PACKAGE INSERT

TENSODOL TABLETS

SCHEDULING STATUS:

S2

PROPRIETARY NAME (AND DOSAGE FORM):

TENSODOL (Tablets)

COMPOSITION:

Each tablet contains:

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

The inactive ingredients include colloidal silicon dioxide, magnesium stearate, maize starch, povidone, quinoline yellow, sodium starch glycollate and talc.

PHARMACOLOGICAL CLASSIFICATION:

A 2.8 Analgesic combination.

PHARMACOLOGICAL ACTION:

TENSODOL has analgesic, antipyretic and antihistaminic properties.

INDICATIONS:

TENSODOL is indicated in mild to moderate pain associated with tension.

CONTRAINDICATIONS:

- hypersensitivity to any of the active ingredients in **TENSODOL**.
- the dosage in renal functional impairment must be reduced.
- **TENSODOL** should be taken with caution in asthmatics
- Respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion, after operation on the biliary tract, acute alcoholism, head injuries and conditions in which intracranial pressure is raised.
- **TENSODOL** should not be given during an attack of bronchial asthma or in heart failure secondary to chronic lung disease.
- **TENSODOL** is contraindicated in patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.
- safety in pregnancy has not been established (see **"PREGNANCY AND LACTATION"**).

WARNINGS AND SPECIAL PRECAUTIONS:

Paracetamol:

TENSODOL 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.

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

Codeine phosphate:

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

This medicine may lead to drowsiness and impaired concentration, which may be 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 phosphate:

- should be used with caution in patients with obstructive bowel disorders, liver impairment, myasthenia gravis, prostatic hypertrophy, impaired renal function or shock.
- should be used with caution or in reduced doses in patients with adrenocortical insufficiency and hypothyroidism.
- dosages should be reduced in debilitated and elderly patients.
- may affect the activity of other medicines by delaying their absorption (see **"INTERACTIONS"**).
- depressant effects are aggravated by alcohol, anaesthetics, hypnotics, sedatives, tricyclic antidepressants and phenothiazines.

Caffeine:

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

Doxylamine succinate:

- 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 by doxylamine succinate (see **"INTERACTIONS"**).
- Doxylamine succinate may mask the warning symptoms of damage caused by ototoxic drugs and may affect the metabolism of drugs in the liver (see **"INTERACTIONS"**).
- Doxylamine succinate may enhance the sedative effects of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillisers (see **"INTERACTIONS"**).

INTERACTIONS:

Codeine may affect the activity of other medicines by delaying their absorption (see **"WARNINGS AND SPECIAL PRECAUTIONS"**). The depressant effects are aggravated by alcohol, anaesthetics, hypnotics, sedatives, tricyclic antidepressants and phenothiazines (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

The effects of atropine and tricyclic antidepressants may be enhanced by the doxylamine succinate (an antihistamine) (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Doxylamine succinate may also mask the warning symptoms of damage caused by ototoxic medicines and may affect the metabolism of medicines in the liver (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Doxylamine succinate may enhance the sedative effects of central nervous system

depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillisers (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

PREGNANCY AND LACTATION:

The safety of TENSODOL in pregnancy and lactation is not known (see **"CONTRAINDICATIONS"**).

DOSAGE AND DIRECTIONS FOR USE:

Adults and children 12 years and older:

Take 2 tablets every 4 hours as needed. Do not exceed 8 tablets per day.

Do not use continuously for longer than 10 days without consulting your doctor.

DO NOT EXCEED THE RECOMMENDED DOSE.

SIDE-EFFECTS:

Paracetamol

- Skin rashes and other allergic reactions may occur. The rash is usually erythematous or urticarial but sometimes more serious and may be accompanied by drug fever and mucosal lesions.
- The use of paracetamol has been associated with the occurrence of neutropenia, pancytopenia and leucopenia.

Codeine phosphate

Codeine may cause respiratory depression, bradycardia, circulatory failure, hypotension, orthostatic hypotension, palpitations, deepening coma, confusion, drowsiness, euphoria, mood changes, restlessness, vertigo, flushing, hypothermia, increased intracranial pressure, miosis, dry mouth, muscle rigidity, nausea, vomiting, constipation, pruritus,

urticaria, sweating, urinary retention, ureteric and biliary spasm and an antidiuretic effect.

Caffeine:

- Side effects of caffeine include nausea, headache and insomnia.
- Large doses may cause restlessness, excitement, muscle tremor, tinnitus, scintillating scotoma, tachycardia and extrasystoles.
- Caffeine increases gastric secretion and may cause gastric ulceration.

Doxylamine succinate

- A common side effect of doxylamine succinate is sedation.
- Other side effects include gastro-intestinal disturbances, headache, blurred vision, tinnitus, elation or depression, irritability, nightmares, anorexia, difficulty in micturition, dryness of the mouth, tightness of the chest, and tingling, heaviness and weakness of the hands.
- Symptoms of stimulation in adults include insomnia, nervousness, tachycardia, tremors, muscle twitching and convulsions.
- Large doses may precipitate fits in epileptics.
- Allergy and anaphylaxis may occur.
- Blood dyscrasias including agranulocytosis and haemolytic anaemia may occur.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Doxylamine succinate:

Overdosage of doxylamine succinate causes sedation.

