AUSTRALIAN PRODUCT INFORMATION – PANAMAX (PARACETAMOL) TABLET AND ELIXIR

1 NAME OF THE MEDICINE

Paracetamol.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

PANAMAX Tablets

Each tablet contains paracetamol 500 mg.
Excipients with known effect: potassium sorbate.

PANAMAX Elixir

Each 5 mL contains paracetamol 120 mg.
Excipients with known effect: benzoic acid, potassium sorbate, saccharin sodium.

PANAMAX 240 Elixir

Each 5 mL contains paracetamol 240 mg.
Excipients with known effect: benzoic acid, potassium sorbate, saccharin sodium, sorbitol solution (70 per cent) (non-crystallising).

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

PANAMAX Tablets

Flat, round, scored, white tablet with bevelled edges, front face marking 'PANAMAX' with break line on the reverse.

PANAMAX Elixir

Clear, red coloured syrup liquid with a fruity odour and taste.

PANAMAX 240 Elixir

Clear light red coloured syrupy liquid.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Relief of pain and discomfort in arthritis, headache, muscular and neuralgic conditions. Reduces fever. Panamax is useful as an analgesic for patients with dyspepsia, ulcers or gout.

4.2 DOSE AND METHOD OF ADMINISTRATION

PANAMAX Tablets

Children

7 to 12 years: 250 to 500 mg (1/2 to 1 tablet) every four to six hours (maximum 4 tablets per day). Take with water.

Adults

500 mg to 1g (1 to 2 tablets) every four to six hours (maximum 8 tablets per day). Take with water.

PANAMAX Elixir

Administer in water or fruit juice at 4 to 6-hourly intervals.

Infants

1 to 3 months: (4–6 kg) 2 to 4 mL;
3 to 6 months: (6–8 kg) 4 to 5 mL;
6 to 12 months: (8–10 kg) 5 to 6 mL.

Children

1 to 2 years: (10-12 kg) 6 to 8 mL;
2 to 4 years: (12-16 kg) 8 to 10 mL;
4 to 6 years: (16-20 kg) 10 to 13 mL;
6 to 8 years: (20-25 kg) 13 to 16 mL;
8 to 10 years: (25-32 kg) 16 to 20 mL;
10 to 12 years: (32-41 kg) 20 to 26 mL.

Administration to infants under 1 month is not recommended.

Recommended dosages are based on 15 mg of paracetamol per kg of body weight.

PANAMAX 240 Elixir

Administer in water or fruit juice if necessary.

Children

5 to 6 years: (18–20 kg) 6 mL;
6 to 8 years: (20–25 kg) 6 to 8 mL;
8 to 10 years: (25–32 kg) 8 to 10 mL;
10 to 12 years: (32–41 kg) 10 to 12 mL.

Adults

10 to 20 mL (maximum 80 mL per day)
If necessary repeat 4 to 6 hourly up to 4 times in 24 hours.
Panamax 240 Elixir is not recommended for children under 5 years of age.

4.3 CONTRAINDICATIONS

Panamax is contraindicated in patients who are hypersensitive to paracetamol or to any other component of the Panamax formulations. It must not be used in patients with known glucose-6-phosphate-dehydrogenase deficiency. Paracetamol should not be used in patients with severe hepatocellular insufficiency. Paracetamol should not be used in patients with active alcoholism as chronic excessive alcohol ingestion predisposes patients to paracetamol hepatotoxicity.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

This medication may be dangerous when used in large amounts or for long periods. Hepatotoxicity may occur with paracetamol even at therapeutic doses, after short treatment duration and in patients without pre-existing liver dysfunction. Hepatotoxicity may develop following as little as 10 to 15g of paracetamol and hepatic failure is known to occur occasionally with the long term use of paracetamol.

To avoid the risk of overdose:

Check that paracetamol is absent from the composition of other medicinal products taken concomitantly.

Patients with known analgesic intolerance or known bronchial asthma must only use Panamax after having consulted a physician (hypersensitivity reactions including bronchospasm possible).

Caution is advised in patients with underlying sensitivity to aspirin and/or to non-steroidal anti-inflammatory drugs (NSAIDs).

Severe cutaneous adverse reactions (SCARs): Life threatening cutaneous reactions Stevens-Johnson Syndrome (SJS), and Toxic Epidermal Necrolysis (TEN) have been reported with the use of paracetamol. Patients should be advised of the signs and symptoms and monitored closely for skin reactions. If symptoms or signs of SJS and TEN (e.g. progressive skin rash often with blisters or mucosal lesions) occur, patients should stop paracetamol treatment immediately and seek medical advice.

Paracetamol should be used upon medical advice in patients with:

- Mild-to-moderate hepatocellular insufficiency
- Severe renal insufficiency and sepsis
- Chronic alcohol use including recent cessation of alcohol intake
- Malnutrition and other sources of low glutathione reserves
- Glucose-6-phosphate-dehydrogenase deficiency
- Gilbert's syndrome

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness and/or pre-disposing factors (see above) who were treated with paracetamol at therapeutic dose for a prolonged period or combination of paracetamol and flucloxacillin. Symptoms of HAGMA may include serious breathing difficulties with deep rapid breathing, drowsiness, nausea and vomiting. Prompt discontinuation of paracetamol and close monitoring is recommended if symptoms of HAGMA appear. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Use in hepatic impairment

PANAMAX should not be administered to patients with severe hepatocellular insufficiency (see Section 4.3 CONTRAINDICATIONS).

