1.3.1.1 Professional Information for Medicines for Human Use

SCHEDULING STATUS

S5

1. NAME OF MEDICINE

HOPYN Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each tablet contains:

Paracetamol	320 mg
Codeine Phosphate	8 mg
Caffeine Anhydrous	32 mg
Meprobamate	150 mg

Preservative:

Nipastat	0,025 % m/m

Sugar free

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

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Category A 2.8 Analgesic Combinations. Uncoated tablets.

Green, round, flat tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PHARMACOLOGICAL ACTION:

HOPYN tablets has analgesic and skeletal muscle relaxing properties.

HOPYN is indicated to relieve mild to moderate pain and fever, and pain associated with tension.

4.2 Posology and method of administration

Posology

DO NOT EXCEED THE RECOMMENDED DOSE. Adult dosage: Two tablets three or four times a day as required.

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

Special Populations

No information available.

Paediatric population:

No information available.

Method of administration: Oral intake

4.3 Contraindications:

Hypersensitivity to any of the excipients of **HOPYN** tablets (see section 2 and section 6.1). **HOPYN** should not be administrated to patients with acute intermittent porphyria or a history of epilepsy. **HOPYN** is contraindicated in respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion, after operations on the biliary tract, acute alcoholism, head injuries and conditions where intracranial pressure is raised as well as in patients with renal or hepatic insufficiency. Use of **HOPYN** during pregnancy should be avoided. **HOPYN** should not be used for patients with heart failure secondary to chronic lung disease, a history of cardiac disease, , patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.

4.4 Special Warnings and Precautions for use:

HOPYN tablets are not recommended for use by pregnant or breastfeeding women (see section 4.6).

If the patient does not respond to this medication, a doctor should be consulted.

The use of this medicine leads to drowsiness which is aggravated by the simultaneous intake of alcohol and it is dangerous to drive a

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vehicle or be in charge of machinery while on treatment with this product.

Do not use continuously for more than 10 days without consulting your doctor.

Paracetamol

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.

Paracetamol dosages in excess of those recommended may cause severe liver damage.

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

Codeine

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

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.

The depressant effects of codeine are enhanced by depressants of the central nervous system such as alcohol, anaesthetics, hypnotics, sedatives, and phenothiazines. The prolonged use of high doses of codeine has produced dependence of the morphine type.

Caffeine

Caffeine should be given with care to patients with a history of peptic ulceration.

Meprobamate

Patients receiving meprobamate should be warned that their tolerance to ingested alcohol and other depressants of the central nervous system may be lowered with consequent impairment of judgement and co-ordination. Symptoms of porphyria may be exacerbated (see section 4.3).

Prolonged use of meprobamate may lead to the development of dependence of the barbiturate alcohol type. Meprobamate may induce the hepatic microsomal enzymes involved in drug metabolism.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute generalized

exanthematous pustulosis (AGEP), eosinophilia and systemic (DRESS)/Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicines. If a patient develops SCAR, treatment with **HOPYN** must immediately be discontinued and appropriate treatment instituted.

4.5 Interactions with other medicines and other forms of interaction

No information available.

Paediatric population

No information available.

4.6 Fertility, pregnancy and lactation

Pregnancy

HOPYN TABLETS is not recommended for use by pregnant women.

Breastfeeding

HOPYN TABLETS is not recommended for use by breastfeeding women.

Fertility

No information available.

4.7 Effects on ability to drive and use machines

The use of this medicine may cause drowsiness and care should be taken when driving or operating machinery. Reduce dosage if necessary.

4.8 Undesirable Effects:

Sensitivity reactions resulting in reversible skin rash or blood disorders may occur.

a. Summary of the safety profile

No information available

b. Tabulated summary of adverse reactions

Codeine	
System Organ Class	**Adverse reaction**
Psychiatric disorders	Changes of mood.
Nervous system disorders	Drowsiness, confusion, vertigo, restlessness, orthostatic hypotension and raised intracranial pressure may occur.
	hypotension and raised intracranial pressure may occur.
Eye disorders	Miosis.
Cardiac disorders	Bradycardia, palpitations.
Gastrointestinal disorders	Codeine may cause nausea, vomiting, constipation and dry mouth.

