PROFESSIONAL INFORMATION

SCHEDULING STATUS: S2

1. NAME OF MEDICINE

SYNDOL TABLETS

Strength

Each tablet contains:

Codeine phosphate	10 mg
Doxylamine succinate	5 mg
Paracetamol	450 mg
Caffeine	30 mg

Pharmaceutical form:

Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each tablet contains:

Paracetamol	450 mg
Caffeine	30 mg
Codeine phosphate	10 mg
Doxylamine succinate	5 mg

Sugar free

For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Tablets

Round, yellow, scored tablet embossed with “S” logo on opposite side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

SYNDOL TABLETS are indicated for the symptomatic relief of tension headache and other somatic pain/tension states such as neuralgia, primary dysmenorrhoea and following trauma and surgery. **SYNDOL TABLETS** calm and soothe the patient and help allay the anxiety that can prolong or aggravate pain.

4.2 Posology and method of administration

Adults and children 12 years and older: 2 tablets every 4 hours as needed. Do not exceed 8 tablets per day.

DO NOT EXCEED THE RECOMMENDED DOSE.

Oral administration.

4.3 Contraindications:

Known hypersensitivity to any of the ingredients.

Safety of use of **SYNDOL TABLETS** during pregnancy and lactation has not been established.

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.

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.

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.

Paracetamol dosages in excess of those recommended may cause severe liver damage. Patients suffering from liver or kidney disease should take paracetamol under medical supervision. Consult your doctor if no relief is obtained with the recommended dosage.

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

Products containing codeine should not be given for prolonged periods.

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

Do not use continuously for more than 10 days without consulting your doctor. Large doses may precipitate fits in epileptics.

SYNDOL Tablets should not be given to children under 12 years of age.

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

The effects of atropine and tricyclic antidepressants may be enhanced.

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

4.5 Interactions with other medicines and other forms of interactions.

Doxylamine succinate has anticholinergic properties and should be used with care in conditions such as glaucoma and prostatic hypertrophy. The effects of atropine and tricyclic antidepressants may be enhanced.

Doxylamine succinate may enhance the sedative effect of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillisers.

Doxylamine may decrease emetic response to apomorphine.

The warning symptoms of damage caused by ototoxic drugs may be masked and the metabolism of drugs in the liver may be affected (see **Undesirable effects**).

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

4.6 Fertility, pregnancy and lactation

Safety of SYNDOL TABLETS during pregnancy and lactation has not been established.

4.7 Effects on ability to drive and use of 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.

Patients should be cautioned about operating vehicles or machinery or engaging in activities which requires them to be fully alert.

4.8 Undesirable effects

Frequency	**System Organ classification**	**Side effects**
Frequent	Nervous system disorders	Sedation, Drowsiness, deep sleep, including inability to concentrate, lassitude, inco-ordination, dizziness, headache, dryness of the mouth,

		nervousness, tremors, muscle twitching and convulsions.
	Vascular disorders	Hypotension.
Frequency Unknown	Blood and lymphatic system disorders	Agranulocytosis, anemia, thrombocytopenia or blood disorders, Blood dyscrasias including and haemolytic anaemia.
	Cardiac disorders	Tightness of the chest and tingling, heaviness and weakness of the hands, tachycardia, Bradycardia, palpitations and extrasystoles.
	Ear and labyrinth disorders	Tinnitus, Vertigo.
	Eye disorders	Scintillating scotoma, Miosis.
	Gastrointestinal disorders	Nausea, vomiting, diarrhoea, constipation, epigastric pain, constipation, dry mouth, gastric ulceration.
	General disorders and administration site conditions	Hypothermia.
	Hepato-biliary disorders	Hepatitis, Biliary spasm
	Immune system disorders	Allergy, anaphylaxis
	Musculoskeletal and connective tissue disorders	Muscle tremor, Muscular weakness
	Psychiatric disorders	Irritability, elation or depression, anorexia, nightmares, insomnia, changes of mood, confusion, restlessness and raised intracranial pressure, excitement.
	Renal and urinary disorders	Renal colic, renal failure, sterile pyuria, Difficulty in micturition, ureteric spasm.

	Skin and subcutaneous tissue disorders	Skin rash, Urticaria, pruritus and sweating.
	Vascular disorders	Orthostatic hypotension, facial flushing.

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

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 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.