Paracetamol

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia, and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion.

Abnormalities of glucose metabolism and metabolic acidosis may occur. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias have been reported.

Symptoms during the first 2 days of acute poisoning do not reflect the potential seriousness of the overdosage. Nausea, vomiting, anorexia and abdominal pain may persist for a week or more. Liver injury may become manifest on the second day, (or later) initially by elevation of serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of prothrombin time.

The liver damage may progress to encephalopathy, coma and death. Cerebral oedema and nonspecific myocardial depression have also occurred. 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.

Prompt treatment is essential.

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.

Any patient who has ingested 5 – 10 g or more of paracetamol (or a child who has had more than 140 mg/kg) in the preceding 4 hours should undergo gastric 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.

Specific therapy with an antidote such as N-acetylcysteine or methionine may be necessary. If decided upon, N-acetylcysteine should be administered intravenously (IV) as soon as possible.

N-acetylcysteine should be administered as soon as possible, preferably within 8 hours of overdosage with paracetamol. There is evidence that it is still effective up to 36 hours after overdosage with paracetamol and may be longer, especially if more than 150 mg/kg of paracetamol was taken.

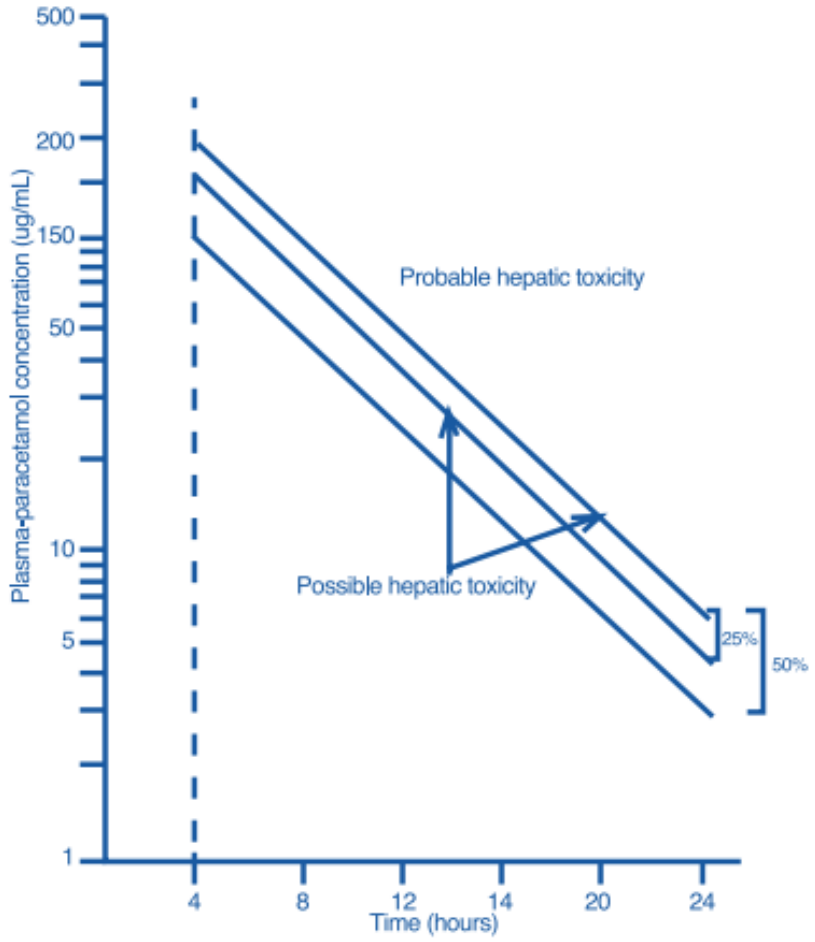
IV: An initial dose of 150 mg/kg in 200 ml dextrose injection, given intravenously over 15 minutes, followed by an intravenous infusion of 50 mg/kg in 500 ml of dextrose injection over the next 4 hours, and then 100 mg/kg in 1 000 ml over the next 16 hours. **The volume of intravenous fluids should be modified for children.**

Orally: 140 mg/kg as a 5 % solution initially, followed by a 70 mg/kg solution every 4

hours for 17 doses. N-acetylcysteine is effective if administered within 8 hours of overdosage.

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.

