**PROFESSIONAL INFORMATION FOR**

**TENSOPYN**

**SCHEDULING STATUS**

S2

## 1. NAME OF THE MEDICINE

**TENSOPYN**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

| | |
|---|---|
| Paracetamol | 450 mg |
| Codeine phosphate | 10 mg |
| Caffeine anhydrous | 30 mg |
| Doxylamine succinate | 5 mg |

Sugar free

For the full list of excipients, see **section 6.1**.

## 3. PHARMACEUTICAL FORM

Tablets.

Yellow, practically odourless, flat faced, bevelled edges, round tablets embossed with a triangle on one side.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

TENSOPYN tablets are indicated for mild to moderate pain associated with tension.

## 4.2 Posology and method of administration

**Posology**

Adults and children over 12 years: one to two tablets every 4 hours, with a maximum of 8 tablets daily.

**DO NOT EXCEED THE RECOMMENDED DOSE.**

Do not use continuously for longer than 5 days without consulting your doctor.

**Special populations**

***Elderly population***

Elderly patients may metabolise or eliminate opioid analgesics more slowly than younger adults; therefore, dose reduction may be necessary (refer to **section 4.4**).

***Renal and hepatic impairment***

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

The dosage in renal functional impairment must be reduced.

**Paediatric population**

The safety and efficacy of TENSOPYN in children under 12 years has not yet been established (see **section 4.3**).

**Method of administration**

TENSOPYN should be taken orally.

## 4.3 Contraindications

TENSOPYN is contraindicated in:

- Patients with a known hypersensitivity to paracetamol, codeine phosphate, caffeine and doxylamine succinate or to any of the excipients used in the formulation of TENSOPYN (see **section 6.1**).
- Children under the age of 12 years.
- Children (aged below 18 years) who undergo surgery for the removal of the tonsils or adenoids to treat obstructive sleep apnoea, as these patients are more susceptible to respiratory problems.
- Severe liver or kidney function impairment.
- Acute intermittent porphyria.
- Respiratory depression especially in the presence of cyanosis and excessive bronchial secretion.
- 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.
- In patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.
- After an operation on the biliary tract.
- Acute alcoholism (see **section 4.4**).
- In patients for whom it is known that they are CYP2D6 ultra-rapid metabolisers (see **section 4.4 and 4.6**).
- Pregnancy and women who are breastfeeding their infants.

## 4.4 Special warnings and precautions for use

**TENSOPYN 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.**

Do not take continuously for more than 5 days without consulting a doctor. Also consult your doctor if no relief is obtained with the recommended dosage.

Do not take concurrently with any other paracetamol or codeine-containing medicine.

TENSOPYN tablets may lead to drowsiness and impaired concentration, which 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.

Dosage more than that recommended may cause severe liver damage.

Care is advised in the administration of TENSOPYN to patients with impaired kidney or liver function and in those with hypertension, hypothyroidism, adrenocortical insufficiency, prostatic hypertrophy, urinary retention, susceptibility to angle-closure glaucoma, shock, obstructive bowel disorders, acute abdominal conditions (e.g. peptic ulcer), recent gastrointestinal surgery, gallstones, myasthenia gravis, a history of cardiac arrhythmias or convulsions, hyperthyroidism, hepatic dysfunction, acute febrile illness, asthma, hypotension, elderly, and in patients with a history of drug abuse or emotional instability.

Codeine may induce faecal impaction, producing incontinence, spurious diarrhoea, abdominal pain and rarely colonic obstruction. Elderly patients may metabolise or eliminate opioid analgesics more slowly than younger adults.

The dosage in renal functional impairment must be reduced. Use with caution in renal disease. Should be taken with caution by asthmatics.

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

It should be given with care to patients with alcohol dependence, chronic malnutrition, or dehydration.

Administration of pethidine and possibly other opioid analgesics to patients taking a monoamine oxidase inhibitor (MAOI) has been associated with very severe and sometimes fatal reactions. See also **section 4.3** regarding contraindication of taking TENSOPYN with MAOIs, because of the doxylamine component.

**Severe Cutaneous adverse reactions (SCARs)**

Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), eosinophilia and systemic (DRESS)/Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicines. If a patient develops SCAR, treatment with TENSOPYN must be discontinued and appropriate treatment instituted.

