1.3.1.1 Clean amended professional information for

MYPRODOL CAPSULES

SCHEDULING STATUS:

S3

1. NAME OF THE MEDICINE

MYPRODOL CAPSULES, 10 mg/200 mg/250 mg, capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains

Codeine phosphate 10 mg

Ibuprofen 200 mg

Paracetamol 250 mg

Sugar free

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsules.

Hard gelatin capsule of size ‘0. The cap is opaque green and the body is opaque red. "RIO" is printed in black on both the cap and body. Contents of the capsule are fine white granular powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MYPRODOL CAPSULES are indicated for the relief of mild to moderate pain of inflammatory origin with or without fever.

4.2 Posology and method of administration

Posology

"DO NOT EXCEED THE RECOMMENDED DOSE."

Adults

One to two capsules four hourly and not more than twelve capsules per twenty-four hours. Consult your doctor if no relief is obtained with the recommended dosage.

Use the lowest effective dose for the shortest possible duration of treatment.

Method of administration

MYPRODOL CAPSULES is administered orally. The capsules must be swallowed with water and not chewed.

Paediatric population

Not recommended for children under twelve years of age.

4.3 Contraindications

- Heart failure,
- Impaired hepatic and renal function,
- Peptic ulceration,
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including MYPRODOL CAPSULES,
- Cardiovascular disease,
- 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,
- Contraindicated in patients taking monoamine oxidase inhibitors or within fourteen days of stopping such treatment,
- Caution is advised in those patients who are receiving coumarin anticoagulants,
- Patients who are sensitive to aspirin should not be given MYPRODOL CAPSULES,
- Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/ foetal renal dysfunction and premature closure of the foetal ductus arteriosus.

4.4 Special warnings and precautions for use

The safety of continuous administration of MYPRODOL CAPSULES has not been established for a period greater than four weeks.

Codeine phosphate:

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

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.

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

Ibuprofen:

- Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with MYPRODOL CAPSULE therapy,
- In view of MYPRODOL CAPSULE's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients,
- Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs including MYPRODOL CAPSULES, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal,
- The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of MYPRODOL CAPSULES, in patients with a history of ulcers, and the elderly,
- When gastrointestinal bleeding or ulceration occurs in patients receiving MYPRODOL CAPSULES treatment with MYPRODOL CAPSULES should be stopped,

- MYPRODOL CAPSULES should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated,
- Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. MYPRODOL CAPSULES should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
- Foetal Toxicity: Limit use of NSAIDs, including MYPRODOL CAPSULES, between 20 and 30 weeks of pregnancy due to the risk of oligohydramnios/foetal renal dysfunction. Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus.
- If NSAID treatment is necessary between 20 weeks and 30 weeks gestation, limit MYPRODOL CAPSULES use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if MYPRODOL CAPSULES treatment extends beyond 48 hours. Discontinue MYPRODOL CAPSULES if oligohydramnios occurs and follow up according to clinical practice.

4.5 Interactions with other medicines and other forms of interaction

- NSAID: Use of two or more NSAIDs concomitantly could result in an increase in side effects.
- Corticosteroids: increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs)
- Anti-coagulants: MYPRODOL CAPSULES may enhance the effects of anti-coagulants such as warfarin

- Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding.

4.6 Fertility, pregnancy and lactation

MYPRODOL CAPSULES are not recommended for use by pregnant or breastfeeding women.

Regular use of non-steroidal anti-inflammatory drugs during the third trimester of pregnancy, may result in persistent pulmonary hypertension of the new-born.
Use of NSAIDs, including MYPRODOL CAPSULES, can cause premature closure of the foetal ductus arteriosus and foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, the use of MYPRODOL CAPSULES dose and duration between 20 and 30 weeks of gestation should be limited and avoided at around 30 weeks of gestation and later in pregnancy (see sections 4.3 and 4.4).
The onset of labour may be delayed and its duration increased.

Fertility

No data on male and female fertility are available

4.7 Effects on ability to drive and use machines

Patients should be advised not to drive or operate machinery if affected by dizziness or sedation. This medicine can impair cognitive function and can affect a patient's ability to drive safely. Patients should

be advised that they do not engage in the above activities until they are aware of the measure to which MYPRODOL CAPSULES affects them.

4.8 Undesirable effects

a. Summary of the safety profile

In view of the product's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

The most commonly observed adverse events are gastro-intestinal in nature.

b. Tabulated summary of adverse reactions

Ibuprofen:

SYSTEM ORGAN CLASS	**ADVERSE REACTIONS**
Blood and lymphatic system disorders	Agranulocytosis and thrombocytopenia.
Immune system disorders	Hypersensitivity reactions.
Psychiatric disorders	Depression.
Nervous system disorders	Drowsiness, nervousness, insomnia.
Eye disorders	Blurred vision and other ocular reactions.
Ear and labyrinth disorders	Dizziness, tinnitus.
Cardiac disorders	Oedema, hypertension and cardiac failure.
Gastrointestinal disorders	Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal.

	Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis.
Hepato-biliary disorders	Abnormalities of liver function tests.
Skin and subcutaneous tissue disorders	Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, skin rash, pruritus.
Renal and urinary disorders	Impairment of renal function.

Paracetamol:

SYSTEM ORGAN CLASS	**ADVERSE REACTIONS**
Blood and the lymphatic system disorders	Blood disorders may occur, haematological reactions have been reported.
Skin and subcutaneous tissue disorders	Sensitivity reactions resulting in reversible skin rash.

