PROFESSIONAL INFORMATION

SCHEDULING STATUS: S2

1. NAME OF THE MEDICINE

BETAPYN TABLETS

Strength

Codeine phosphate	10 mg
Doxylamine succinate	5 mg
Paracetamol	450 mg
Caffeine anhydrous	50 mg

Pharmaceutical form

Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each BETAPYN tablet contains:

Codeine phosphate	10 mg
Doxylamine succinate	5 mg
Paracetamol	450 mg
Caffeine anhydrous	50 mg

Sugar free

For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Tablets

Round, yellow, flat tablets, bisected on one side of 12,7 mm and embossed with “BETAPYN” on reverse side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic treatment of mild to moderate pain and/or fever.

4.2 Posology and method of administration

Posology

Adults and children over 12 years:

1 or 2 tablets taken orally, repeated 4-hourly if necessary. Do not exceed 8 tablets per day.

DO NOT EXCEED THE RECOMMENDED DOSE.

4.3. Contraindications:

- Sensitivity to paracetamol or any of the components.
- Severe liver function impairment.
- Caffeine should be given with care to patients with peptic ulceration.
- Safety of BETAPYN during pregnancy and lactation has not been established.

- BETAPYN is contraindicated in respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion.
- It is also contraindicated in the presence of acute alcoholism, head injuries, and conditions in which intracranial pressure is raised.
- It should not be given during an attack of bronchial asthma or in heart failure secondary to chronic lung disease.

4.4 Special warnings and precautions for use

This product 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.

Patients suffering from liver or kidney disease should take paracetamol under medical supervision.

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

Codeine should be given with caution to patients with hypothyroidism, adrenocortical insufficiency, impaired liver function, prostatic hypertrophy or shock. It should be used with caution in patients with inflammatory or obstructive bowel disorders. The dosage should be reduced in elderly and debilitated patients. Should be used with caution in patients with myasthenia gravis. The prolonged use of high doses of codeine has produced dependence of the morphine type.

Exceeding the prescribed dose, together with prolonged and continuous use of this medication, may lead to dependency and addiction.

This medicine contains **Doxylamine succinate**, and may lead to drowsiness and impaired concentration, which may be aggravated by simultaneous intake of alcohol or other central nervous system depressant agents. Doxylamine succinate, and should be used with care in patients with glaucoma and prostatic hypertrophy. Patients should be advised, particularly at

the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents. (See Interaction with other medicines and other forms of interactions).

Do not administer to children under 12 years of age.

4.5 Interaction with other medicines and other forms of interactions

This medicine may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants **(see Special warnings and precautions for use).**

Doxylamine may decrease emetic response to apomorphine.

The effects of atropine and tricyclic antidepressants may be enhanced.

4.6 Fertility, pregnancy and lactation

Safety of BETAPYN during fertility, pregnancy and lactation has not been established.

4.7 Effects on ability to drive and use machines

This medicine may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants. Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

4.8 Undesirable effects

Frequency	System organ class	Undesirable effects
Frequent	Nervous system disorders	Insomnia, drowsiness, confusion, sedation, deep sleep, inability to concentrate, lassitude, incoordination, dizziness, headache, dry mouth, nervousness, tremors, convulsions.
	Vascular disorders	Headache, facial flushing, vertigo, orthostatic hypotension, hypotension**.**
Frequency Unknown	Blood and the lymphatic system disorders	Neutropenia, pancytopenia and leucopoenia, agranulocytosis, anaemia, thrombocytopenia, haemolytic anaemia.
	Cardiac disorders	Tachycardia, extrasystoles, bradycardia, palpitation.
	Ear and labyrinth disorders	Tinnitus, vertigo.
	Eye disorders	Scintillating scotoma, miosis.
	Gastrointestinal disorders	Increases in gastric secretions and gastric ulceration, nausea, vomiting, constipation, dry mouth, gastrointestinal disturbances, diarrhoea.
	General disorders and administration site conditions	Hypothermia.
	Hepato-biliary disorders	Hepatitis, biliary spasm.
	Immune system disorders	Allergy, anaphylaxis.

	Musculoskeletal, connective tissue and bone disorders	Muscle tremor, muscular weakness.
	Psychiatric disorders	Irritability, anxiety, neurosis, restlessness, excitement, mood changes, raised intracranial pressure.
	Renal and urinary disorders	Renal colic, renal failure, sterile pyuria, difficulty in micturition, ureteric spasm.
	Skin and subcutaneous tissue disorders	Urticaria, pruritus and sweating. Skin rashes and other allergic reactions may occur. The rash is usually erythematous or urticarial but sometimes more serious and may be accompanied by fever and mucosal lesions.

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. 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.

One may also report to Adcock Ingram Limited using the following email:

Adcock.AEReports@adcock.com

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 -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 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.