**Mental health disorders**

Caution should be practiced in patients with a personal or family history of mental health disorders or substance abuse as they are at an increased risk for addiction and abuse.

**Risks from concomitant use of opioids and benzodiazepines**

Concomitant use of opioids, including codeine, and sedative medicines such as benzodiazepines or related medicines may result in sedation, respiratory depression, coma, and death. Because of these risks, concomitant prescribing of sedative medicines, such as benzodiazepines or related medicines, with opioids should be reserved for patients for whom alternative treatment options are not possible.

If a decision is made to prescribe codeine concomitantly with sedative medicines such as benzodiazepines, the lowest effective dose should be used, and the duration of treatment should be as short as possible. The patients should be monitored closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their close contacts to be aware of these symptoms (see **section 4.5**).

*Opioid use disorder (abuse and dependence)*

Tolerance, physical and psychological dependence and opioid use disorder (OUD) may develop upon repeated administration of opioids such as codeine. Abuse or intentional misuse of TENSOPYN may result in overdose and/or death.

Patients should be informed about the risks and signs of OUD as well as serious clinical outcomes. If these signs occur, patients should be advised to contact their doctor.

Withdrawal symptoms, such as restlessness and irritability may occur once the medicine is stopped.

Opioid-induced Hyperalgesia (OIH) and Allodynia

Opioid pain medicines have been associated with opioid-induced hyperalgesia (OIH), a condition where opioids cause an increase in pain (called hyperalgesia) or an increased sensitivity to pain (called allodynia). Increases in pain typically occur following a dose

increase and resolve quickly following proper diagnosis and management of the condition. Symptoms of OIH include (but may not be limited to) increased levels of pain upon opioid dosage increase, decreased levels of pain upon opioid dosage decrease, or pain from ordinarily non-painful stimuli (allodynia).

**Risks from concomitant use of opioids and alcohol**

Concomitant use of opioids, including codeine, with alcohol may result in sedation, respiratory depression, coma and death. Concomitant use with alcohol is not recommended (see **section 4.5**).

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver diseases.

**CYP2D6 metabolism**

Codeine is metabolised by the liver into morphine, its active metabolite. If a patient has a deficiency or is completely lacking this enzyme an adequate analgesic effect will not be obtained. However, if the patient is an extensive or ultra-rapid metaboliser, there is an increased risk of developing side effects of opioid toxicity even at commonly prescribed doses. These patients convert codeine into morphine rapidly resulting in higher-than-expected serum morphine levels.

General symptoms of opioid toxicity include confusion, somnolence, shallow breathing, small pupils, nausea, vomiting, constipation and lack of appetite. In severe cases this may include symptoms of circulatory and respiratory depression, which may be life-threatening and very rarely fatal.

**Paediatric population**

Children with conditions associated with respiratory problems should not take codeine, as in TENSOPYN. Overdosage is very dangerous in young children.

## 4.5 Interaction with other medicines and other forms of interaction

The speed of absorption of paracetamol may be increased by metoclopramide, domperidone and absorption reduced by cholestyramine.

**Antithrombotic medicines**

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

**CNS depressants**

TENSOPYN may enhance the sedative effects of CNS depressants such as alcohol, barbiturates, anaesthetics, hypnotics, other opioid analgesics, anxiolytic sedatives, antipsychotics, tricyclic antidepressants and phenothiazines, resulting in increased CNS depression. It may also have an additive antimuscarinic action with other medicines, such as atropine and some antidepressants.

**Benzodiazepines**

The concomitant use of opioids with sedative medicines, such as benzodiazepines or related medicines, increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dosage and duration of concomitant use should be limited (see **section 4.4**).

**Alcohol and opioids**

The concomitant use of alcohol and opioids increases the risk of sedation, respiratory depression, coma, and death because of additive CNS depressant effect. Concomitant use with alcohol is not recommended (see **section 4.4**).

**Diuretics and antihypertensives**

The hypotensive actions of diuretics and anti-hypertensive medicines may be potentiated when used concurrently with opioid analgesics. Concurrent use of hydroxyzine with codeine may result in increased analgesia as well as increased CNS depressant and hypotensive effects.

**Neuromuscular blocking medicines**

The respiratory depressant effect caused by neuromuscular blocking medicines may be additive to the central respiratory depressant effects of opioid analgesics. Quinidine can inhibit the analgesic effect of codeine.

