PROFESSIONAL INFORMATION

SCHEDULING STATUS S1

1. NAME OF MEDICINE

JP PARACETAMOL 500 mg (tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each tablet contains:

Paracetamol		500 mg
Preservatives:	Nipastat	0,1 % m/m
	Benzoic Acid	0,06 % m/m

Sugar free

Contains sodium metabisulphite (see section 4.4)

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM:

Green, round, flat bevel edged tablet with a central break-line on one side

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

For the relief of mild to moderate pain and fever such as headaches, toothache and pain associated with colds and flu

4.2. Posology and method of administration

DO NOT EXCEED THE RECOMMENDED DOSE

Adults: One or two tablets repeated every 3-4 hours if necessary, but not more than 8 tablets to be taken in any 24 hour period.

Paediatric population

Children 6 to 12 years: Half to one tablet repeated every 3-4 hours if necessary, but not more than 4 doses in any 24 hour period.

Children under 6 years:

Not recommended. Paracetamol syrup should rather be considered for use if such a medicine is necessary.

Method of administration

Oral

4.3. **Contraindications**

Hypersensitivity to paracetamol or any of the other ingredients in JP PARACETAMOL 500 mg listed in section 6.1.

Severe liver function impairment.

4.4. **Special warnings and precautions for use**

JP PARACETAMOL 500 mg contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or Poison Centre must be contacted immediately.

Dosages in excess of those recommended may cause severe liver damage. Patients suffering from liver or kidney disease should take paracetamol under medical supervision. Do not use continuously for more than 10 days without consulting a doctor. Excessive and prolonged use of this medicine may be dangerous.

Special precautions:

1. Consult a doctor if no relief is obtained from the recommended dosage.
2. Store in a safe place out of reach of children

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), eosinophilia and systemic (DRESS)/Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicines. If a patient develops SCAR, treatment with JP PARACETAMOL 500 mg must immediately be discontinued and appropriate treatment instituted (see section 4.8).

JP PARACETAMOL 500 mg contains sodium metabisulphites

May rarely cause severe hypersensitivity reactions and bronchospasm.

4.5. Interaction with other medicines and other forms of interaction

Hepatotoxic medicines: Increased risk of hepatotoxicity.

Enzyme-inducing medicines: Increased risk of hepatotoxicity and possible decrease in therapeutic effects of JP PARACETAMOL 500 mg.

Metoclopramide: Absorption of JP PARACETAMOL 500 mg may be accelerated.

Probenecid: Pre-treatment with probenecid can decrease JP PARACETAMOL 500 mg clearance and increase its half-life.

Cholestyramine: Absorption of JP PARACETAMOL 500 mg is reduced if given within one hour of cholestyramine.

Salicylates: Prolonged concurrent use of JP PARACETAMOL 500 mg with salicylates increases the risk of adverse renal effects.

Antibiotics / antibacterials: Chronic use of isoniazid, an antibiotic drug often prescribed for tuberculosis, may increase the risk of liver damage when combined with JP PARACETAMOL 500 mg, even at

recommended doses. Plasma-paracetamol concentrations considered as an indication for antidote treatment should be halved in patients receiving enzyme inducing drugs such as rifampicin.

Warfarin and anticoagulants: concurrent, regular daily use of high-dose administration of paracetamol may enhance the anticoagulant effect with an increased risk of bleeding – use with caution. Increased monitoring of anticoagulant therapy may be appropriate for those taking paracetamol regularly.

Antiepileptics: plasma-paracetamol concentrations considered an indication for antidote treatment should be halved in patients receiving enzyme inducing drugs such as carbamazepine, phenobarbital, phenytoin, or primidone.

Antivirals: paracetamol enhances the antiviral effect of interferon alfa.

4.6. **Fertility, pregnancy and lactation**

Safe for use in pregnancy and lactation at the recommended doses.

4.7. Effects on ability to drive and use machines

JP PARACETAMOL has no or negligible influence on the ability to drive and use machines (see section 4.8).

4.8. **Undesirable effects**

Blood and lymphatic system disorders

The use of paracetamol has been associated with the occurrence of neutropenia, pancytopenia and leucopenia, agranulocytosis, thrombocytopenia and anaemia.

Metabolism and nutrition disorders

Frequency unknown: pyroglutamic aciduria (5-oxoprolinuria) and high-anion gap metabolic acidosis

Ear and labyrinth disorders

Frequency unknown: Hearing loss

Cardiac disorders

Frequency unknown: hypertension

Renal and urinary disorders:

Less frequent: Renal colic, renal failure and sterile pyuria

Frequency unknown: nephropathy

Hepatobiliary disorders:

Less frequent: Hepatitis

Gastrointestinal disorders:

Less frequent: Pancreatitis.

Frequency unknown: Nausea and vomiting

Skin and subcutaneous tissue disorders

Less frequent: Hypersensitivity reactions resulting in reversible skin rash may occur. The rash is usually ertythematous or urticarial, but sometimes more serious and may accompanied by fever and mucosal lesions. More mild rashes and other hypersensitivity reactions also occur occasionally.

