SCHEDULING STATUS

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1 NAME OF THE MEDICINE

GO PAIN PARACETAMOL Tablets, 500 mg film-coated tablets

2 QUALITIVE AND QUANTITIVE COMPOSITION

Each film-coated GO PAIN PARACETAMOL Tablet contains 500 mg paracetamol.

Sugar free.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets (tablets)

White to off-white coloured film-coated tablets debossed with “PARA 500” one side and score line on the other side.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

Posology

Children under 6 years: Not recommended.

Children 6 – 12 years: ½ - 1 tablet every 6 hours. Not more than 4 tablets to be taken in any 24-hour period.

Children over 12 years: 1 tablet every 4 – 6 hours. Not more than 4 tablets to be taken in any 24-hour period.

Adults: 1 – 2 tablets every 4 – 6 hours. Not more than 8 tablets to be taken in any 24-hour period.

DO NOT EXCEED THE RECOMMENDED DOSE

Method of administration

For oral use.

4.3 Contraindications

- Hypersensitivity to paracetamol, or any of the other ingredients in GO PAIN PARACETAMOL Tablets (see section 6.1).
- Severe liver function impairment.

4.4 Special warnings and precautions for use

GO PAIN PARACETAMOL Tablets contain 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.
- Consult a doctor or pharmacist if pain or fever persists or gets worse at the recommended dosage, or if new symptoms occur.
- Do not use this product continuously without consulting a medical practitioner:

Pain – for more than 7 days in adults (5 days for children); and fever – for more than 3 days.

- Patients suffering from hepatitis or alcoholism or recovering from any form of liver disease should not take excessive quantities of GO PAIN PARACETAMOL Tablets.
- Caution is recommended in patients with moderate renal failure and patients on dialysis, as plasma concentrations of GO PAIN PARACETAMOL Tablets and its conjugates are increased.
- Use with caution in renal impairment, chronic malnutrition, or dehydration.
- Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Stevens–Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS)/ drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruption (FDE) have been reported in patients treated with paracetamol containing medicines. If a patient develops SCAR, treatment with GO PAIN PARACETAMOL Tablets must immediately be discontinued and appropriate treatment instituted (see Section 4.8).

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 GO PAIN PARACETAMOL Tablets.

Metoclopramide: Absorption of GO PAIN PARACETAMOL Tablets may be accelerated.

Domperidone: Absorption of GO PAIN PARACETAMOL Tablets may be accelerated.

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

Cholestyramine: Absorption of GO PAIN PARACETAMOL Tablets is reduced if given within one hour of cholestyramine.

Salicylates: Prolonged concurrent use of GO PAIN PARACETAMOL Tablets with salicylates increases the risk of adverse renal effects.

Antibiotics: Chronic use of isoniazid, an antibiotic medicine often prescribed for tuberculosis, may increase the risk of liver damage when combined with GO PAIN PARACETAMOL Tablets, even at recommended

doses.

Warfarin and anticoagulants: Concurrent, chronic, high-dose administration of GO PAIN PARACETAMOL Tablets 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.

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

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

4.6 Fertility, pregnancy and lactation

Pregnancy

GO PAIN PARACETAMOL Tablets is generally considered safe for use in pregnant patients, if used infrequently (not daily or on most days).

Breastfeeding

GO PAIN PARACETAMOL Tablets is distributed into breastmilk, in amounts too small to be considered harmful to a breastfed infant. No significant adverse effects have been seen in breastfed infants whose mothers' received paracetamol.

Fertility

No data on fertility are available.

4.7 Effects on ability to drive and use machines

GO PAIN PARACETAMOL Tablets has no or negligible influence on mental and/or physical abilities to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision.

4.8 Undesirable effects

Tabulated list of adverse reactions

System Organ Class	Undesirable effect

	Frequent	**Less frequent**	**Frequency not known**
Blood and the lymphatic system disorders		Agranulocytosis, thrombocytopenia, leukopenia, pancytopenia, neutropenia, anaemia	
Immune system disorders			Hypersensitivity reactions are characterised by urticaria, dyspnoea and hypotension. Angioedema can also occur.
Metabolism and nutrition disorders		Pyroglutamic aciduria (5-oxoprolinuria) and high-anion gap metabolic acidosis	
Ear and labyrinth disorders			Hearing loss
Cardiac disorders			Possible increase in the risk of hypertension
Gastrointestinal disorders		Pancreatitis	
Hepatobiliary disorders		Hepatitis	
Renal and urinary disorders		Renal colic, renal failure and sterile pyuria	Nephropathy

Skin and subcutaneous tissue disorders		Dermatitis, skin rashes, severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Stevens–Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS)/ drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruption (FDE)	

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 to SAHPRA via the "6.04 Adverse Drug Reaction 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 directly to a hospital. A delay in starting treatment may mean that the 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.

