# NEW ZEALAND DATA SHEET

## 1. PRODUCT NAME

FEBREX TABLETS, Paracetamol 500 mg, tablet

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:
Paracetamol (BP) 500 mg/tablet

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

## 3. PHARMACEUTICAL FORM

FEBREX Tablets
Uncoated Tablet White capsule shaped tablet with break line on one side

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

For fast effective temporary relief of pain and discomfort associated with headache, muscular aches, period pain, arthritis/osteoarthritis, toothache, migraine, cold & flu symptoms, tension headache, sinus pain/headache and backache. Reduces fever.

### 4.2 Dose and method of administration

FEBREX Tablets

*Adults and children aged 12 years and over:* 1 to 2 tablets every four to six hours as required. Maximum of 8 tablets in 24 hours. Maximum daily dose: 4000 mg.

Do not use for more than a few days at a time in adults without medical advice.

*Children 7 to 12 years:* ½ to 1 tablet every four to six hours as required. Maximum of 4 tablets in 24 hours.

Should not be used for more than 48 hours for children 7 – 17 except on medical advice.

*Children under 7 years:* Not recommended for children under the age of 7 years.

Take orally with water or other fluid.

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: 4 hours.

4.3 Contraindications

These products are contraindicated in patients with a previous history of hypersensitivity to paracetamol or any of the excipients.

## 4.4 Special warnings and precautions for use

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.

Paracetamol should be used with caution in patients with:

- Impaired liver function: Underlying liver disease increases the risk of paracetamol-related liver damage
- 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 liver or kidney impairment must seek medical advice before taking this medication. The restrictions related to the use of paracetamol products in patients with liver or kidney impairment are primarily a consequence of the paracetamol content of the drug.

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.

If symptoms persist, medical advice must be sought.

Keep out of sight and reach of children.

Contains sugars, as lactose monohydrate.

Use in children: Not recommended for children under seven years of age.

## 4.5 Interactions 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 FEBREX medication is prolonged.

Paracetamol absorption is increased by substances that increase gastric emptying, eg metoclopramide.

Paracetamol absorption is decreased by substances that decrease gastric emptying, eg 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 drugs.

Paracetamol excretion may be affected and plasma concentrations altered when given with probenecid.

Colestyramine reduces the absorption of paracetamol if given within one hour of paracetamol.

## 4.6 Fertility, pregnancy and lactation

*Use in pregnancy*
As with the use of any medicine during pregnancy, pregnant women should seek medical advice before taking paracetamol.

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.

*Use in lactation*
Paracetamol is excreted in breast milk but not in a clinically significant amount at recommended dosages. Available published data do not contraindicate breast-feeding.

## 4.7 Effects on ability to drive and use machines
Paracetamol 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<br>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

Experience following overdose with paracetamol indicates that the clinical signs of liver injury occur usually after 24 to 48 hours and have peaked after 4 to 6 days.

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.

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.

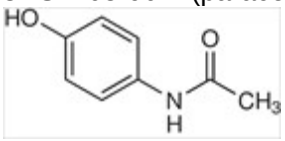
Administration of N-acetylcysteine may be required.

In cooperative adults, activated charcoal may reduce absorption of the medicine if given within one hour after ingestion.

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

CAS: 103-90-2 (paracetamol)



Paracetamol MW 151.17
ATC code Paracetamol, N02BE01

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 is given by mouth or rectally (suppositories) for mild to moderate pain and fever.

The lack of peripheral prostaglandin inhibition confers important pharmacological properties such as the maintenance of the protective prostaglandins within the gastrointestinal tract. Paracetamol is, therefore, particularly suitable for patients with a history of disease or on concomitant medication, where peripheral prostaglandin inhibition would be undesirable (such as, for example, those with a history of gastrointestinal bleeding or the elderly).

5.2 Pharmacokinetic properties

*Absorption*
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Food intake delays paracetamol absorption.

*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 in the liver and excreted in the urine mainly as 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 200 mg/kg or 10 g total paracetamol ingested) and, if left untreated, can cause irreversible liver damage.

Paracetamol is metabolised differently by infants and 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 as unmodified paracetamol with 85% to 90% of the administered dose eliminated in the urine within 24 hours of ingestion. The elimination half-life varies from one to three hours. The mean plasma half-life is about 2.3 hours.

## 6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

*FEBREX Tablets*

Lactose, Maize starch, Purified water, Sodium Starch Glycollate, Povidone, Magnesium sterate, Silica colloidal anhydrous.

6.2 Incompatibilities
No known incompatibilities.

6.3 Shelf life

*FEBREX Tablets*
36 months from date of manufacture.

6.4 Special precautions for storage

*FEBERX Tablets*
Store below 25°C Protect from moisture.

6.5 Nature and contents of container

*FEBREX Tablets*

Bottle Pack: 1000 tablets (Prescription)
Blister Pack: 100 x 10 tablets (Prescription)
Blister Pack: 2 x 10 tablets (OTC - General Sale)
Blister Pack: 5 x 10 tablets (OTC - Pharmacy Only)
Blister Pack: 10 x 10 tablets (OTC - Pharmacy Only)

6.6 Special precautions for disposal and other handling
No special requirements

## 7. MEDICINE SCHEDULE

Packs of under 20 – General sale
Packs of 20 and more – Pharmacy only

## 8. SPONSOR

Miro Healthcare Ltd
Hayes Knight, 5 William Laurie Place
Auckland 0632 New Zealand

## 9. DATE OF FIRST APPROVAL

## 10. DATE OF REVISION OF TEXT

20 October 2021

Summary table of changes

| Section changes | Summary of new changes |
|---|---|
| All | Transferred to new data sheet template |
| 4.2 | Addition of advice to:<br>Use for shortest duration of treatment<br>Oral administration only<br>Maximum daily dose: 4000 mg |
| 4.5 | Addition of advice that occasional doses have no significant effect on the anticoagulant effect of warfarin and other coumarins. |
| 4.6 | Addition of advice to seek medical advice before using if pregnant. |
| 4.9 | Addition of the expected timing of clinical signs of liver injury and that acute pancreatitis has been observed. |

| Section changes | Summary of new changes |
|---|---|
| All | All data is kept as per innovator product Panadol.<br>Brand name Panadol is changed to Febrex<br>Data related to Mini Caps is deleted. |
| 3 | Pharmaceutical form updated as per Febrex.<br>"White capsule shaped tablet with breakline on one side." |
| 6.1 | List of excipient changed as per Febrex formulation |
| 6.3 | Shelf life changed as per Febrex formulation |
| 6.4 | Special precaution for storage changed as per Febrex formulation |
| 6.5 | Nature and contents of container changed as per Febrex formulation |
| 7 | Medicine schedule changed as per Febrex formulation |
| 8 | Sponsor updated to Miro Healthcare ltd |
| 6.4 | Storage condition updated |
| 6.5 | Nature and contents of container |
| 10 | Date of revision of test updated |