**Antidiarrhoeal medicines**

Concurrent use of codeine with antidiarrhoeal and antiperistaltic medicines, such as loperamide and kaolin, may increase the risk of severe constipation. Concomitant use of antimuscarinics or medicines with antimuscarinic action may result in an increased risk of severe constipation, which may lead to paralytic ileus and/or urinary retention.

Codeine may delay the absorption of mexiletine and thus reduce the antiarrhythmic effect of the latter. Codeine may antagonise the gastrointestinal effects of metoclopramide, cisapride and domperidone. Cimetidine inhibits the metabolism of opioid analgesics resulting in increased plasma concentrations.

Naloxone antagonises the analgesic, CNS and respiratory depressant effects of opioid analgesics. Naltrexone also blocks the therapeutic effect of opioids.

*Doxylamine*: Monoamine oxidase inhibitors (MAOIs) or within 14 days of stopping treatment with these products as there is a risk of serotonin syndrome (see **section 4.3 and 4.4**).

Concomitant administration of pethidine and possibly other opioid analgesics to patients taking MAOIs has been associated with very severe and sometimes fatal reactions such as severe CNS excitation or depression, including hypertension or hypotension.
Although this has not been documented with codeine, it is possible that a similar interaction may occur and therefore the use of codeine should be avoided while the patient is taking MAOIs and for 2 weeks after MAOI discontinuation.

*Incompatibilities*: Codeine has been reported to be incompatible with phenobarbitone sodium forming a codeine-phenobarbitone complex, and with potassium-iodide, forming crystals of codeine periodide. Acetylation of codeine phosphate by aspirin has occurred in solid dosage forms containing the two medicines, even at low moisture levels.

*Interference with laboratory tests*: Opioid analgesics interfere with a number of laboratories tests including plasma amylase, lipase, bilirubin, alkaline phosphatase, lactate dehydrogenase, alanine aminotransferase and aspartate aminotransferase. Opioids may also interfere with gastric emptying studies as they delay gastric emptying and with hepatobiliary imaging using technetium Tc 99m disofenin as opioid treatment may cause constriction of the sphincter of Oddi and increase biliary tract pressure.

The metabolism of paracetamol is possibly accelerated by carbamazepine, phenytoin, phenobarbital, primidone (there have also been isolated reports of hepatotoxicity).

## 4.6 Fertility, pregnancy and lactation

### Pregnancy

TENSOPYN is contraindicated in pregnancy (see **section 4.3**).

Codeine crosses the placenta. There is no adequate evidence of safety in human pregnancy and a possible association with respiratory and cardiac malformations has been reported. Regular use during pregnancy may cause physical dependence in the foetus leading to withdrawal symptoms in the neonate.

Use of opioid analgesia during labour may cause respiratory depression in the neonate, especially the premature neonate. These medicines should not be given during the delivery of a premature baby.

### Breastfeeding

TENSOPYN is contraindicated in women who are breastfeeding their infants (see **section 4.3**). Codeine should not be used during breastfeeding.

Paracetamol is excreted in breast milk but not in a clinically significant amount.

At normal therapeutic doses, codeine and its active metabolites may be present in breast milk at very low doses and is unlikely to adversely affect the breast fed infant. However, if the patient is an ultra-rapid metaboliser of CYP2D6, higher levels of the active metabolites

may be present in breast milk and on very rare occasions may result in symptoms of opioid toxicity in the infant, which may be fatal (see **section 4.3** and **4.4**).

### 4.7 Effects on ability to drive and use machines

The use of TENSOPYN 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.

### 4.8 Undesirable effects

**Tabulated list of adverse reactions**

The following adverse reactions have been classified according to the following categories, *frequent, less frequent* and *frequency unknown*.