Paracetamol should be used with caution in patients with mild-to-moderate hepatocellular insufficiency. These patients must seek medical advice before taking this medication. Underlying liver disease increases the risk of paracetamol-related liver damage.

Use in renal impairment

PANAMAX 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

PANAMAX Tablet is not recommended for children under 7 years of age.

PANAMAX Elixir is not recommended for infants under 1 month of age.

PANAMAX 240 Elixir is not recommended for children under 5 years of age.

Effect on Laboratory Tests

Uric acid and blood glucose: Intake of paracetamol may affect the laboratory determination of uric acid by phosphotungstic acid and of blood glucose by glucose oxidase-peroxidase.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Paracetamol may increase the risk of bleeding in patients taking warfarin and other antivitamin K. Anticoagulant dosage may require reduction and patients should be monitored for appropriate coagulation and bleeding complications.

Paracetamol absorption is increased by drugs which increase gastric emptying e.g. metoclopramide and domperidone and decreased by drugs which decrease gastric emptying e.g. propantheline, antidepressants with anticholinergic properties, narcotic analgesics.

Paracetamol may increase chloramphenicol concentrations by slowing down excretion, entailing the risk of increased toxicity. The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes, such as antiepileptics (such as phenobarbital, phenytoin, carbamazepine, topiramate), barbiturates, hypnotics, rifampicin and alcohol.

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

Cholestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol. Chelating resin can decrease the intestinal absorption of paracetamol and potentially decrease its efficacy if taken simultaneously. In general, there must be an interval of more than 2 hours between taking the resin and taking paracetamol, if possible.

Co-administration of flucloxacillin with paracetamol may lead to high anion gap metabolic acidosis due to pyroglutamic acidosis, particularly in patients with risk factors (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

When used concurrently with zidovudine, an increased tendency for neutropenia may develop. Combination of Panamax and zidovudine should be avoided.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy – Pregnancy Category A

Drugs which have 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. Paracetamol can be

used during pregnancy if clinically needed however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Paracetamol can cross the placenta; however, no teratogenic effects have been observed in rats or mice, after doses of up to 250 mg/kg.

A woman in the third trimester of pregnancy ingested 22.5 g paracetamol. Early treatment with oral acetylcysteine resulted in good outcome for both mother and foetus.

Use in lactation

Paracetamol is excreted in breast milk. The amount available for ingestion by the infant has been reported variously as less than 0.1% of a single 500 mg dose and as 0.04 to 0.23% of a single 650 mg dose. Maternal ingestion of paracetamol in usual analgesic doses does not appear to present a risk to the nursing infant.

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)

Reports of adverse reactions are rare. Although the following reactions have been reported: dyspepsia, sweating, erythema, urticaria, anaphylactic shock, angioneurotic oedema, difficulty breathing, drop in blood pressure, nausea, allergic reactions such as skin rashes, hypersensitivity reactions and haematological reactions, including thrombocytopenia, leukopenia, neutropenia, agranulocytosis and pancytopenia. Bronchospasm may be triggered in patients having a tendency of analgesic asthma. Toxic Epidermal Necrolysis (TEN), Stevens-Johnson Syndrome (SJS), acute generalised exanthematous pustulosis, fixed drug eruption (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE) and cytolytic hepatitis, which may lead to acute hepatic failure, have also been reported. Overdosage with paracetamol if left untreated can result in severe, sometimes fatal liver damage and rarely, acute renal tubular necrosis.

Haemolytic anaemia, particularly in patients with underlying glucose 6-phosphate-dehydrogenase deficiency has been reported. Kounis syndrome has been reported, as has high anion gap metabolic acidosis due to pyroglutamic acidosis in patients with pre-disposing factors (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

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 http://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Elderly persons, small children, patients with liver disorders, chronic alcohol consumption or chronic malnutrition, as well as patients concomitantly treated with enzyme-inducing drugs are at an increased risk of intoxication, including fatal outcome.

Symptoms

Toxic symptoms include vomiting, abdominal pain, hypotension and sweating. Nausea, vomiting, anorexia, pallor and abdominal pain generally appear during the first 24 hours of overdosage with paracetamol. Overdosage with paracetamol may cause hepatic cytolysis which can lead to hepatocellular insufficiency, gastrointestinal bleeding, metabolic acidosis, encephalopathy, disseminated intravascular coagulation, coma and death. Increased levels of hepatic transaminases, lactate dehydrogenase and bilirubin with a reduction in prothrombin level can appear 12 to 48 hours after acute overdosage. Overdosage can also lead to pancreatitis, acute renal failure and pancytopenia. The most serious adverse effect of acute overdosage of paracetamol is a dose-dependent, potentially fatal hepatic necrosis. In adults, hepatotoxicity may occur after ingestion of a single dose of 12 g (24 tablets) of paracetamol; a dose of 25 g (50 tablets) or more is potentially fatal. Symptoms during the first 2 days of acute poisoning by paracetamol do not reflect the potential seriousness of the intoxication. Major manifestations of liver failure such as jaundice, hypoglycaemia and metabolic acidosis may take at least 3 days to develop.

