NEW ZEALAND DATA SHEET

1 PRODUCT NAME

Paracetamol Osteo (Pharmacy Health)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:
Paracetamol 665 mg/tablet

Excipients:
For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Modified-release tablet, coated

Presentation
White to off-white, capsule shaped, biconvex tablets, plain on both sides. Tablet cannot be halved.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of persistent pain associated with osteoarthritis for up to 8 hours.

4.2 Dose and method of administration

Dose
Adults and children aged 12 years and over: Swallow 2 tablets with water or other fluid, three times a day, every 6 to 8 hours as required. Swallow whole do not crush or chew.
Maximum of 6 tablets in 24 hours.
Do not use for more than a few days at a time in adults except on medical advice. Should not be used for more than 48 hours for children aged 12 – 17 years, except on medical advice.

Children under 12 years: Do not give to children under 12 years of age.

Take orally with water or other fluid. Do not chew or suck, as it impairs the modified release properties.

Method of administration
Take with water or other fluid.
Can be taken with or without food.
The 3 doses should be equally spaced throughout the day.
The tablets must not be crushed.
Do not exceed the stated dose.

The lowest dose necessary to achieve efficacy should be used for the shortest duration of treatment.
Should not be used with other paracetamol-containing products. Minimum dosing interval: 6 hours.
Maximum daily dose for children 12 years of age to adults: 4000 mg.

4.3 Contraindications

This product is contraindicated in patients with a previous history of hypersensitivity to paracetamol or to any of the excipients listed in Section 6.1.

4.4 Special warnings and precautions for use

Identified precautions
Contains paracetamol. Do not use with any other paracetamol-containing products.
The concomitant use with other products containing paracetamol may lead to an overdose.
Paracetamol overdose may cause liver failure which may require liver transplant or lead to death.
If symptoms persist, medical advice must be sought.
Keep out of sight and reach of children.

Use in hepatic impairment
Paracetamol should be used with caution in patients with impaired liver function: Underlying liver disease increases the risk of paracetamol-related liver damage.
Patients who have been diagnosed with liver impairment must seek medical advice before taking this medication.
Cases of hepatic dysfunction/failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index, are chronic heavy users of alcohol or have sepsis.
In patients with glutathione depleted states the use of paracetamol may increase the risk of metabolic acidosis.

Use in renal impairment
Paracetamol should be used with caution in patients with impaired kidney function:
Administration of paracetamol to patients with moderate to severe renal impairment may result in accumulation of paracetamol conjugates.
Patients who have been diagnosed with kidney impairment must seek medical advice before taking this medication.

Use in the elderly
No data available.

Paediatric use
Do not give to children under 12 years of age.

Effects on laboratory tests
No data available.

4.5 Interaction with other medicines and other forms of interaction

The following interactions with paracetamol have been noted:

- The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect. Anticoagulant dosage may require reduction if paracetamol and anticoagulants are taken for a prolonged period of time.
- 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 concentrations.
- The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes such as alcohol and anticonvulsant agents.
- Paracetamol excretion may be affected, and plasma concentrations altered when given with probenecid.
- Cholestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol.

4.6 Fertility, pregnancy and lactation

Effects on fertility
No data available.

Use in Pregnancy (Category A)
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.

As with the use of any medicine during pregnancy, pregnant women should seek medical advice before taking paracetamol. The lowest effective dose and shortest duration of treatment should be considered.

Use in Lactation
Paracetamol is excreted in breast milk. Human studies with paracetamol have not identified any risk to lactation or the breast-fed offspring. These results are based on immediate release preparations 4 of paracetamol. There is no data available on the excretion of modified-release paracetamol preparations in breast milk. However, it is not expected that Paracetamol Osteo (Pharmacy Health) would provide any increase in the excretion of paracetamol in breast milk as this product is designed to maintain rather than increase plasma paracetamol concentrations compared to immediate release preparations. Maternal ingestion of paracetamol in usual analgesic doses does not appear to present a risk to the breastfed infant.

4.7 Effects on ability to drive and use machines

Paracetamol Osteo (Pharmacy Health) is unlikely to cause an effect on the ability to drive or use machinery.

4.8 Undesirable effects

Adverse events from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by System Organ Class and frequency.

The following convention has been utilised for the classification of undesirable effects: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000), not known (cannot be estimated from available data).

Adverse event frequencies have been estimated from spontaneous reports received through post-marketing data.

Body System	Undesirable Effect	Frequency
Blood and lymphatic system disorders	Thrombocytopenia	Very rare
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including, among others, skin rashes, angioedema, Stevens Johnson syndrome and Toxic Epidermal Necrolysis	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm, especially in patients sensitive to aspirin and other NSAIDs	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare

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. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/}

4.9 Overdose

Because Paracetamol Osteo 665 (Pharmacy Health) is a sustained-release formulation of paracetamol, absorption will be prolonged in overdose. It is recommended that for the management of overdose, where Paracetamol Osteo 665 (Pharmacy Health) is suspected, that an additional plasma paracetamol level be obtained 4-6 hours after the initial measurement. If either level is above or close to the treatment line on the paracetamol overdose nomogram, administration of antidote would be indicated.

