1.3.1.1 Professional Information for Medicines for Human Use

SCHEDULING STATUS:

S0

1. NAME OF THE MEDICINE

PAINOGESIC SYRUP 120 mg /5 ml syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml syrup contains:

Paracetamol 120 mg

Preservatives:

Alcohol 11,2 % v/v

Sugar free

Tartrazine free

Contains sweeteners: Inverted sugar 2 ml and Glycerin 5 ml

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Syrup

A red raspberry flavoured syrup.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

PAINOGESIC SYRUP is indicated for the relief of mild to moderate pain and fever.

4.2. Posology and method of administration

Posology

DO NOT EXCEED THE RECOMMENDED DOSE.

Infants:

3 months to 1 year: 2,5 to 5 ml (60 to 120 mg)

Children:

1 to 5 years: 5 to 10 ml (120 to 240 mg)

6 to 12 years: 10 to 20 ml (240 to 480 mg)

Always administer using a medicine measure or a syringe.

Repeat dosage every 4 to 6 hours if needed to a maximum of 4 doses per 24 hours.

Method of administration

Dose to be taken orally.

Shake the bottle before use.

4.3. Contraindications

Hypersensitivity to paracetamol or to any of the ingredients of **PAINOGESIC SYRUP** listed in section 6.1

Severe liver function impairment.

4.4. Special warnings and precautions for use

PAINOGESIC SYRUP 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 of **PAINOGESIC SYRUP** in excess of those recommended may cause severe liver damage.
Consult a medical practitioner if pain or fever persists or gets worse at the recommended dosage, if new symptoms occur or if redness and swelling is present, as these could be signs of a more serious condition.
Do not use this product continuously for more than 10 days without consulting your doctor.

PAINOGESIC SYRUP contains inverted sugar

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Patients suffering from hepatitis or alcoholism, or recovering from any form of liver disease, should not take excessive quantities of **PAINOGESIC SYRUP**.

Paracetamol should be given with care to patients with impaired kidney or liver function.

Use with caution in renal disease, alcohol dependence, chronic malnutrition or dehydration.

High Anion gap metabolic acidosis (HAGMA)

Caution is advised if **PAINOGESIC SYRUP** is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of **PAINOGESIC SYRUP**. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), StevenJohnson syndrome (SJS), acute generalised exanthematous pustulosis (AGEP), drug rash with eosinophilia and systemic symptoms (DRESS) or drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicines. If a patient develops SCARs,

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

4.5. Interaction with other medicines and other forms of interaction

Hepatotoxic medicines - increased risk of hepatotoxicity.

Enzyme inducing medicines - increased risk of hepatotoxicity. Possible decrease in therapeutic effects of **PAINOGESIC SYRUP**.

Metoclopramide - Absorption of **PAINOGESIC SYRUP** may be accelerated.

Cholestyramine - Absorption of **PAINOGESIC SYRUP** is reduced if given within one hour of cholestyramine.

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

Warfarin and Anticoagulants - concurrent, chronic, high-dose administration of **PAINOGESIC SYRUP** may increase the anticoagulant effect.

Paracetamol is recommended as the general analgesic and antipyretic of choice in patients on oral anticoagulant therapy. However, caution is needed since, although it has no effect on the gastric mucosa or on platelet function, some studies (with warfarin, anisindione, dicoumarol, or phenprocoumon) and isolated reports have found an increased risk of bleeding in patients taking regular doses of paracetamol while on an oral anticoagulant. An increase in INR has also been reported in controlled studies of the use of paracetamol in patients stabilised on warfarin. Increased monitoring of anticoagulant therapy may be appropriate for those also taking paracetamol regularly.

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

Probenecid - Pre-treatment with probenecid can decrease paracetamol clearance and increase its plasma half-life. Although urinary excretion of the sulphate and glucuronide conjugates of paracetamol are reduced, that of paracetamol is unchanged.

