PROFESSIONAL INFORMATION

SCHEDULING STATUS: **S3**

1. PROPRIETARY NAME OF THE MEDICINE

ADCO-NAPACOD TABLETS

Strength

Codeine Phosphate 10 mg

Paracetamol 500 mg

Pharmaceutical form

Tablets

Pink, flat, round, bevelled edge, bisected tablets measuring ½" (12,7 mm) in diameter.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Adco-Napacod tablet contains:

Codeine phosphate	10 mg
Paracetamol	500 mg

Preservative:

Nipastat/Salistat (total parabens)	0,185 % m/m

Sugar free

Date of approval: 09 January 2023

Sewela Ann Ramaphakela

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Date: 2023.01.26 11:36:49 +02'00'

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet

Pink, flat, round, bevelled edge, bisected tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

For the relief of mild to moderate pain and fever.

4.2 Posology and method of administration

Posology

Adults: 1 to 2 tablets, repeated 6 hourly if necessary.

Paediatric population

Children 7 to 12 years: ½ to 1 tablet, repeated 6 hourly if necessary.

Children under 6 years: Not recommended.

DO NOT EXCEED THE RECOMMENDED DOSE. DO NOT USE CONTINUOUSLY FOR LONGER THAN 10 DAYS WITHOUT CONSULTING YOUR DOCTOR.

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4.3 CONTRAINDICATIONS

- Hypersensitivity to any of the active ingredients.
- 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 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.
- Patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.

4.4 Special warnings and precautions of use

This product contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdose a doctor, hospital or Poison Centre must be contacted immediately.

- Dosages of paracetamol in excess of those recommended may cause severe liver damage.
- Consult your doctor if no relief is obtained with the recommended dosage.
- Do not use continuously for longer than ten days without consulting your doctor (See Posology).
- Store in a safe place, out of reach of children.

- Patients suffering from liver or kidney disease should take paracetamol under medical supervision.
- May delay the absorption of other medicines administered concomitantly.
- 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 and sedatives, and phenothiazines.
- Exceeding the prescribed dose, together with prolonged and continues use of this medicine, may lead to dependence and addiction.

Paediatric population

Not recommended for children under 6 years “See Posology”.

4.5 Interaction with other medicines and other forms of interaction

May delay the absorption of other medicines administered concomitantly.

Paracetamol:

Hepatotoxic medicines - increased risk of hepatotoxicity.

Enzyme inducing medicines - increased risk of hepatotoxicity. Possible decrease in therapeutic effects of ADCO-NAPACOD.

Metoclopramide and domperidone - absorption of ADCO-NAPACOD may be accelerated.

Cholestyramine - absorption of ADCO-NAPACOD is reduced if given within one hour of cholestyramine.

Prolonged concurrent use of ADCO-NAPACOD with salicylates increases the risk of adverse renal effects.

Codeine:

Central nervous system depressants -The depressant effects of codeine are enhanced by depressants of the central nervous system such as alcohol, anaesthetics, hypnotics and sedatives, and phenothiazines (see **Special warnings and precautions for use**).

4.6 Fertility, pregnancy and lactation

Safety and/or efficacy has not been established.

4.7 Effects on ability to drive and use machines

Codeine has depressant effects which may be enhanced by nervous system depressants such as central nervous system depressants such as alcohol, anaesthetics, hypnotics and sedatives, and phenothiazines.

ADCO-NAPACOD May cause drowsiness and confusion **(See undesirable effects codeine).** Patients should be warned against activities requiring mental alertness, judgment and/or sound coordination and vision.

4.8 Undesirable effects:

System Organ classification	**Frequency**	**Side effects**
Blood and lymphatic system disorders	Less frequent	• Agranulocytosis, • Thrombocytopenia, • Leukopenia**,** • Pancytopenia, • Neutropenia, • Anaemia.
Metabolism and nutrition disorders	Frequency unknown	• Pyroglutamic aciduria (5-oxoprolinuria), • high-anion gap metabolic acidosis, • Dry mouth.

Psychiatric disorders	Frequent	• Drowsiness, • Confusion, • Restlessness.
	Frequency Unknown	• Euphoria.
Cardiac disorders	Frequency unknown	• Bradycardia, • Palpitations.
Renal and urinary disorders	Less frequent	• Renal colic**,** • Renal failure**,** • Sterile pyuria**.**
	Frequency unknown	• Nephropathy**,** • Micturition**.**
Hepatobiliary disorders	Less frequent	• Hepatitis**.**
Gastrointestinal disorders	Less frequent	• Pancreatitis.
	Frequency unknown.	• nausea, • vomiting, • constipation, • Ureteric or biliary spasm.

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Skin and subcutaneous disorders	Less frequent	• skin rash, • Dermatitis**.**
	Frequency unknown	• Urticaria, • Pruritus.
Nervous system disorders	Frequency unknown	• Sweating, • Facial flushing, • Vertigo, • Hypothermia, • Change of mood, • Raised intracranial pressure.
Eye disorders	Frequency unknown	• Miosis.
General disorders and administrative site conditions.	Frequency unknown	Hypersensitivity reactions characterised by dyspnoea and orthostatic hypotension.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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:

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https://www.sahpra.org.za/Publications/Index/8.

