported. Skin rashes and hypersensitivity reactions occur occasionally. Overdosage with paracetamol if left untreated can result in severe, sometimes fatal liver damage and rarely, acute renal tubular necrosis.

Adverse effects with non-prescription (OTC) or short-term use ibuprofen are rare and may include:

- gastrointestinal – gastrointestinal bleeding, dyspepsia, heartburn, nausea, loss of appetite, stomach pain, diarrhoea;
- central nervous system (CNS) – dizziness, fatigue, headache, nervousness;
- hypersensitivity reactions – skin rashes and itching. Rarely exfoliative dermatitis and epidermal necrolysis have been reported with ibuprofen;
- rare cases of photosensitivity;
- cardiovascular – risks of myocardial infarct and stroke. These risks are minimal at Maxigesic® recommended maximum daily doses but increase with longer duration of treatment, and in the elderly. Fluid retention and in some cases oedema have been reported with all NSAIDs. These effects are rare at non-prescription doses.

Allergic reactions such as skin rash, itching, swelling of the face or breathing difficulties may also occur. These are usually transient and reversible on cessation of treatment.

High anion gap metabolic acidosis with frequency "Not known" (cannot be estimated from the available data): Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at https://www.tga.gov.au/reporting-problems.

4.9 Overdose

Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage.

Symptoms

Paracetamol

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may proceed to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop in the absence of severe liver damage. Cardiac arrhythmias have been reported. Liver damage is likely in adults who have taken 10 g or more of paracetamol, due to excess quantities of a toxic metabolite becoming irreversibly bound to liver tissue.

Ibuprofen

Symptoms include nausea, abdominal pain and vomiting, dizziness, convulsion and rarely, loss of consciousness. Clinical features of overdose with ibuprofen which may result are depression of the central nervous system and the respiratory system.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Paracetamol

Although the exact site and mechanism of analgesic action is not clearly defined, paracetamol appears to produce analgesia by elevation of the pain threshold.

Ibuprofen

Ibuprofen possesses analgesic, antipyretic and anti-inflammatory properties, similar to other non-steroidal anti-inflammatory drugs (NSAIDs). Its mechanism of action is unknown, but is thought to be through peripheral inhibition of cyclooxygenases and subsequent prostaglandin synthesise inhibition.