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

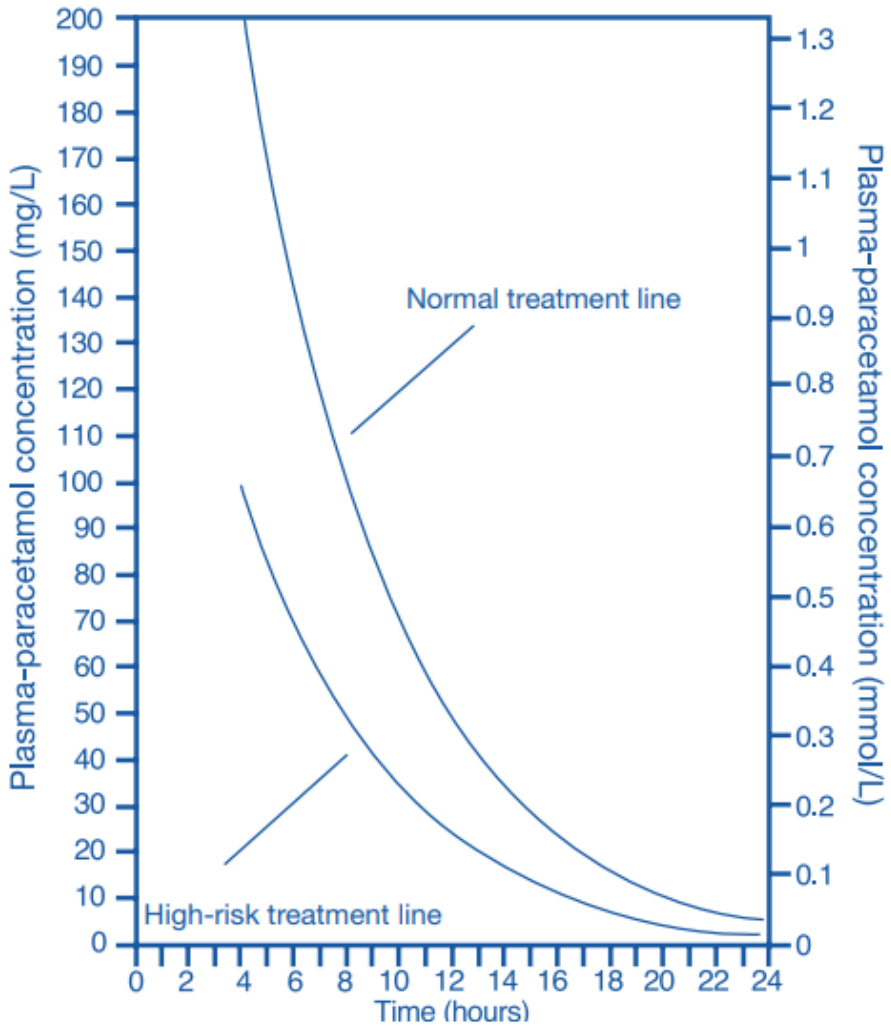


Adapted from Rumack BH, Matthew HJ. Acetaminophen poisoning and toxicity
Pediatrics 1975; 55; 871-6

Notes for the use of this chart:

1. The time coordinates refer to time after ingestion.
2. Plasma-paracetamol concentrations drawn before 4 hours may not represent peak concentrations.
3. The graph should be use only in relation to a single acute ingestion.
4. The solid line 25% below the standard nomogram is included to allow for possible errors in plasma assays and estimated time from ingestion of an overdose.
5. The solid line 50% below the standard nomogram is to assess the possible hepatic toxicity in patients recieving enzyme-inducing drugs, with malnutrition or a history of alcohol abuse, or have not eaten for a few days.
6. The value of such charts is uncertain if the patient is first seen 15 hours or more after ingestion, or has taken modified release preparations of paracetamol.

Figure 2. A linear plot of plasma-paracetamol concentration against hours after ingestion



Courtesy of PA Routledge. Note for the use of this chart:

1. The time coordinates refer to time after ingestion.
2. Plasma-paracetamol concentrations drawn before 4 hours may not represent peak concentrations.
3. The graph should be used only in relation to a single acute ingestion.
4. Patients whose plasma-paracetamol concentrations are above the normal treatment lines should be treated.
5. Patients on enzyme-inducing drugs, with malnutrition or a history of acohol abuse, or who have not eaten for a few days should be treated if their plasma-paracetamol concentrations are above the "High-risk treatment line".
6. The value of such charts is uncertain if the patient is first seen 15 hours or more after ingestion, or has taken modified release preparations of paracetamol.

Monitor all patients with significant ingestions for at least 96 hours.

Codeine phosphate

Symptoms of overdosage with codeine phosphate include the following: nausea, vomiting, restlessness, sensory disturbances, muscle tremor, diuresis, palpitations, stupor, shock, central stimulation with exhilaration, convulsions, drowsiness, respiratory

depression, hypotension with circulatory failure, respiratory collapse, cyanosis and coma. In acute poisoning the stomach should be emptied by aspiration and lavage. Intensive supportive therapy may be necessary to correct respiratory failure and shock. The specific antagonist nalaxone may be used to counteract severe respiratory depression.

IDENTIFICATION:

A yellow, flat, bevelled edge tablet, scored on one side.

PRESENTATION:

Blister strips of 10 tablets each, packed in 20's or 40's.

Plastic containers, packed in 20's or 40's.

STORAGE INSTRUCTIONS:

Store below 25 ºC in a dry place.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

28/2.8/0383

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Cipla Medpro (Pty) Ltd

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Mispel Street,

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DATE OF PUBLICATION OF THIS PACKAGE INSERT:

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