Antibacterials - The plasma-paracetamol concentrations considered an indication for antidote treatment should be halved in patients receiving enzyme inducing medicines such as rifampicin. Severe hepatotoxicity at therapeutic doses or moderate overdoses of

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paracetamol has been reported in patients receiving isoniazid, alone or with other medicines for tuberculosis.

Antivirals - Severe hepatotoxicity has occurred after use of paracetamol in a patient taking zidovudine and co-trimoxazole. However, neither short-term nor long-term studies (the latter also in an individual patient) have shown any alteration of zidovudine elimination in patients taking zidovudine and paracetamol.

Interferon alfa - Paracetamol has also been found to enhance the antiviral effect of interferon alfa.

Flucloxacillin - Caution should be taken when **PAINOGESIC SYRUP** is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risks factors (see section 4.4)

4.6. Fertility, pregnancy and lactation

Safety and efficacy in pregnancy and breastfeeding have not been established.

Fertility

No data available.

4.7. Effects on ability to drive and use machines

PAINOGESIC SYRUP has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

Tabulated list of adverse reactions

System Organ Class	**Frequency**	**Adverse Reaction**
Blood and lymphatic system disorders	Less frequent	agranulocytosis, thrombocytopenia, leucopenia, pancytopenia, neutropenia, 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	Possible increase in the risk of 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	Dermatitis, skin rashes, and other allergic reactions such as Stevens Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Acute Generalised Exanthematous Pustulosis (AGEP). The rash is usually erythematous or urticarial but sometimes more serious and accompanied by fever and mucosal lesions. More mild rashes and

		other hypersensitivity reactions also occur occasionally.
General disorders and administrative site conditions	Frequency Unknown	Hypersensitivity reactions characterised by urticaria, dyspnoea, and hypotension.

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

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 to10 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.

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.

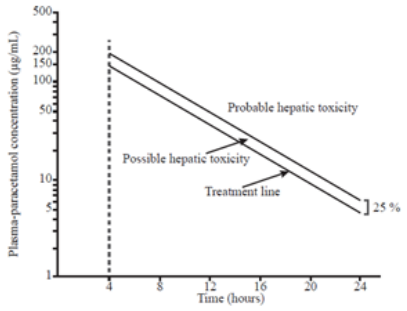
Management:

Although evidence is limited it is recommended that any adult person who has ingested 5 to 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. An initial dose of 150 mg/kg N-acetylcysteine in 200 ml dextrose injection given intravenously over 15 minutes, followed by an infusion of 50 mg/kg in 500 ml dextrose injection over the next four hours, and then 100 mg/kg in 1 000 ml dextrose injection over the next sixteen hours. The volume of intravenous fluid 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 every four hours for seventeen doses.

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

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

The class of the medicine: A 2.7 Antipyretics or antipyretic and anti-inflammatory analgesics.

ATC code: N02BE01

Paracetamol has analgesic and antipyretic properties.

It 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 hour. The plasma half-life is about 2 hours.

Distribution

Plasma protein binding is variable. Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk.

Elimination

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

Special Populations

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Ethanol 96 % v/v

Glycerin

Hexacol red (2G Supra CI no. 18050)

Invert sugar

Propylene glycol

Purified water

Raspberry essence

Spirits chloroform

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6.2. Incompatibilities

Not applicable

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store in a cool place at or below 25 ˚C. Protect from light.

KEEP OUT OF REACH OF CHILDREN.

6.5. Nature and contents of container

100 ml amber or white opaque plastic bottles.
2.5 L amber bottles.

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 27/2.7/0015

9. DATE OF FIRST AUTHORISATION

20/04/2005

10. DATE OF REVISION OF TEXT

24/01/2024

REFERENCES:

Reference 1: PANADO® PAEDIATRIC SYRUP – STRAWBERRY:

PI, Adcock Ingram Limited: 18 April 2023

Reference 2: VARIPAN SUGAR FREE SYRUP: PI,

Lebasi Pharmaceuticals (Pty) Ltd: 20 November 2023