PROFESSIONAL INFORMATION

SCHEDULING STATUS

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1. NAME OF THE MEDICINE

PANADO ® PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR (Syrup)

Paracetamol 120 mg/5 ml Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml syrup contains:

Paracetamol	120 mg
Preservatives:	
Methylparaben	0,10 % m/v
Propylparaben	0,015 % m/v

Sugar free

Tartrazine free

Colourant free

Contains sweeteners: Sodium saccharin 4 mg and sodium cyclamate 7,5 mg

Contains sorbitol 280 mg and antioxidant sodium metabisulphite

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Syrup

A clear slightly viscous colourless syrup with an odour of grape.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

PANADO® PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR is indicated for the symptomatic treatment of mild to moderate pain and fever.

4.2 Posology and method of administration

DO NOT EXCEED THE RECOMMENDED DOSE.

Infants:

Under 3 months:	10 mg/kg (0,41 ml/kg)
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)

While symptoms persist, to be repeated every 4 hours if needed to a maximum of 4 doses per 24 hours for not longer than 5 days.

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 **PANADO®** **PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR** listed in section 6.1.
- Severe liver function impairment.

4.4 Special warnings and precautions for use

PANADO® PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR 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 **PANADO PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR** 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.

Patients with the rare hereditary condition of sorbitol intolerance should not take **PANADO PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR**. Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

Patients suffering from hepatitis or alcoholism, or recovering from any form of liver disease, should not take excessive quantities of **PANADO PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR**

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.

Serious skin reactions such as Acute Generalized Exanthematous Pustulosis (AGEP), Stevens - Johnson syndrome (SJS), and Toxic Epidermal Necrolysis (TEN), have been reported infrequently in patients receiving paracetamol. The use of **PANADO® PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR** should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity such as swelling, itching, red severe rash, (see Section 4.8).

Sodium metabisulphite 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.
- Possible decrease in therapeutic effects of **PANADO® PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR**
- Metoclopramide - Absorption of **PANADO® PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR** may be accelerated.
- Cholestyramine - Absorption of **PANADO® PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR** is reduced if given within one hour of cholestyramine.
- Prolonged concurrent use of **PANADO® PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR** with salicylates increases the risk of adverse renal effects
- Warfarin and Anticoagulants- concurrent, chronic, high-dose administration of **PANADO® PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR** 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 drugs 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 drugs such as rifampicin. Severe hepatotoxicilty 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:

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:

PANADO® PAEDIATRIC ALCOHOL FREE – GRAPE FLAVOUR has no or negligible influence on the ability to drive and use machines**.**

4.8 Undesirable effects:

Blood and lymphatic system disorders:

Less frequent: Agranulocytosis, thrombocytopenia, leucopenia, pancytopenia, neutropenia, anaemia.

Metabolism and nutrition disorders

The following side effects have been reported and frequencies are unknown:

Pyroglutamic aciduria (5-oxoprolinuria) and high-anion gap metabolic acidosis

Ear and labyrinth disorders

The following side effect has been reported and the frequency is unknown: Hearing loss

Cardiac disorders

The following side effect has been reported and the frequency is unknown: Possible increase in the risk of hypertension

Renal and urinary disorders:

Less frequent: Renal colic, renal failure and sterile pyuria.

The following side effect has been reported and the frequency is unknown: Nephropathy

Hepatobiliary disorders:

Less frequent: Hepatitis.

Gastrointestinal disorders:

Less frequent: Pancreatitis.
The following side effects have been reported and frequencies are 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 (TENS), 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
Hypersensitivity reactions characterised by urticaria, dyspnoea, and hypotension.

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 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 to10 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.

Management:

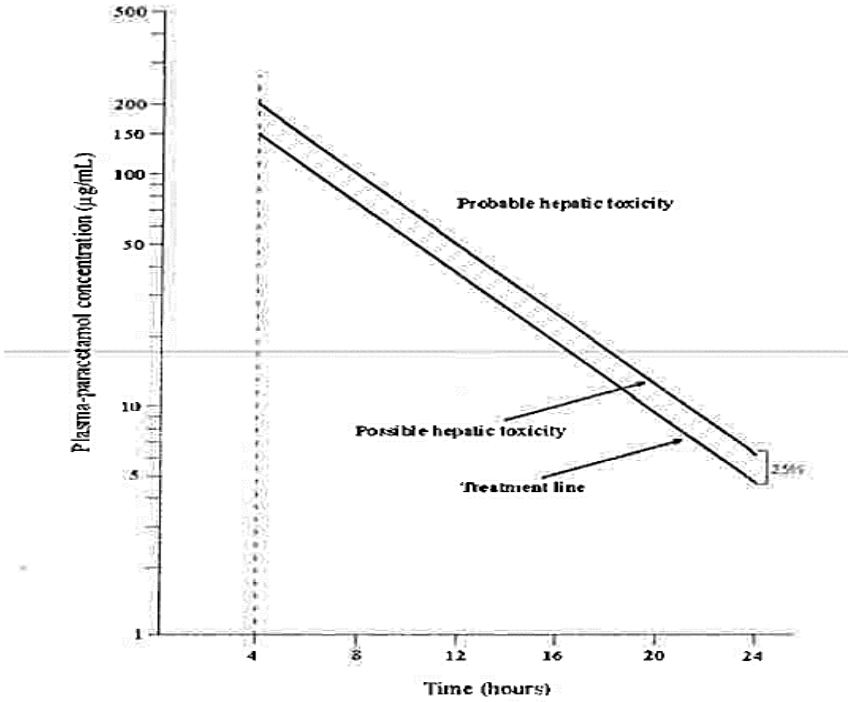
Although evidence is limited it is recommended that any adult person who has ingested 5 – 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours, should have the stomach emptied by lavage (emesis may be adequate for children) and a single dose of 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. 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 ingestions for at least ninety-six hours.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

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

5.3 Preclinical safety data:

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polyvinylpyrrolidone K25, Polyethylene Glycol 1500, Glycerol, Methyl paraben, Propyl paraben, Sorbitol, Sodium Cyclamate, Saccharin Sodium, Xanthan Gum, Flavour Weintrauben Aroma Grape, Sodium Citrate, Citric Acid, Sodium Metabisulphite, Purified Water.

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 at or below 25 °C. Exposure to air should be kept to a minimum.

6.5 Nature and contents of container:

50 ml bottles (clear glass and clear PVC) packed in unit cartons.
100 ml bottle (clear glass, PVC and PET) packed in unit cartons.

6.6 Special precautions for disposal

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited
1 New Road,
Erand Gardens,
Midrand, 1685

Customer Care: 0860 ADCOCK/232625

8. REGISTRATION NUMBER:

50/2.7/1083

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25 January 2022

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07 October 2022

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