Symptoms:

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 dysrhythmias have been reported.

After maternal overdosage during pregnancy, foetal metabolism of paracetamol that crosses the placenta can produce hepatotoxic metabolites, causing foetal hepatotoxicity.

Treatment for paracetamol overdosage:

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 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.

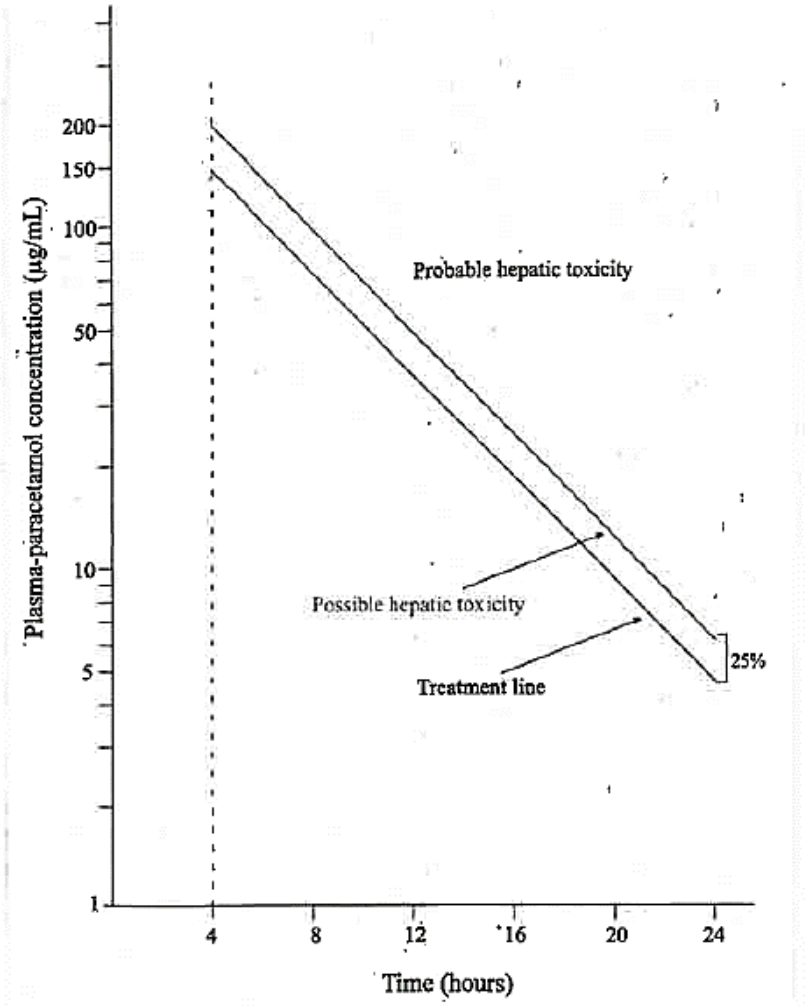

Figure 1: *A semi-logarithmic plot of plasma-paracetamol concentration against hours after ingestion*

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 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” (refer to paracetamol nomogram above). Prothrombin index correlates best with survival.

Monitor all patients with significant ingestions for at least ninety-six hours. Hepatic tests must be carried out at the beginning of treatment and repeated every 24 hours. In most cases hepatic transaminases return to normal in one to two weeks with full restitution of the liver function. In very severe cases, however, liver transplantation may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

ATC code: N02BE01

Paracetamol has analgesic and antipyretic activity.

The mechanism of action is associated with inhibition with prostaglandin synthesis.

5.2 Pharmacokinetic properties

Absorption:

Paracetamol is readily absorbed from the gastrointestinal tract, with peak plasma concentrations occurring approximately 10 – 60 minutes after oral doses.

Distribution:

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

Biotransformation:

Paracetamol is mainly metabolised in the liver, following two major hepatic pathways: glucuronic acid conjugation and sulphuric acid conjugation. The metabolites of paracetamol are mainly excreted in the urine. Less than 5 % is excreted as unchanged paracetamol.

Elimination:

The elimination half-life of paracetamol varies from about 1 – 3 hours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Povidone (K-30)

Pregelatinized starch

Sodium starch glycolate

Stearic acid

Tablet coating:

Opadry Clear® 03B19277 (hypromellose 2910 6cps and macrogol MW 40)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Store in the original package/container.

6.5 Nature and contents of container

Blister Pack

- 10 tablets in blister pack (PVC-aluminium) packed in an outer carton as 20 tablets.

HDPE bottles

- 24 tablets in HDPE bottles (high-density polyethylene) with polypropylene child resistant closures with heat seal and pulp liner

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACORP (PTY) LTD

29 Victoria Link

Route 21 Business Park

Irene, 1078, RSA

8 REGISTRATION NUMBER(S): 56/2.7/0503

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:

5 September 2023

10 DATE OF REVISION OF TEXT