SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

MYPRODOL® SUSPENSION, 10 mg/200 mg/250 mg, suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 ml contains codeine phosphate 10 mg, ibuprofen 200 mg and paracetamol 250 mg.

Excipient(s) with known effect:

Preservative (sodium benzoate): 0,1 % *m/v*

Sugar free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension.

An opaque pink suspension with a blackcurrant taste and odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MYPRODOL® SUSPENSION is 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

Two to four medicine measures (10 to 20 ml) four hourly and not more than twenty-four medicine measures in twenty-four hours.

Paediatric population

3 to 5 years…….2,5 to 5 ml three to four times daily

6 to 12 years……...5 to 10 ml three to four times daily

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

Consult your doctor if no relief is obtained with the recommended dosage.

Method of administration

For oral administration. Shake the bottle before use.

4.3 Contraindications

- Impaired hepatic and renal function.
- Cardiovascular disease.
- Heart failure.
- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including MYPRODOL® SUSPENSION.

- Active or history of recurrent ulcer/haemorrhage/perforations.
- 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® SUSPENSION.
- 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 (see sections 4.4 and 4.6).
- MYPRODOL® SUSPENSION is contraindicated for the use in new-born babies as it contains sodium benzoate (see section 4.4) and may increase jaundice.

4.4 Special warnings and precautions for use

MYPRODOL® SUSPENSION is not recommended for use by pregnant or breastfeeding women (see section 4.6).

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

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

- Ibuprofen should be used with care in patients with impaired renal function.
- 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® SUSPENSION therapy. In view of ibuprofen's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.
- Caution is required in patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) and should only be treated with diclofenac after careful consideration.
- Elderly: The elderly has an increased frequency of adverse reactions to NSAIDs including ibuprofen in MYPRODOL® SUSPENSION, 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® SUSPENSION, in patients with a history of ulcers, and the elderly.
- When gastrointestinal bleeding or ulceration occurs in patients receiving MYPRODOL® SUSPENSION, treatment with MYPRODOL® SUSPENSION should be stopped.
- MYPRODOL® SUSPENSION should be given with caution to patients with a history of

gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastroesophageal 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 necrolyis have been reported. MYPRODOL® SUSPENSION should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
- Use of NSAIDs such as ibuprofen in MYPRODOL® SUSPENSION during the third trimester of pregnancy, may result in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased (see section 4.3 and 4.6).
- Foetal Toxicity: Limit use of NSAIDs, including MYPRODOL® SUSPENSION, between 20 to 30 weeks of pregnancy due to the risk of oligohydramnios/foetal renal dysfunction. Avoid use of NSAIDs in women around 20 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus (see sections 4.3 and 4.6).
- If NSAID treatment is necessary between 20 weeks and 30 weeks gestation, limit MYPRODOL® SUSPENSION use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if MYPRODOL® SUSPENSION treatment extends beyond 48 hours. Discontinue MYPRODOL® SUSPENSION if oligohydramnios occurs and follow up according to clinical practice (see sections 4.3 and 4.6).
- Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as MYPRODOL® SUSPENSION. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents

with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophillia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue MYPRODOL® SUSPENSION and evaluate the patient immediately.

Codeine phosphate

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

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

MYPRODOL® SUSPENSION contains sodium benzoate (excipient)

This medicine contains 10 mg sodium benzoate in each 10 ml which is equivalent 0,1 % *m/v*.

Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in newborn

babies (up to 4 weeks old) (see section 4.3).

MYPRODOL® SUSPENSION contains sodium

This medicinal product contains 26,88 mg sodium per 10 ml, equivalent to 1,344 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interactions with other medicines and other forms of interaction

- NSAIDs: 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® SUSPENSION 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

Pregnancy

MYPRODOL® SUSPENSION is not recommended for use by pregnant women (see section 4.4).

Use of non-steroidal anti-inflammatory medicines (such as ibuprofen) during the third trimester of pregnancy, may result in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased (see section 4.3).

Use of NSAIDs, including MYPRODOL® SUSPENSION, 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® SUSPENSION 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.

Breastfeeding

MYPRODOL® SUSPENSION is not recommended for use by breastfeeding women (see section 4.4).

Fertility

No data on male and female fertility is available.

4.7 Effects on ability to drive and use machines

MYPRODOL® SUSPENSION has moderate influence on the ability to drive and use machines, as it may cause dizziness, drowsiness and blurred vision.

It is not always possible to predict to what extent MYPRODOL® SUSPENSION may interfere with the daily activities of a patient.
Patients should ensure that they do not engage in the above activities until they are aware of the measure to which MYPRODOL® SUSPENSION affects them.