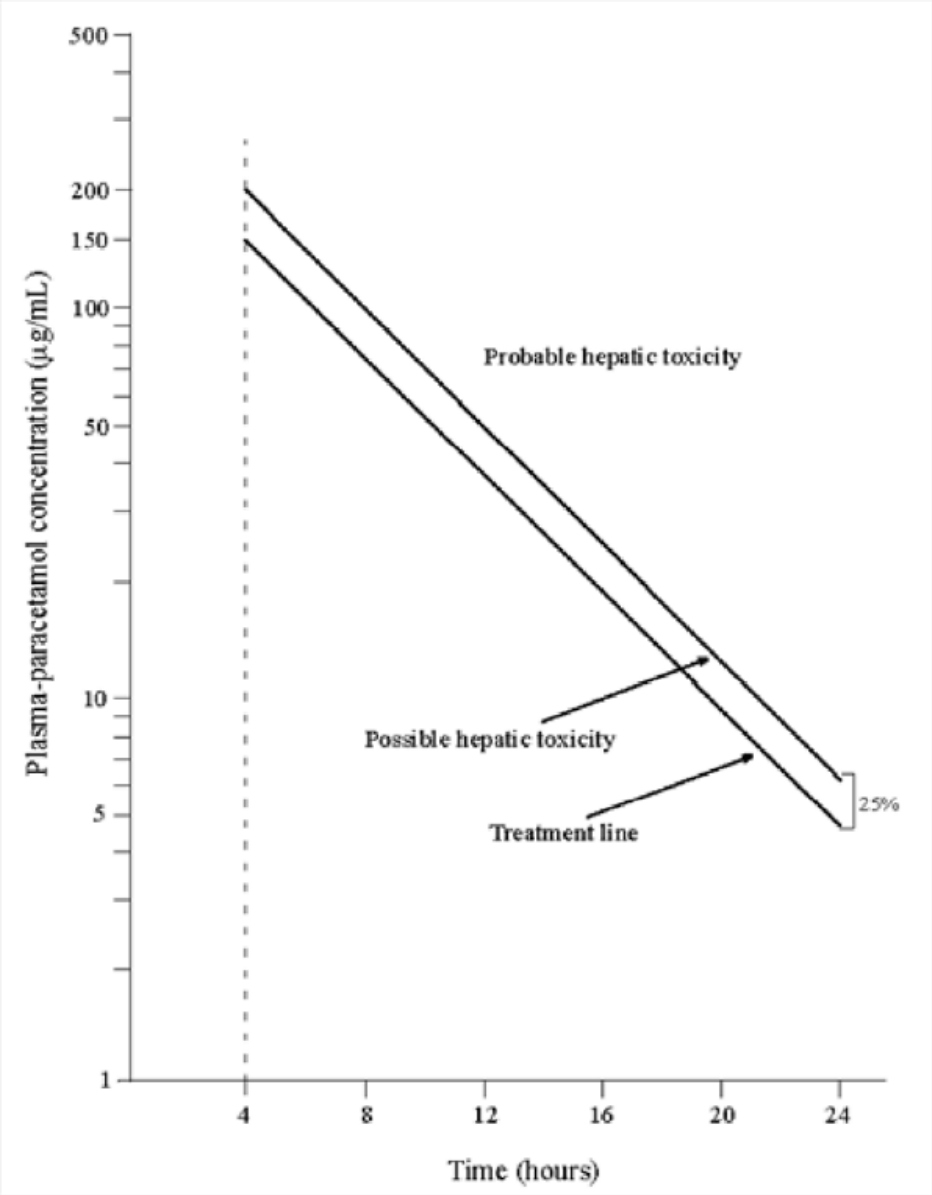
Treatment for paracetamol overdosage: Although evidence is limited it is recommended that any adult person who has ingested 5 - 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours, should have the stomach emptied by lavage (emesis may be adequate 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.



(Reference: Martindale 37th Edition)

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

Doxylamine succinate:

Overdosage of doxylamine succinate causes sedation. Overdosage may be fatal, especially in infants and children in whom the main symptoms are central nervous system stimulation and antimuscarinic effects, including ataxia, excitement, hallucinations, muscle tremor, convulsions, dilated pupils, dry mouth, flushed face and hyperpyrexia. Deepening coma, cardiorespiratory collapse and death may occur within 18 hours. In adults, the usual symptoms are central nervous system depression with drowsiness, coma and convulsions. Hypotension may also occur. Treatment of antihistamine overdose is symptomatic and supportive.

Codeine phosphate:

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

Caffeine:

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.

In the event of overdosage consult a doctor or take the patient to the nearest hospital immediately. Specialized 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 paracetamol 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 with paracetamol. If hyperexcitability, hallucinations or convulsions occur, treat with barbiturates (cautiously), gastric lavage and supportive therapy. Gastric lavage and supportive therapy are advised if drowsiness is excessive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

A 2.8 Analgesic combinations

Mechanism of action

Paracetamol is an effective, well-documented analgesic preparation. Codeine is a proven analgesic agent, which has a suggested central action.

Doxylamine succinate is an ethanolamine type antihistamine with mild sedative, anti-allergic and anti-emetic properties. Because of its sedative action, it reduces the psychic tension component of tension headache and other somatic pain/tension states.

Caffeine has a mild stimulant effect on the cerebral cortex and relieves fatigue.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium, magnesium stearate, maize starch, povidone, pregelatinised starch, talc and yellow colourant.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

48 months

6.4 Special precautions for storage

Store at or below 25 ºC

6.5 Nature and contents of container

Blister packs of 10, 18, 20, 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 THE APPLICANT CERTIFICATE OF REGISTRATION:

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand,1685

0860ADCOCK (232625)

8. REGISTRATION NUMBERS

B675 (Act 101/1965)

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORISATION

(Old medicine letter)

Submitted: 19/04/2016

10. DATE OF REVISION OF THE TEXT

30 November 2021

Botswana: B9316250 S3
Namibia: NS1 05/2.8/0165

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