If an overdose is taken or suspected, contact the Poisons Information Centre immediately for advice (0800 764 766), or the patient should go to the nearest hospital straight away. This should be done even if they feel well because of the risk of delayed, serious liver damage.

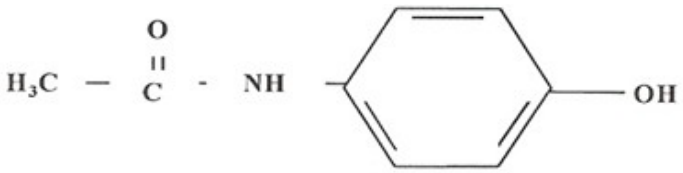
Treatment
Paracetamol overdose may cause liver failure which may require liver transplant or lead to death. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity.
Immediate medical management is required in the event of an overdose, even if the symptoms of overdose are not present.
Administration of N-acetylcysteine may be required.
In cases of overdose, methods of reducing absorption of ingested drug are important.
Activated charcoal may reduce absorption of the medicine if given within one hour after oral ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected.

Further information on the management of modified-release paracetamol overdose can be found in the "Guidelines for the management of paracetamol poisoning in Australia and New Zealand" available at https://www.mja.com.au/journal/2015/203/5/summary-statement-new-guidelines- management-paracetamol-poisoning-australia-and

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

CAS: 103-90-2 (paracetamol)



C8H9NO2 151.2 103-90-2
ATC code Paracetamol, N02BE01

Mechanism of action
Paracetamol is a para-aminophenol derivative that exhibits analgesic and anti-pyretic activity. Its mechanism of action is believed to include inhibition of prostaglandin synthesis, primarily within the central nervous system. It does not possess anti- inflammatory activity. It provides relief from mild to moderate pain and fever.
The sustained release of paracetamol provides pain relief, which may last up to 8 hours.

Clinical trials
No data available

5.2 Pharmacokinetic properties

Paracetamol Osteo (Pharmacy Health) is a modified-release dose of paracetamol.

Absorption
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Food intake delays paracetamol absorption.
Paracetamol Osteo 665 (Pharmacy Health) is formulated to provide a sustained-release dose of paracetamol.
Coadministration of Paracetamol Osteo 665 with food leads to a small increase in bioavailability and a small delay in Tmax.
When administered under repeat dose conditions according to the recommended dosage of two tablets every 6 to 8 hours, Paracetamol Osteo 665 tablets achieve mean plasma concentrations above the minimum therapeutic level for analgesia of 4 µg/mL throughout the dosage interval.

Distribution
Paracetamol is distributed into most body tissues. Binding to the plasma proteins is minimal at therapeutic concentrations but increases with increasing doses.

Metabolism
Paracetamol is metabolised extensively in the liver and excreted in the urine mainly as inactive glucuronide and sulphate conjugates.
The metabolites of paracetamol include a minor hydroxylated intermediate which has hepatotoxic activity. This intermediate metabolite is detoxified by conjugation with glutathione. However, it can accumulate following paracetamol overdosage (more than 150 mg/kg or 10 g total paracetamol ingested) and, if left untreated, can cause irreversible liver damage.
Paracetamol is metabolised differently by premature infants, new-borns, infants and young children compared to adults, the sulphate conjugate being predominant.

Excretion
Paracetamol is excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted unchanged. Approximately 85% of a dose of paracetamol is excreted in urine as free and conjugated paracetamol within 24 hours of ingestion.
Administration of paracetamol to patients with moderate to severe renal impairment may result in accumulation of paracetamol conjugates. The elimination half-life varies from one to three hours.

5.3 Preclinical safety data

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hypromellose, Maize starch, Povidone, Croscarmellose sodium, Magnesium stearate, Titanium dioxide, Macrogol 400.

6.2 Incompatibilities

Data not available.

6.3 Shelf life

48 months from date of manufacture

6.4 Special precautions for storage

Store at or below 30^{o}C.

6.5 Nature and contents of container

Blister pack of 96 tablets

6.6 Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

Pharmacist Only Medicine

8 SPONSOR

Noumed Pharmaceuticals Ltd
Auckland, New Zealand
Phone: 0800 527 545

9 DATE OF FIRST APPROVAL

26th January 2023

10 DATE OF REVISION OF THE TEXT

6th April 2023

SUMMARY TABLE OF CHANGES

Section	Summary of change
6.1	Remove claims of free from ingredient.
6.3	Shelf life changed to 48 months.
6.4	Storage conditions changed to Store below 30°C.