Serious cutaneous adverse reactions (SCAR) include toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute g eneralized exanthematous pustulosis (AGEP), eosinophilia and systemic (DRESS) / Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) (see section 4.4).

General disorders and administrative site conditions

Hypersensitivity reactions characterised by urticaria, dyspnoea, and hypotension.

Post-marketing experience

The risk of SCARs is very serious, potentially life-threatening / fatal and appear to be unpredictable.

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9. **Overdose**

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person to a hospital directly. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed. Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than
5 -10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of drugs that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms (see section 4.8)

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning do not reflect the potential seriousness of the overdosage. Liver damage may become apparent 12 to 48 hours, or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias

have been reported.

Treatment for Paracetamol overdosage:

Although evidence is limited it is recommended that any adult person who has ingested 5 - 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours, should have the stomach emptied by lavage (emesis may be adequate for children) and a single dose of 50 g activated charcoal given via the lavage tube. Ingestion of amounts of paracetamol smaller than this may require treatment in patients susceptible to paracetamol poisoning (see above). In patients who are stuperose or comatose endotracheal intubation should precede gastric lavage in order to avoid aspiration.

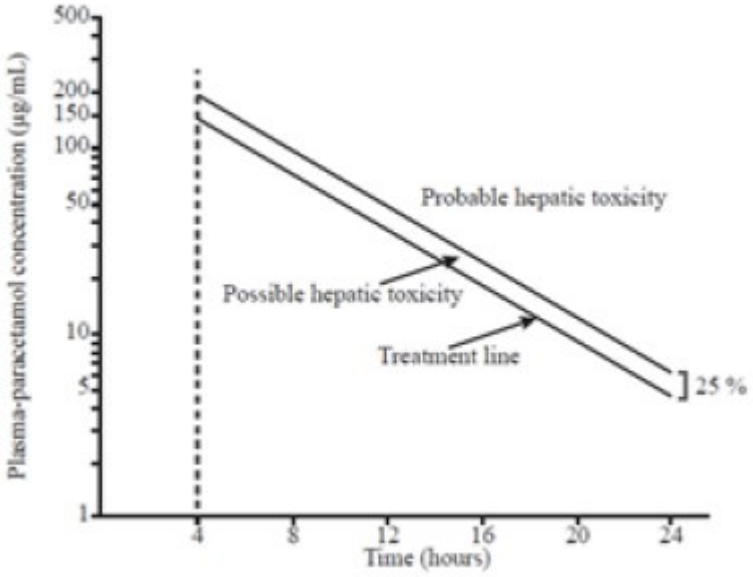
N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken.

IV: An initial dose of 150 mg/kg in 200 ml dextrose injection, given intravenously over 15 minutes, followed by an intravenous infusion of 50 mg/kg in 500 ml of dextrose injection over the next 4 hours, and then 100 mg/kg in 1 000 ml over the next 16 hours. The volume of intravenous fluids should be modified for children.

Orally: Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by a 70 mg/kg solution every 4 hours for 17 doses.

A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours, may be misleading. Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their 4-hour plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the nomogram below. The nomogram should be used only

in relation to a single acute ingestion.



Source: Martindale, The Complete Drug Reference. 37th edition

Those, whose plasma paracetamol levels are above the "normal treatment line", should continue N- acetylcysteine treatment with 100 mg/kg IV over sixteen hours repeatedly until recovery. Patients with increased susceptibility to liver damage as identified above, should continue treatment if concentrations are above the "high risk treatment line". Prothrombin index correlates best with survival.

Monitor all patients with significant ingestions for at least ninety-six hours.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacological class:

A 2.7 Anti-pyretic or anti-pyretic and anti-inflammatory analgesics

ATC code: N02BE01

Pharmacological action

Paracetamol has analgesic and anti-pyretic actions

5.2. Pharmacokinetic properties

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring after 0,5 to 1 hour after oral administration.

Once absorbed, the plasma half-life of paracetamol is about 2 hours.

It is distributed into most body tissues. Plasma-protein binding varies. It crosses the placenta and is presented in breast milk.

Paracetamol is metabolised predominantly in the liver conjugation with glucuronic acid (about 60 %), sulphuric acid (about 35 %) and cysteine (about 3 %) and excreted in the urine primarily as inactive conjugated metabolites.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Starch maize, sodium starch glycolate, gelatine, Nipastat sodium, benzoic acid, sodium metabisulphite, purified talc, magnesium stearate, Deep Apple Green F1620 (CI 47005, 42090, 15985, 44090, 16255)

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

HDPE containers: 36 months

Polypropylene bucket: 24 months

Store in a well-closed container protected from light. Store at or below 25°C. Exposure to air should be minimal.

6.4. **Nature and contents of container**

White HDPE container of 50, 100 and 1000 tablets

White polypropylene bucket containing 5000 tablets.

6.5. Special precautions for storage

None

6.6. Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Gulf Drug Company (Pty) Ltd

22 Burnside Drive,

Old Mill Industrial Park, Mount Edgecombe 4300

8. REGISTRATION NUMBER:

B/2.7/1644

9. DATE OF FIRST AUTHORISATION

28 September 1992

10. DATE OF REVISION OF TEXT

27 September 2023