4.8 Undesirable effects

a. Summary of the safety profile

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal.

b. Tabulated summary of adverse reactions

Ibuprofen	
SYSTEM ORGAN CLASS	**ADVERSE REACTIONS**
Blood and lymphatic system disorders	Agranulocytosis and thrombocytopenia have occasionally been reported.
Immune system disorders	Hypersensitivity reactions.
Psychiatric disorders	Nervousness, depression and insomnia.
Nervous system disorders	Dizziness and drowsiness.
Eye disorders	Blurred vision and other ocular reactions.
Ear and labyrinth disorders	Tinnitus.
Cardiac disorders	Oedema, hypertension and cardiac failure.
Gastrointestinal disorders	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; pruritus; Drug Reaction with Eosinophillia and Systemic

	Symptoms (DRESS) (see section 4.4).
Renal and urinary disorders	Impairment of renal function. Acute reversible renal failure has been reported.
Paracetamol:	
SYSTEM ORGAN CLASS	**ADVERSE REACTIONS**
Blood and lymphatic system disorders:	Haematological reactions have been reported.
Immune system disorders:	Sensitivity reactions resulting in reversible skin rash or blood disorders may occur.
Codeine phosphate:	
SYSTEM ORGAN CLASS	**ADVERSE REACTIONS**
Psychiatric disorders:	Changes of mood.
Nervous system disorders:	Drowsiness, confusion and restlessness. Raised intracranial pressure may occur.
Eye disorders:	Miosis.
Ear and labyrinth disorders:	Vertigo.
Cardiac disorders:	Bradycardia and palpitations.
Vascular disorders:	Orthostatic hypotension.
Gastrointestinal disorders:	Nausea, vomiting, constipation and dry mouth.
Skin and subcutaneous tissue disorders:	Sweating and facial flushing. Reactions such as urticarial and pruritus may occur.
Renal and urinary disorders:	Micturition may be difficult and there may be ureteric or biliary spasm.

General disorders and administrative site conditions:	Hypothermia.

c. Description of selected adverse reactions

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

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 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**

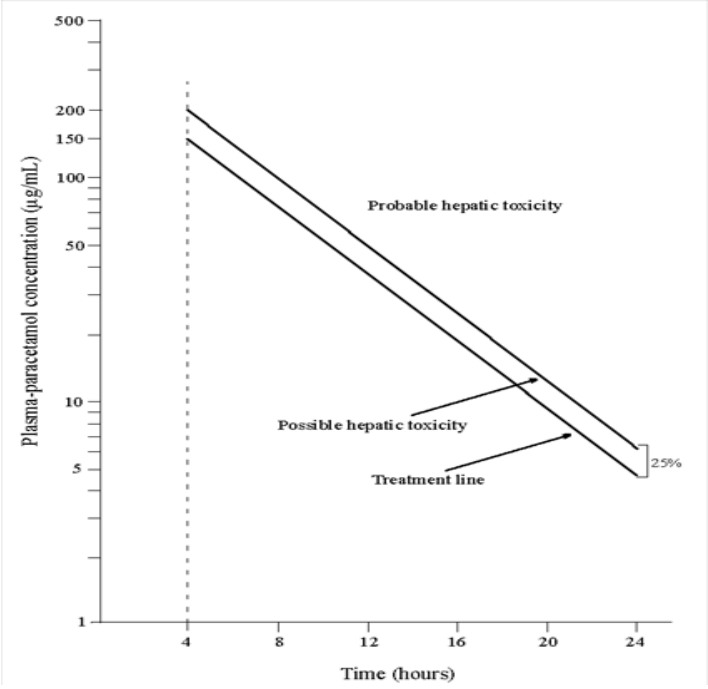
volume of intravenous fluid should be modified for children.

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.

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 Analgesics combinations

MYPRODOL® SUSPENSION has an analgesic, anti-inflammatory and antipyretic action.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Blackcurrant NE 53984,

Citric acid anhydrous,

Disodium edetate,

Glycerine,

Kaolin light,

Polyethylene glycol 4000,

Polyvinylpyrrolidone (PVP) K25,

Purified water,

Raspberry red H 1277,

Sodium benzoate,

Sodium citrate,

Sodium cyclamate,

Sodium metabisulphite,

Sodium saccharin 500,

Sodium dihydrogen phosphate dehydrate,

Xanthan gum TF.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 30 °C in well-closed containers.

Protect from light.

6.5 Nature and contents of container

100 ml amber round glass bottle, with a polypropylene lined (with an expanded polyethylene liner) white screw cap.

200 ml amber round glass bottle, with a polypropylene lined (with an expanded polyethylene liner) white screw cap.

200 ml amber round PVC bottle with a low-density polyethylene white snap-on cap.

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,

1685

Midrand

Customer Care: 0860 ADCOCK 232625

8. REGISTRATION NUMBER(S)

Y/2.8/119

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22 June 1994

10. DATE OF REVISION OF THE TEXT

18 July 2023

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