Codeine phosphate:

SYSTEM ORGAN CLASS	**ADVERSE REACTIONS**
Psychiatric disorders	Confusion, restlessness, changes of mood.
Nervous system disorders	Drowsiness.
Eye disorders	Miosis.
Ear and labyrinth disorders	Vertigo.

Cardiac disorders	Bradycardia, palpitations.
Vascular disorders	Hypothermia, raised intracranial pressure, orthostatic hypotension, facial flushing.
Gastrointestinal disorders	Nausea, vomiting, constipation, dry mouth.
Hepato-biliary disorders	Biliary spasm.
Skin and subcutaneous tissue disorders	Sweating, urticaria, pruritus
Renal and urinary disorders	Micturition may be difficult and there may be ureteric spasm.

c. Description of selected adverse reactions

Ibuprofen

Acute reversible renal failure has been reported. Ibuprofen should be used with care in patients with impaired renal function.

Codeine phosphate

Codeine phosphate 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 depressant effects of codeine are enhanced by depressants of the central nervous system such as alcohol, anaesthetics, hypnotics and sedatives, and phenothiazines.

The prolonged use of high doses of codeine has produced dependence of the morphine type.

d. Paediatric population

MYPRODOL CAPSULES are not recommended for use for children under twelve years of age (see section 4.2).

e. Other special populations

The dosage should be reduced in elderly and debilitated patients.

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 provders 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

Paracetamol

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 medicines 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.

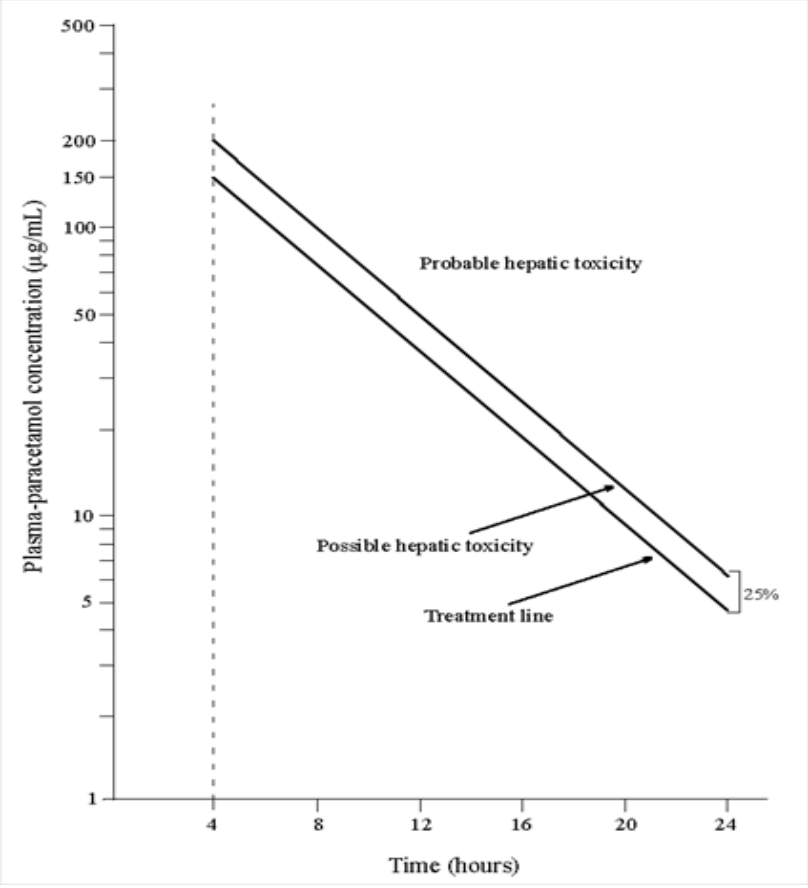
N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken. An initial dose of 150 mg/kg 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.

A semi-logarithmic plot of plasma-paracetamol concentration against hours after ingestion. (Reference: Martindale).



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.

Ibuprofen

The most likely symptoms of overdosage are epigastric pain and nausea.

Codeine phosphate

Symptoms of overdosage include excitement and, in children, convulsions may occur. Large doses produce respiratory depression.

Treatment of overdosage is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

Category and class: A: 2.8 Analgesic combinations

MYPRODOL CAPSULES have an analgesic, anti-inflammatory and antipyretic action.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule fill

Colloidal silica

Magnesium stearate

Maize starch

Potassium sorbate.

Gelatine capsule shell

Opaque Green Cap

Opaque Red Body

Printing ink

Capsule shell colourants:

Brilliant blue FCF, E 133

Erythrosine, E 127

Quinoline yellow, E 104

Sunset yellow, E 110

Titanium dioxide, E 171

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 ºC in well-closed containers.

6.5 Nature and contents of container

- A white high density polypropylene (HDPP) securitainer with a low density polyethylene (LDPE) snap on lid or a white high density polyethylene container with a high density polyethylene (HDPE) screw cap containing 30 capsules.
- Push through clear PVC and aluminium blister packs of 10 capsules in unit cartons of 10, 30, 60 or 100 capsules.

Not all pack sizes may be marketed.

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:

T/2.8/244

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

7 May 1987

10. DATE OF REVISION OF THE TEXT

To be allocated on approval.

Botswana (S3): B9300580 Namibia (NS2): 90/2.8/00146

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