Treatment

Despite lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention.

Determinations of the plasma concentration of paracetamol are recommended.

Plasma concentration of paracetamol should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable).

Where paracetamol intoxication is suspected, intravenous administration of SH group donators such as acetylcysteine within the first 10 hours after ingestion is indicated. Although acetylcysteine is most effective if initiated within this period, it can still offer some degree of protection if given as late as 48 hours after ingestion; in this case it is taken for longer.

If the history suggests that 12 g paracetamol or more has been ingested, administer one of the following antidotes:

Acetylcysteine 20% iv

Administer intravenously, 20% acetylcysteine immediately without waiting for positive urine test or plasma level results. For dosage instructions refer to the acetylcysteine 20% iv product information.

Oral Methionine

For dosage instructions refer to the methionine product information.

Further measures will depend on the severity, nature and course of clinical symptoms of intoxication and should follow standard intensive care protocols.

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 has analgesic and antipyretic effects.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

After oral administration, paracetamol is absorbed rapidly and completely from the small intestine; peak plasma levels occur 10 to 60 minutes after oral administration. Food intake delays paracetamol absorption.

Distribution

Paracetamol is uniformly distributed throughout most body fluids; the apparent volume of distribution is 1 to 1.2 L/kg. Paracetamol can cross the placenta and is excreted in breast milk. Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

Metabolism

Paracetamol is metabolised by the hepatic microsomal enzyme system. In adults at therapeutic doses, paracetamol is mainly conjugated with glucuronide (45-55%) or sulfate (20-30%). A minor proportion (less than 20%) is metabolised to catechol derivatives, and mercapturic acid compounds via oxidation. Paracetamol is metabolised differently by infants and children compared to adults, the sulfate conjugate being predominant.

Excretion

Paracetamol is excreted in the urine mainly as the glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged paracetamol. 85-90% of the administered dose is eliminated in the urine within 24 hours of ingestion. The elimination half-life is about 1 to 4 hours.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

PANAMAX Tablets

The inactive ingredients are: maize starch, purified talc, pregelatinised maize starch, povidone, stearic acid and potassium sorbate.

PANAMAX Elixir

The inactive ingredients are: macrogol 1500, propylene glycol, glycerol, tutti frutti flavour, raspberry flavour, benzoic acid, potassium sorbate, Lycasin, saccharin sodium, ponceau SX and purified water.

PANAMAX 240 Elixir

The inactive ingredients are: macrogol 1500, allura red AC, propylene glycol, glycerol, saccharin sodium, sorbitol solution (70 per cent) (non-crystallising), benzoic acid, potassium sorbate, raspberry flavour, imitation candied sugar and purified water.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

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.

6.5 NATURE AND CONTENTS OF CONTAINER

PANAMAX Tablet

Blister packs of 50 and 100 tablets.

PANAMAX Elixir

100 mL.

PANAMAX 240 Elixir

200 mL.

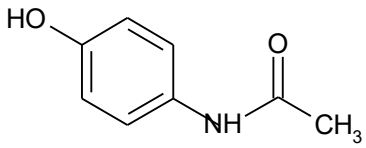
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

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

6.7 PHYSICOCHEMICAL PROPERTIES

Paracetamol is a white or almost white, crystalline powder. It is sparingly soluble in water, freely soluble in alcohol and very slightly soluble in methylene chloride. It has a melting point between 168°C and 172°C.

Chemical structure



MW 151.17

Chemical Formula

$C_8H_9NO_2$

Chemical Name

N-(4-Hydroxyphenyl)acetamide

CAS number

103-90-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

PANAMAX Tablet

Pharmacy Medicine (Schedule 2) pack size: 50

Pharmacist Only Medicine (Schedule 3) pack size: 100

PANAMAX Elixir and PANAMAX 240 Elixir

Pharmacy Medicine (Schedule 2)

8 SPONSOR

sanofi-aventis australia pty ltd
12-24 Talavera Road
Macquarie Park NSW 2113
Freecall: 1800 818 806
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

PANAMAX Tablets

10 September 1991

PANAMAX Elixir

30 August 1991

PANAMAX 240 Elixir

14 July 1994

10 DATE OF REVISION

25 August 2025

Summary table of changes

Section Changed	Summary of new information
4.3	Update for clarity and to achieve an appropriate level of consistency with the currently approved PI document for the similar S4 medicine, PANADEINE FORTE
4.4	Safety update to include the risk of high anion gap metabolic acidosis (HAGMA) due to pyroglutamate acidosis. Update for clarity and to achieve an appropriate level of consistency with the currently approved PI document for the similar S4 medicine, PANADEINE FORTE.
4.5	Safety update to include the risk of HAGMA due to pyroglutamate acidosis Correction of cross-referencing

4.8	Safety update to include the risk of HAGMA due to pyroglutamate acidosis Correction of cross-referencing