PROFESSIONAL INFORMATION

SCHEDULING STATUS: **S2**

1. NAME OF MEDICINE

ADCO-DOL, 10 mg /5 mg/ 450 mg/ 45 mg, tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Codeine phosphate 10 mg

Doxylamine succinate 5 mg

Paracetamol 450 mg

Caffeine 45 mg

Sugar free.

For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Tablets.

Yellow, circular, flat tablet, scored on one side only, and embossed with "ADCO" above and "DOL" below the score line.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ADCO-DOL tablets for adults and children over 12 years.

Symptomatic relief of mild to moderate pain, pain associated with tension, and fever.

4.2 Posology and method of administration

Adults and children over 12 years: One or two tablets repeated four hourly if necessary. Do not exceed eight tablets per day.

DO NOT EXCEED THE RECOMMENDED DOSE.

Method of administration

ADCO-DOL should be taken orally, with a sufficient amount of water.

4.3 Contraindications

- Sensitivity to active ingredients or the excipients listed in Section 6.1.
- 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.

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.
The effects of atropine and tricyclic antidepressants may be enhanced.
This medicine may lead to drowsiness and impaired concentration which is aggravated by the simultaneous intake of alcohol or other central nervous system depressant agents (see INTERACTIONS). Patients should be warned against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration may lead to accidents.

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

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

Large doses may precipitate fits in epileptics.
Consult your doctor if no relief is obtained with the recommended dosage.
Do not use continuously for more than ten days without consulting your doctor.
ADCO-DOL tablets should not be given to children under 12 years of age.

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.
The effects of atropine and tricyclic antidepressants may be enhanced (Refer to **Special warnings and precautions for use**).
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**).
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 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 in 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 warned against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration may lead to accidents.

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 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, 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.

One may also report to Adcock Ingram Limited using the following email: Adcock.AEReports@adcock.com

4.9 Overdose

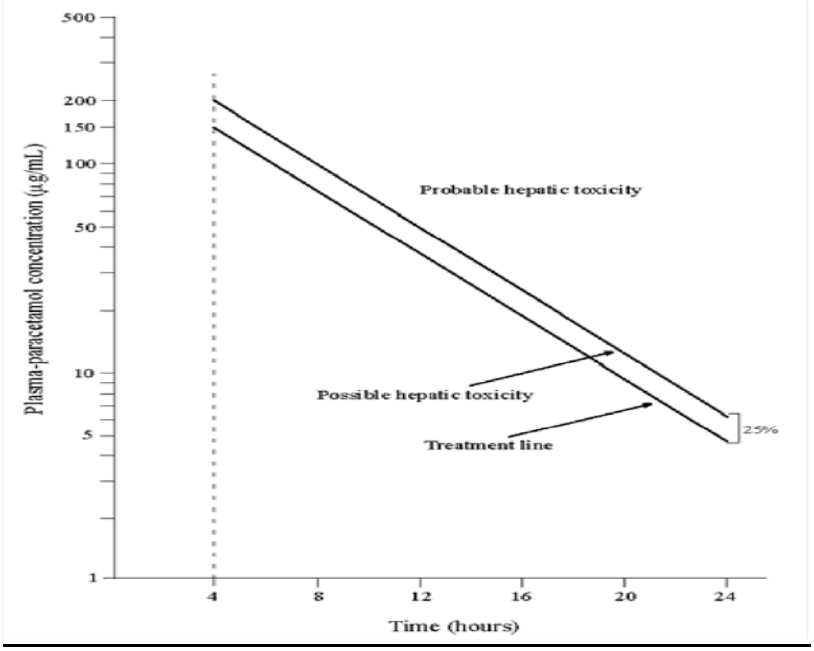
Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person directly to a hospital. A delay in starting treatment may mean the antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.

Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 -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.



(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, cardiorespitratory 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. Specialised treatment is essential as soon as possible.
The latest information regarding the treatment of overdosage can be obtained from the nearest poison centre, but in the event of this not being available, empty the stomach by aspiration and lavage. Supportive therapy may be required.
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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

A: 2.8 Analgesic combinations

Mechanism of action
ADCO-DOL tablets have antipyretic, analgesic and antihistaminic properties.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colour sunset yellow FCF lake, colour quinoline yellow lake, colour quinoline yellow WS, gelatin, maize starch, magnesium stearate, purified talc, sodium starch glycolate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 ºC.

Protect from light and moisture.

Do not remove the blister pack from the outer carton until required for use.

6.5 Nature and contents of container

Blister packs of 20, 40 tablets.

Securitainers of 20 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION:

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand, 1685

Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER.

U/2.8/159

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORISATION

16 August 1988.

10. DATE OF REVISION OF THE TEXT

Date of the latest approved PI: 18 May 2023.

Namibia: NS1 90/2.8/0083

Botswana: BOT1803275 1D

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