Skin and subcutaneous tissue disorders	Sweating and facial flushing. Reactions such as urticaria and pruritus may occur
Renal and urinary disorders	Renal and urinary disorders Micturition may be difficult and there may be ureteric or biliary spasm.
General disorders and administration site conditions	Hypothermia.
Caffeine	
SYSTEM ORGAN CLASS	**ADVERSE REACTIONS**
Nervous system disorders	Nervous system disorders Caffeine may cause restlessness, excitement, muscle tremor.
Eye disorders	Eye disorders Scintillating scotoma.
Ear and labyrinth disorders	Tinnitus.
Cardiac disorders	Tachycardia and extrasystoles.
Gastrointestinal disorders	Caffeine increases gastric secretions and may cause gastric ulceration.
Meprobamate	
SYSTEM ORGAN CLASS	**ADVERSE REACTIONS**
Blood and lymphatic system disorders	Blood disorders including agranulocytosis, eosinophilia,

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	leukopenia, thrombocytopenia, and aplastic anaemia have been reported.
Nervous system disorders	The most frequent side effect of meprobamate is drowsiness. Paraesthesia, weakness, headache, excitement, dizziness, ataxia.
Eye disorders	Disturbances of vision.
Cardiac disorders	Hypotension, tachycardia and cardiac arrhythmias may occur.
Gastrointestinal disorders	Nausea, vomiting, diarrhoea.
Skin and subcutaneous tissue disorders	Hypersensitivity reactions may occur. They may be limited to skin rashes, urticaria and purpura or may be more severe with angioneurotic oedema, bronchospasm, or anuria. Erythema multiforme has been reported as well as Fixed drug eruptions (FDE), Drug-induced hypersensitivity syndrome (DIHS).

c. 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. See section 4.4

d. Paediatric population

No information available.

e . Other special population(s)

No information available.

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

In the event of overdosage consult a doctor or take the patient to the nearest hospital immediately. Specialised treatment is essential as soon as possible. The latest information regarding the treatment of overdosage can be obtained from the nearest poison centre.
Symptoms of overdosage include nausea and vomiting. Liver damage, which may be fatal, may only appear after a few days.

Kidney failure has been described following acute intoxication.

Acute meprobamate overdosage can produce stupor, coma, convulsions, shock, circulatory and respiratory collapse. Because meprobamate is rapidly absorbed from the gastrointestinal tract, gastric lavage must be carried out shortly after ingestion and must be thorough.

In paracetamol overdose prompt treatment is essential.

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 to 10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of medicine 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.

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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 sever 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 to 10 g 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.

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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 (IV)** 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.

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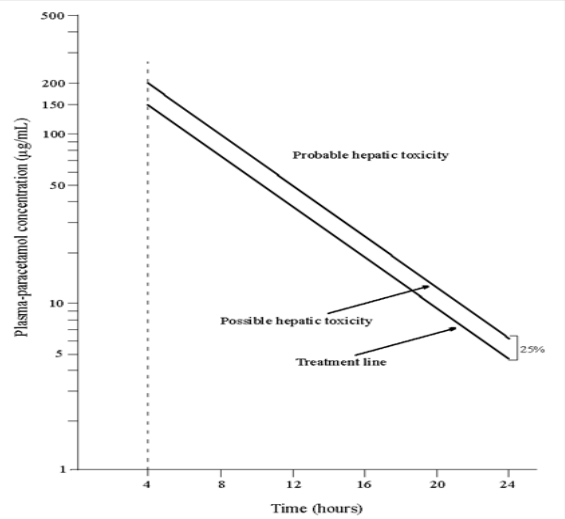
A semi-logarithmic plot of plasma-paracetamol concentration against hours after ingestion.

Reference: Martindale, The Complete Drug Reference.



Those whose plasma paracetamol levels are above the “normal treatment line”, should continue Nacetylcysteine 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.

For overdose with an extended/modified release preparation the value of the nomogram is unknown. As there is no information on the plasma

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levels of paracetamol after an overdose of extended/modified release paracetamol preparations, all patients with suspected or known overdose with such preparations should receive N-acetylcysteine.
Because of lack of data for extended/modified release formulations, a level below the “treatment line” of the nomogram may not exclude the possibility of toxicity.
Monitor all patients with significant ingestions for at least ninety-six hours.

5. PHARMACOLOGICAL PROPERTIES

Category and class: A 2.8 Analgesic combinations.

HOPYN tablets have analgesic, antipyretic and tranquilising properties.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Apple green colourant, colloidal silicone dioxide, magnesium stearate, nipastat, povidone, powdered acacia, purified talc and starch maize.

6.2 Incompatibilities

No data available.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

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Store in a dry place below 25°C. Protect from light.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

Packaged in blister packs of 10 in container pack sizes of 20's and 100's.

White HDPE jar with white HDPE screw caps (not lined)in pack sizes of 500's and 1000's. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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:

A28/2.8/0422

9. DATE OF FIRST AUTHORISATION

13/08/1994

10. DATE OF REVISION OF TEXT

22 January 2024

Reference 1: STOPAYNE tablets packaging insert, Adcock Ingram (Pty) Ltd, approved 05 June 2021 on the SAHPRA repository

Reference 2: SAHPRA clinical letter regarding Paracetamol containing medicines- Risk of Fixed Drug Eruptions (FDE) and Drug-induced Hypersensitivity Syndrome (DIHS) dated 22 April 2023