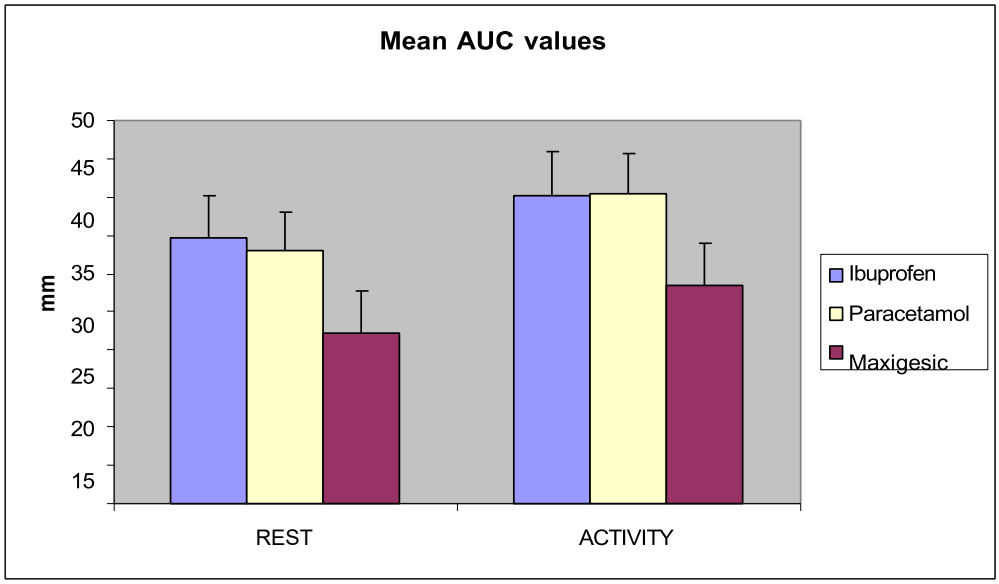
Clinical trials

A prospective, parallel group, double-blind comparison of the analgesic effect of Maxigesic®, paracetamol alone, or ibuprofen alone in 135 patients with post-operative dental pain for 48 hours following oral surgery was conducted. The oral surgery was conducted under local or general anaesthetic with one dose of oral analgesic (2 tablets of paracetamol 500 mg or ibuprofen 300 mg or Maxigesic®) given pre-operatively. Total dose in the 24 hours were paracetamol 4000 mg, ibuprofen 1200 mg and Maxigesic®. Analgesia, the primary efficacy end point, was a time-corrected AUC (Area Under the Curve) calculated from 100 mm VAS (Visual Analogue Scale) pain scores over 48 hours at both rest and on activity.

The primary end points, assessed on the Intent to Treat (ITT) population, showed the mean time-adjusted AUCs over 48 hours calculated from the VAS pain scores for Maxigesic® were significantly lower than for paracetamol at rest (22.344 [SE 3.2] and 33.016 [3.005], respectively [p=0.007]), and on activity (28.377 [SE 3.396] and 40.364 [SE 3.271], respectively [p=0.006]).

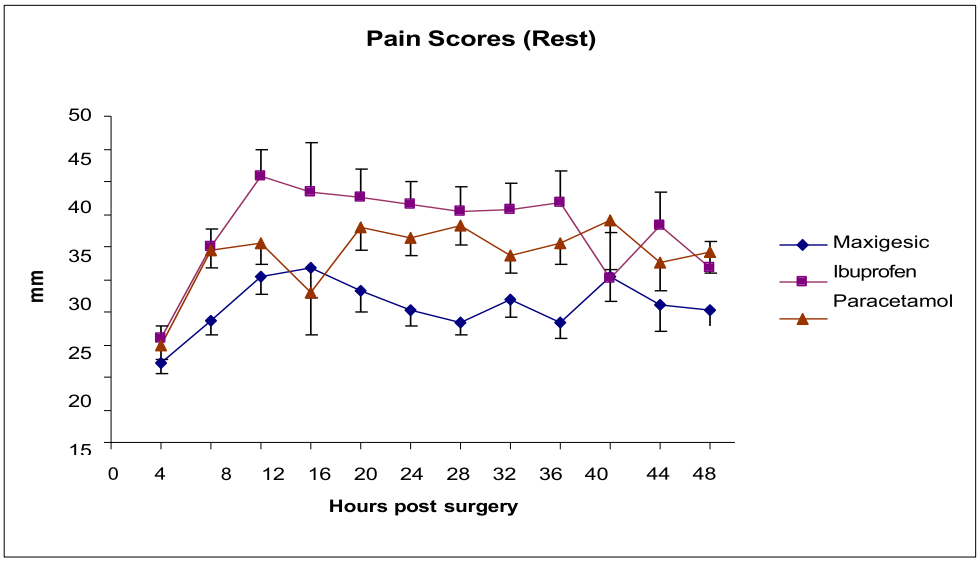
A similar outcome is seen for the Maxigesic® comparison where the AUCs over 48 hours showed the VAS for the combination drug were significantly lower than for ibuprofen at rest (22.344 [SE 3.2] and 34.78 [SE 3.22], respectively [p=0.003]), and during activity (28.377 [SE 3.396] and 40.217 [SE 3.418], respectively [p=0.007]).

