1.3.1.1 Professional Information for Medicines for Human Use

SCHEDULING STATUS:

S0 ALL PACK SIZES CONTAINING **LESS THAN** 25 TABLETS.

SCHEDULE STATUS :

S1 ALL PACK SIZES CONTAINING **MORE THAN** 25 TABLETS.

1. NAME OF THE MEDICINE

PAINOGESIC TABLETS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 500 mg paracetamol

Contains Sugar: Powdered sucrose 20 mg

Contains preservatives: Nipastat 0, 1 % m/m & Benzoic acid 0,06 % m/m

For a full list of excipients, **see section 6.1**

3. PHARMACEUTICAL FORM

A flat green tablet, 12,7 mm in diameter, with a breakline on the one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

PAINOGESIC is indicated for the symptomatic relief of:

- Mild to moderate pain.
- Fever.

4.2. Posology and method of administration

Posology

DO NOT EXCEED THE RECOMMENDED DOSE.

Usual adult dose

One tablet every 3 hours or one to two tablets (0,5 to 1 g) every 4 - 6 hours up to a maximum of 4 g daily (8 tablets).

Paediatric population

Usual paediatric dose

6 to 12 years:

250 - 500 mg (half to one tablet) three to four times a day as required.

Not suitable for children under 6 years of age.

Method of administration

PAINOGESIC Is for oral administration.

4.3. Contraindications

- Hypersensitivity to the paracetamol or any of the excipients listed in section 6.1
- Severe renal function impairment.
- Severe liver function impairment.

4.4. Special warnings and precautions for use

PAINOGESIC 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 medical practitioner, hospital or Poison Centre must be contacted immediately.

- Dosages in excess of those recommended may cause severe liver damage.

- Consult a medical practitioner if no relief is obtained from the recommended dosage.
- Do not use continuously for more than 10 days without consulting a medical practitioner.
- Do not use with any other paracetamol-containing products.
- Patients should be advised to consult their medical practitioner. if their headaches become persistent.
- Caution should be exercised in patients with glutathione depleted states, as the use of paracetamol may increase the risk of metabolic acidosis (see section 4.9).
- Use with caution in patients with glutathione depletion due to metabolic deficiencies. if symptoms persist, medical advice must be sought.

SEVERE CUTANEOUS ADVERSE REACTIONS

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 **PAINOGESIC** must immediately be discontinued and appropriate treatment instituted.

4.5. Interaction with other medicines and other forms of interaction

Concomitant use of **PAINOGESIC** with hepatotoxic medicines or medicines that induce liver enzymes may increase the risk of hepatotoxicity of **PAINOGESIC**. Possible decrease in therapeutic effects of **PAINOGESIC**.

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine.

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.

Probenecid may decrease the clearance and increase the plasma half-life of paracetamol.

Prolonged concurrent use of **PAINOGESIC** with salicylates increases the risk of adverse renal effects.

Chronic use of isoniazid may increase the risk of liver damage when combined with **PAINOGESIC**, even at recommended doses.

4.6. Fertility, pregnancy and lactation

Pregnancy

Safety and efficacy in pregnancy have not been established.

Breastfeeding

Safety and efficacy in lactation have not been established.

Fertility

There are no fertility data

4.7. Effects on ability to drive and use machines

None

4.8. Undesirable effects

Tabulated list of adverse reactions

System Organ Class	**Frequency**		
	Frequent	***Less frequent***	***Not known***
Blood and lymphatic system disorders		Agranulocytosis, thrombocytopenia, leucopenia, pancytopenia, neutropenia, anaemia.	
Immune system disorders		Anaphylaxis Cutaneous hypersensitivity reactions including, among others, skin rashes and angioedema. Very rare cases of serious skin reactions have been reported.	
Respiratory, thoracic and mediastinal disorders		Bronchospasm*	
Gastrointestinal disorders		Pancreatitis.	
Hepatobiliary disorders		Hepatitis. Hepatic dysfunction	
Skin and subcutaneous tissue disorders		Dermatitis, Skin rashes, and other allergic reactions. The rash is usually erythematous or urticarial but sometimes more serious and	Fixed drug eruptions (FDE), Drug-induced hypersensitivity

		accompanied by fever and mucosal lesions.	syndrome (DIHS)
Renal and urinary disorders		Renal colic, renal failure and sterile pyuria	

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatic sensitive to aspirin or to other NSAIDs.

Post Marketing experience

The risk of fixed drug eruptions (FDE) and Drug-induced hypersensitivity syndrome (DIHS) has been associated with the use of paracetamol containing medicines.

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

4.9 Overdose

Symptoms

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and possible 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 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

In the event of an overdosage, consult a doctor immediately, or take the person directly to a hospital. 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 medicines that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

N-acetylcysteine should be administered to all cases of suspected overdosage as soon as possible preferably within 8 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. An initial dose of 150 mg/kg N- acetylcysteine in 200 ml dextrose injection over the next 4 hours and then 100 mg/kg in 1000 ml dextrose injection over the next 16 hours. The volume of intravenous fluids should be modified for children.

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

A plasma paracetamol level should be determined 4 hours after ingestion in all cases of suspected overdosage. Levels done before 4 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.

Those whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/kg IV over 16 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 ingestion for at least 96 hours.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and Class: A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesics

Pharmacological action

Paracetamol has analgesic and antipyretic actions.

Pharmacodynamic effects:

Paracetamol acts predominantly by inhibiting prostaglandin synthesis.

5.2. Pharmacokinetic properties

Absorption

Following oral administration paracetamol is well absorbed, with peak plasma concentrations obtained after 0,5 to 1 hours. Once absorbed the plasma half-life is about 2 hours.

Distribution

Plasma protein binding is variable.

Metabolism/Biotransformation

Paracetamol is metabolised in the liver primarily by conjugation with glucuronic acid (about 60 %), sulphuric acid (about 35 %) and cysteine (about 3 %).

Elimination

Paracetamol renally excreted primarily as conjugated metabolites.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Benzoic acid

Chloroform spirits

Green apple (TF 1196)

Magnesium stearate

Modified starch

Nipastat

Powdered sucrose

Purified water

Starch maize

6.2. Incompatibilities

Not applicable

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store in a well closed container protected from light, Store in a cool (at or below 25 °C), dry place. Exposure to air should be kept to a minimum.

KEEP OUT OF REACH OF CHILDREN.

6.5. Nature and contents of container

White polypropylene securitainers of 100 tablets.

White/Amber PVC/HOPE containers of 100, 500 and 1000 tablets.

H.D.P.E. buckets of 5000 tablets.

Blister packs of 10 and 20 tablets.

Patient ready packs of different pack sizes.

6.6. Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product.

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

7. NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Innovata Pharmaceuticals (Pty) Ltd

Crownwood Office Park

100 Northern Parkway

Ormonde

Johannesburg

2091

South Africa

8. REGISTRATION NUMBER

A 34/2.7/0466

9. DATE OF FIRST AUTHORISATION

31/02/2002

10. DATE OF REVISION OF TEXT

13/06/2023