May also report to Adcock Ingram Limited using the following email:

Adcock.AEReports@adcock.com

4.9 Overdose

Paracetamol overdosage symptoms 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.

Codeine phosphate overdosage symptoms include narcosis followed sometimes by a feeling of exhilaration and then convulsions, nausea and vomiting. Contracted pupils. Increased pulse. Respiratory depression.

Prompt Treatment is essential. In the event of overdosage, consult a doctor immediately, or take the person directly 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.

Date of approval: 09 January 2023

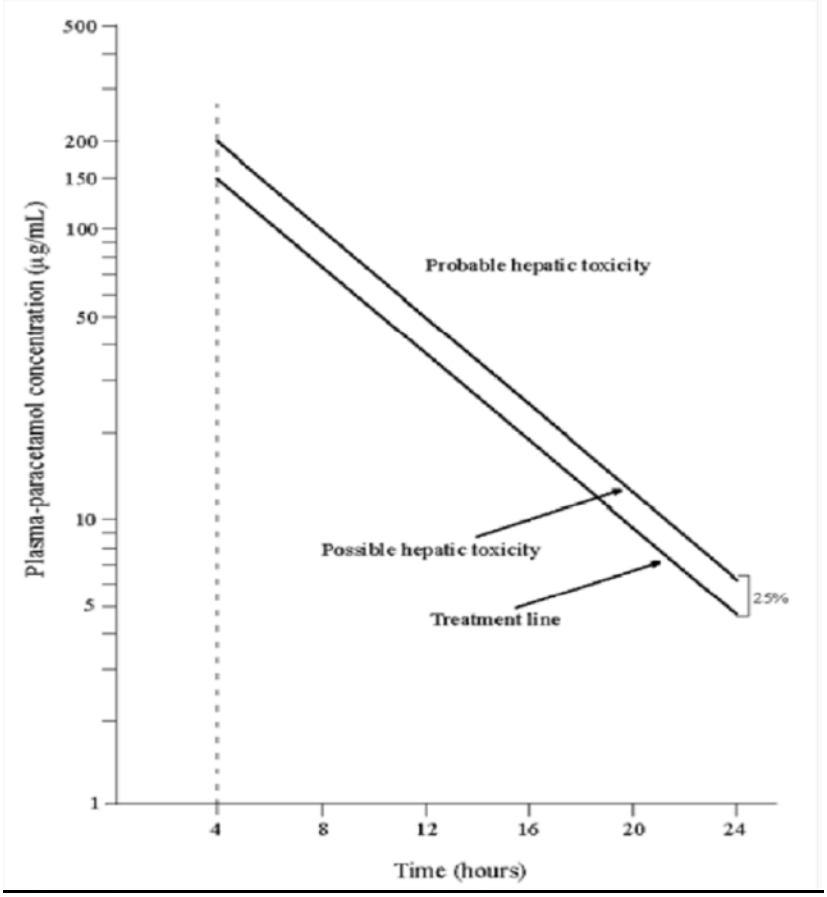

Figure 1. A semi-logarithmic plot of plasma-paracetamol concentration against hours after ingestion.

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.

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

The latest information regarding the treatment of overdosage can be obtained from the nearest poison center.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A: 2.8 Central nervous system depressants. Combination analgesics.

Mechanism of action:

Analgesic and antipyretic.

5.2 Pharmacokinetics

Paracetamol

Absorption:

Following oral administration, paracetamol is well absorbed, with peak plasma concentrations obtained after 0, 5 to 1 hour.

Distribution:

Once absorbed, the plasma half-life is about 2 hours.

Plasma protein binding is variable.

Metabolism:

Paracetamol is metabolised in the liver primarily by conjugation with glucuronic acid (about 60 %), sulphuric acid (about 35 %) and cysteine (about 3 %).

Excretion:

Paracetamol is renally excreted primarily as conjugated metabolites.

Codeine

Once absorbed, codeine is metabolized by the liver. Codeine's metabolites are excreted chiefly as inactive forms in the urine. A small fraction, approximately 10% of administered codeine is *O*-demethylated to morphine, and free and conjugated morphine can be found in the urine after therapeutic doses of codeine. The half-life of codeine in plasma is 2-4 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gelatin (200 – 220 gm), raspberry red powder IH 7804, maize starch, magnesium stearate.

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6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 Years

6.4 Special precautions for storage

Store in airtight containers at or below 25 °C. Protect from light.

6.5 Nature and contents of container:

Packs of 100 and 500 not currently marketed.

Packs of 1 000 and 5 000.

Not all pack sizes are marketed.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road

Erand Gardens

Date of approval: 09 January 2023

Midrand, 1685

0860ADCOCK (232625)

8. REGISTRATION NUMBER:

B/2.8/1401

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION:

15 November 1969

10. DATE OF REVISION OF THE TEXT

09 January 2023

Date of approval: 09 January 2023