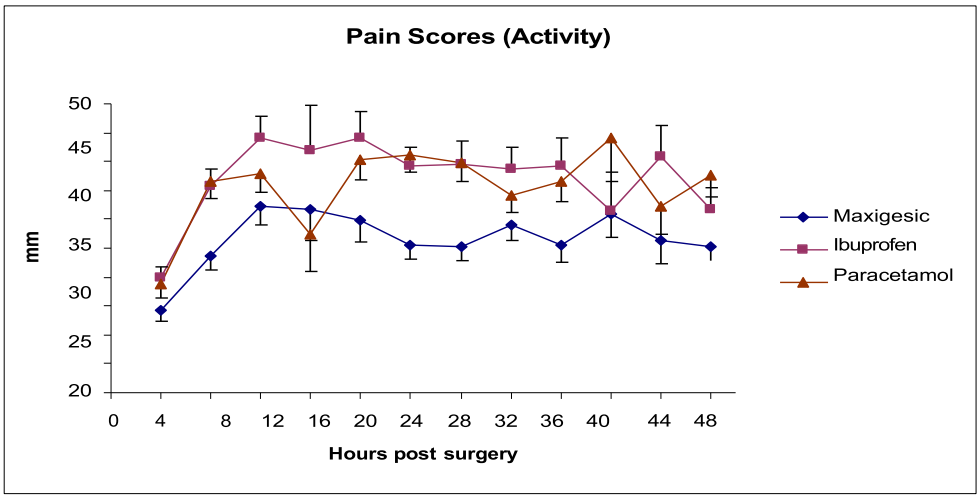
Figure 1: Means of time-adjusted AUC at rest and on activity by treatment groups.



A presentation of the pain records during the 48 hours also shows the Maxigesic® analgesic effect showed lower mean pain scores than either of its two active ingredients at almost all time points at both rest and during activity (Figure 2).

Figure 2: Pain score plot – scores given are those rated during each 4-hour period post-surgery.





A double-blind, placebo-controlled, randomised, parallel group comparison trial was conducted in 159 participants experiencing pain from removal of 2-4 molars. Three different possible doses of Maxigesic® were evaluated and compared with that of placebo [N=49].The doses corresponded to half [N=46], one [N=34] or two tablets [N=30] of Maxigesic® given four times a day for 24 hours.

The mean-adjusted Sum of Pain Intensity Difference [SPID] in all the Maxigesic® doses were significantly [p=0.004-0.002] higher than placebo consistent with each possible dose of Maxigesic® being more effective than placebo.

The results demonstrating the SPID, response rate, maximum VAS pain scores and percentage of patients requiring rescue medication for all four study groups (placebo, half, one and two tablet doses) are presented in the table below.

	Maxigesic® (two tablets) N=30	Maxigesic® (one tablet) N=34	Maxigesic® (half tablet) N=46	Placebo N=49
		SPIDs (mm)		
Mean (SD)	**20.12(18.01)**	**20.44(20.78)**	**19.25(19.99)**	**6.63(19.79)**
P value	0.004	0.002	0.002	**-**
		Response Rate* (%)		
Yes (%)	50.00%	44.10%	45.70%	18.4%
P value	**0.003**	**0.011**	**0.008**	**-**
		Maximum VAS Pain Scores (mm)		
Mean (SD)	**51.13(13.22)**	**55.38(17.61)**	**54.98(15.92)**	**61.20(18.34)**
P value	0.009	**0.063**	**0.062**	**-**
		Percentage of Participants Requiring Rescue Medication (%)		
Yes (%)	53.30%	61.80%	56.50%	81.60%
P value	**0.007**	**0.044**	**0.008**	**-**

**Response rate = percentage of patients with a decrease of at least 50% in VAS pain score within 6 hours after the first dose.*

5.2 Pharmacokinetic properties

Absorption

Paracetamol is absorbed from the gastrointestinal tract with peak plasma concentration occurring about 10 to 60 minutes after oral administration.

Ibuprofen is absorbed following oral administration with maximum plasma concentrations usually achieved in 60 to 120 minutes.

Distribution

Paracetamol is distributed into most body tissues. Ibuprofen is highly protein bound.

Metabolism

Paracetamol is metabolised extensively in the liver and excreted in the urine, mainly as inactive glucuronide and sulphate conjugates. Less than 5% is excreted unchanged. The metabolites of paracetamol include a minor hydroxylated intermediate which has hepatotoxic activity. This active intermediate is detoxified by conjugation with glutathione, however, it can accumulate following paracetamol overdosage and if left untreated has the potential to cause severe and even irreversible liver damage.

Paracetamol is metabolised differently by premature infants, newborns, and young children compared with adults, the sulphate conjugate being most predominant.

Ibuprofen is highly bound (90-99%) to plasma proteins and is extensively metabolised to inactive compounds in the liver, mainly by glucuronidation.

