SCHEDULING STATUS

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1. NAME OF THE MEDICINE

CETAPON JUNIOR PAEDIATRIC SYRUP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains: 120 mg Paracetamol

Preserved with Benzoic acid 0,3% m/v

Sugar free. Tartrazine free.

Contains sweetener (6 mg sodium saccharin per 5 ml)

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Syrup.

A green syrupy liquid with a characteristic smell of peppermint.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of mild to moderate pain and fever.

4.2 Posology and method of administration

Children: **7 - 12 years**: up to 20ml.

1 - 6 years: 5 - 10ml.

3 months to 1 year: 2,5 - 5ml.

Repeat dosage 3 to 4 hourly, if necessary, but not more than 4 doses in 24 hours.

DO NOT EXCEED THE RECOMMENDED DOSE.

Do not use continuously for more than ten days without consulting your doctor.

Method of administration

Dose to be taken orally.

Contraindications

Hypersensitivity to paracetamol or any of the other ingredients (see section 6.1).

Severe liver function impairment.

4.4 Special warnings and precautions for use

Cetapon Junior Paediatric 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 Cetapon Junior Paediatric 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.

Patients suffering from hepatitis or alcoholism, or recovering from any form of liver disease, should not take excessive quantities of Cetapon Junior Paediatric 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.

Severe cutaneous adverse reactions (SCARs): Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson 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 Cetapon Junior Paediatric 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 Cetapon Junior Paediatric Syrup.

Metoclopramide - Absorption of Cetapon Junior Paediatric Syrup may be accelerated.

Cholestyramine - Absorption of Cetapon Junior Paediatric Syrup is reduced if given within one hour of cholestyramine.

Prolonged concurrent use of Cetapon Junior Paediatric Syrup with salicylates increases the risk of adverse renal effects.

Warfarin and Anticoagulants- concurrent, chronic, high-dose administration of Cetapon Junior Paediatric 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 paracetamol has been reported in patients receiving isoniazid, alone or with other medicines for tuberculosis.

Flucloxacillin: Caution is advised when paracetamol is administered concomitantly with flucloxacillin due to the increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with a risk factor for glutathione deficiency such as severe renal impairment, sepsis, malnutrition and chronic alcoholism. Close monitoring is recommended in order to detect the appearance of acid base disorders, namely HAGMA, including the search of urinary 5-oxoproline.

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 breastfeeding:

Safety and efficacy in pregnancy and breastfeeding have not been established. No data available on fertility.

4.7 Effects on ability to drive and use machines:

Cetapon Junior Paediatric 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	**Undesirable effect**		
	Frequent	**Less frequent**	**Frequency not known**

Blood and lymphatic system disorders:		Agranulocytosis, thrombocytopenia, leucopoenia, pancytopenia, neutropenia, anaemia.	
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.	Nausea and vomiting
Hepatobiliary disorders:		Hepatitis	
Skin and subcutaneous tissue disorders:		Dermatitis, skin rash and other allergic reactions such as toxic epidermal necrolysis (TEN), Stevens-Johnson 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) (see section 4.4). The rash is usually erythematous or urticarial but sometimes more serious and accompanied by fever and mucosal lesion. More mild rashes and other hypersensitivity reactions also occur occasionally.	
Renal and urinary disorders: Less frequent		Renal colic, renal failure and sterile pyuria	Nephropathy
Investigations			Increased transaminases. Low level transaminase elevations may occur in some patients taking therapeutic doses of paracetamol, as in Cetapon Junior Paediatric Syrup. These elevations are not accompanied with liver failure and usually resolve with continued therapy or discontinuation of

			paracetamol, as in Cetapon Junior Paediatric Syrup.

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 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 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 drugs that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of overdose: 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 of 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. The nomogram should be used only in relation to a single acute ingestion.

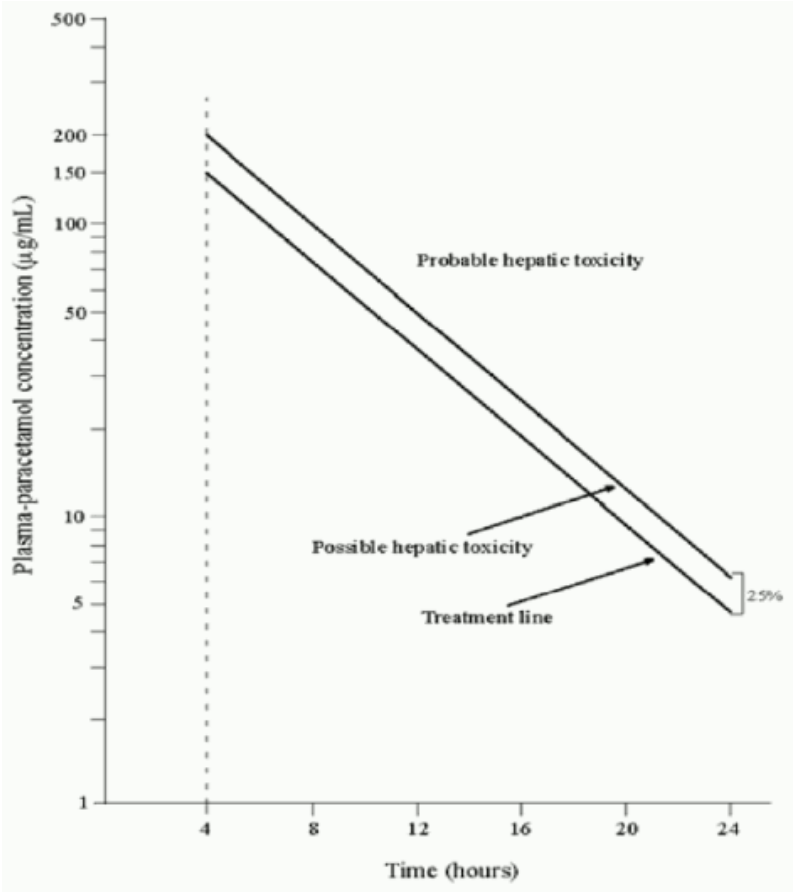


Figure 1. A semi-logarithmic plot of plasma-paracetamol concentration against hours after ingestion. (*Reference: Martindale – 37th Edition*).

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 96 hours.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Paracetamol has analgesic and antipyretic actions.

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerin, propylene glycol, polyethylene glycol, povidone, sodium benzoate, sodium saccharin, quinoline yellow, sunset yellow, brilliant blue, peppermint flavour and purified water.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store in a cool place at or below 25^0C. Protect from light.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

In amber bottles of 50 ml and 100 ml.

6.6 Special precautions for disposal and other handling

Not applicable.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Resmed Healthcare,

71 Rochdale Road, Springfield Park, Durban, 4051.

8. REGISTRATION NUMBERS

Q/2.7/96

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20/09/1982

10. DATE OF REVISION OF THE TEXT