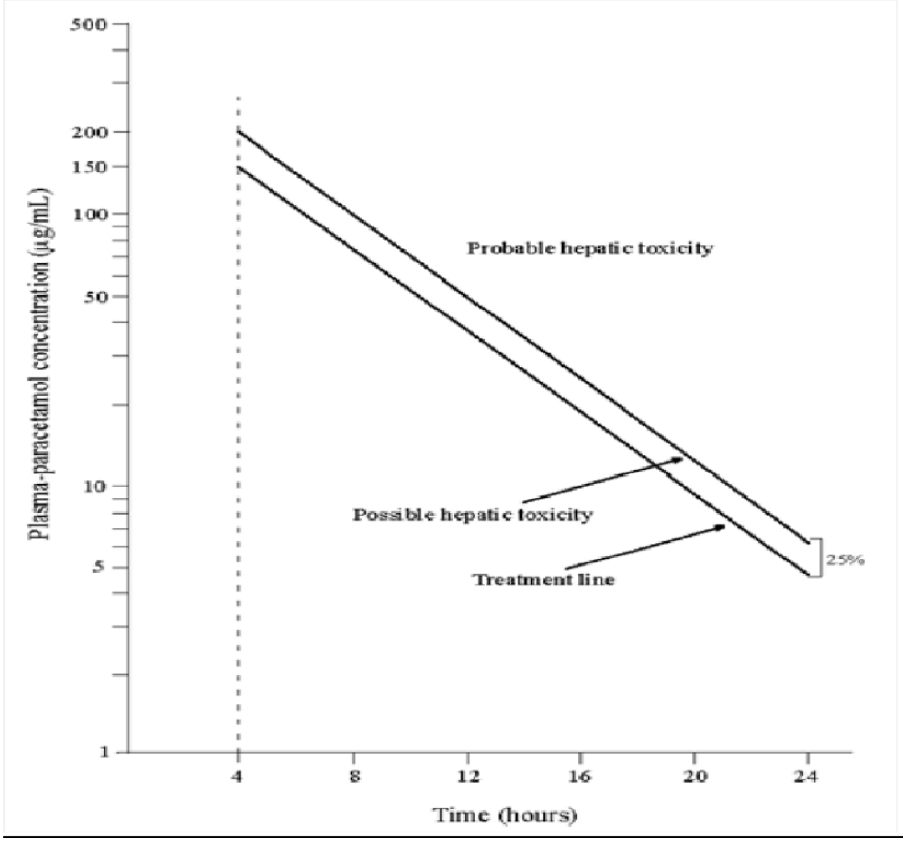
Treatment for paracetamol overdosage:

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 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.

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.



(Reference: Martindale 37th Edition)

Codeine phosphate: Symptoms of overdosage with codeine include excitement and in children, convulsions may occur. Treatment is symptomatic and supportive.

Doxylamine succinate: The most common symptom of overdosage is impaired consciousness and additionally psychotic behaviour.

Caffeine: Overdose may cause diuresis, tachycardia, irritability, nervousness, restlessness, gastrointestinal disturbances and CNS stimulation such as agitation, excitement, insomnia and tremors. The management of caffeine toxicity is generally symptomatic and supportive (e.g., hydration). For acute ingestion gastric lavage is advised.

5. PHARMACEUTICAL PROPERTIES

5.1 Pharmacodynamic properties

A 2.8 Analgesic combinations

Mechanism of action

BETAPYN tablets combine the analgesic and antipyretic action of paracetamol with the analgesic action of codeine phosphate. Doxylamine succinate has sedative and antihistaminic properties and in combination with the above analgesics is of value, especially in tension states.

NOTE: BETAPYN tablets may be used to advantage by people who cannot tolerate aspirin e.g., aspirin sensitivity, peptic ulcer patients, acute and chronic gastritis, and patients on steroid therapy.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colour yellow 14037, hydrogenated cottonseed oil, magnesium stearate, microcrystalline cellulose, nipastat/salistat (total parabens) 0,124 % m/m, pregelatinized starch, starch maize, sodium starch glycollate.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 30 °C in a cool, dry place.

Do not remove the blister pack from the outer carton until required for use.

Store in a safe place, out of reach of children.

6.5 Nature and contents of container

PVC/Aluminium foil blister packs of 18, 20 and 40 tablets.

All pack sizes may not be marketed simultaneously.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand,1685

Date of approval: 30 November 2021

Customer Care: 0860 ADCOCK/232625

8. REGISTRATION NUMBER:

BETAPYN: F/2.8/7

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of Registration: 6 May 1974

10. DATE OF REVISION OF THE TEXT:

Date of the latest approved PI: 30 November 2021

Namibia NS1 90/2.8/00101
Botswana S1D BOT1803273
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