The metabolic pathways of paracetamol and ibuprofen are distinct and there should be no drug interactions where the metabolism of one affects the metabolism of the other. A formal study using

human liver enzymes to investigate such a possibility failed to find any potential drug interaction on the metabolic pathways.

In another study, the effect of ibuprofen on the oxidative metabolism of paracetamol was evaluated in healthy volunteers under fasting conditions. The study results indicated that ibuprofen did not alter the amount of paracetamol undergoing oxidative metabolism, as the amount of paracetamol and its metabolites (glutathione-, mercapturate-, cysteine-, glucuronide- and sulfate-paracetamol) were similar when administered alone, as paracetamol, or with the concomitant administration of ibuprofen (as a fixed combination Maxigesic®).

Excretion
Paracetamol elimination half-life varies from about 1 to 3 hours.

Both the inactive metabolites and a small amount of unchanged ibuprofen are excreted rapidly and completely by the kidney, with 95% of the administered dose eliminated in the urine within four hours of ingestion. The elimination half-life of ibuprofen is in the range of 1.9 to 2.2 hours.

Pharmacokinetic/pharmacodynamic relationship(s)
A specific study to investigate possible effects of paracetamol on the plasma clearance of ibuprofen and vice versa did not identify any drug interactions.

5.3 Preclinical safety data

Genotoxicity
There is nothing in the available information on ibuprofen and paracetamol to suggest an increased or novel risk of genotoxicity with co-administration of ibuprofen and paracetamol.

Carcinogenicity
There is nothing in the available information on ibuprofen and paracetamol to suggest an increased or novel risk of carcinogenicity with co-administration of ibuprofen and paracetamol.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium (E468)
Magnesium stearate (E470b)
Maize starch
Microcrystalline cellulose (E460)
Talc
Film coating (Opadry white) comprising:
HPMC 2910/Hypromellose 15 cP (E464)
Lactose monohydrate

Macrogol/PEG 4000 (E1521)
Titanium dioxide (E171)
Trisodium citrate (E331)

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine (see section 4.5, Interactions with other medicines and other forms of interactions).

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

Store below 30°C in a dry place, protected from light.

6.5 Nature and contents of container

Maxigesic® tablets are supplied in PVC/aluminium blister packs, in cartons containing 8, 10, 12, 16, 20, 24, or 30 tablets. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

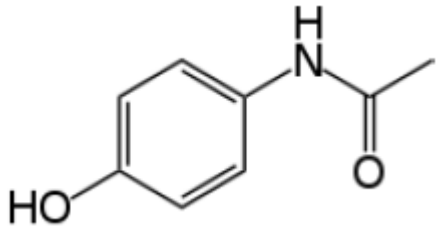
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 Physicochemical properties

Paracetamol

Chemical structure

Chemical name: N-acetyl-p-aminophenol.



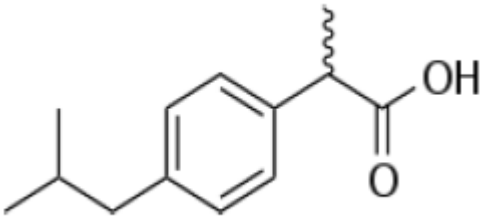
CAS number

103-90-2

Ibuprofen

Chemical structure

Chemical name: (±)-2-(p-isobutylphenyl)propionic acid.



CAS number

15687-27-1

7. MEDICINE SCHEDULE (POISONS STANDARD)

Pack sizes of 8, 10, or 12 tablets: Schedule 2 (Pharmacy Medicine).
Pack sizes of 16, 20, 24 or 30 tablets: Schedule 3 (Pharmacist Only Medicine).

8. SPONSOR

AFT Pharmaceuticals Pty Ltd
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NSW 2113
AUSTRALIA
Phone: 1800 238 74276
Email: customer.service@aftpharm.com

9. DATE OF FIRST APPROVAL

23 December 2013

10. DATE OF REVISION

13 June 2025

Summary table of changes

Section changed	Summary of new information
4.4, 4.5, 4.8	Safety related change.