| **MedDRA system organ class** | **Frequency** | **Side effects** |
|---|---|---|
| Blood and lymphatic system disorders | *Less frequent* | Haematological reactions including thrombocytopenia, leucopenia, pancytopenia, neutropenia, agranulocytosis, thrombocytopenic purpura, unusual bleeding or bruising, blood dyscrasias, including agranulocytosis, eosinophilia, and haemolytic anaemia. |
| Immune system disorders | *Less frequent* | Sensitivity reactions, angioedema. |

| | | |
|---|---|---|
| | *Frequency unknown* | Hypersensitivity, anaphylaxis. |
| Endocrine disorders | *Frequency unknown* | Pancreatitis. |
| Psychiatric disorders | *Frequent* | Drowsiness, confusion. |
| | *Less frequent* | Excitement, feelings of unreality, mental depression, lassitude, deepening coma, irritability, nightmares, anorexia, nervousness. |
| | *Frequency unknown* | Psychomotor impairment, extrapyramidal effects, sleep disturbances, insomnia, restlessness, changes in mood, euphoria, decreased libido, hallucinations. |
| Nervous system disorders | *Frequent* | CNS depression. |
| | *Less frequent* | Dry mouth, sweating, faintness, sedation, vertigo, headache, raised intracranial pressure, paraesthesia. |
| | *Frequency unknown* | Slight drowsiness to deep sleep, lassitude, dizziness, incoordination (although paradoxical stimulation may occasionally occur, especially in children), photosensitivity, |

| | | |
|---|---|---|
| | | convulsions, tremor, CNS stimulation, anxiety. |
| Eye disorders | *Less frequent* | Scintillating scotoma. |
| | *Frequency unknown* | Blurred vision, miosis. |
| Ear and labyrinth disorders | *Frequency unknown* | Tinnitus. |
| Cardiac disorders | *Less frequent* | Fast, slow, or pounding heartbeat, extrasystole. |
| | *Frequency unknown* | Palpitations, arrhythmias, bradycardia, tachycardia. |
| Vascular disorders | *Less frequent* | Swelling of face, hypotension, hypertension, orthostatic hypotension, circulatory failure, hyperthermia. |
| Respiratory, thoracic and mediastinal disorders | *Less frequent* | Increased sweating, irregular breathing, shortness of breath, wheezing or troubled breathing, respiratory depression, tightness of the chest, bronchospasm. |
| | *Frequency unknown* | Thickened respiratory-tract secretions. |
| Gastrointestinal disorders | *Frequent* | Constipation, nausea and vomiting. |
| | *Less frequent* | Diarrhoea, gastric ulceration, gastro-intestinal disturbances, |

| | | |
|---|---|---|
| | | colic, epigastric pain, bloody or black, tarry stools, sore throat, increased gastric reflux, abdominal pain. |
| Hepato-biliary disorders | *Less frequent* | Biliary spasms. |
| | *Frequency unknown* | Jaundice. |
| Skin and subcutaneous tissue disorders | *Less frequent* | Rashes, skin eruptions, urticaria, pruritus, purpura, yellow eyes or skin, pinpoint red spots on skin, allergic reactions, hives or itching, sores, ulcers, or white spots on lips or in the mouth, skin rash. This rash is usually erythematous or urticarial, but sometimes more serious and may be accompanied by drug fever and mucosal lesions. Redness or flushing of face. |
| | *Frequency Unknown* | Risk of fixed drug eruptions (FDE) and Drug-induced hypersensitivity syndrome. |
| Musculoskeletal, connective tissue and bone disorders | *Less frequent* | Trembling or uncontrolled muscle movements or muscle rigidity, muscular weakness and |

| | | |
|---|---|---|
| | | incoordination, weakness of the hands. |
| | *Frequency unknown* | Myalgia. |
| Renal and urinary disorders | *Less frequent* | Bloody or cloudy urine, sudden decrease in amount of urine. |
| | *Frequency unknown* | Urinary difficulty or retention, difficult micturition, ureteric or biliary spasms, antidiuretic effect. |
| Reproductive system and breast disorders | *Frequency unknown* | Decreased potency. |
| General disorders and administrative site conditions | *Less frequent* | Unusual tiredness or weakness. |
| | *Frequency unknown* | Fever, sweating, hair loss, hypothermia. |

**Post-Marketing Experience**

| **MedDRA system organ class** | **Frequency** | **Side Effects** |
|---|---|---|
| Skin and subcutaneous tissue disorders. | *Frequency unknown* | Risk of fixed drug eruptions (FDE) and Drug-induced hypersensitivity syndrome (DIHS). |

**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 requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found

on the SAHPRA website, or to Cipla Medpro (Pty) Ltd. by email: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free).

## 4.9 Overdose

***Paracetamol***

**Prompt treatment is essential.** In the event of an overdosage, consult a doctor immediately, or take the person to a hospital directly. A delay in starting treatment may mean that 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 to 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.

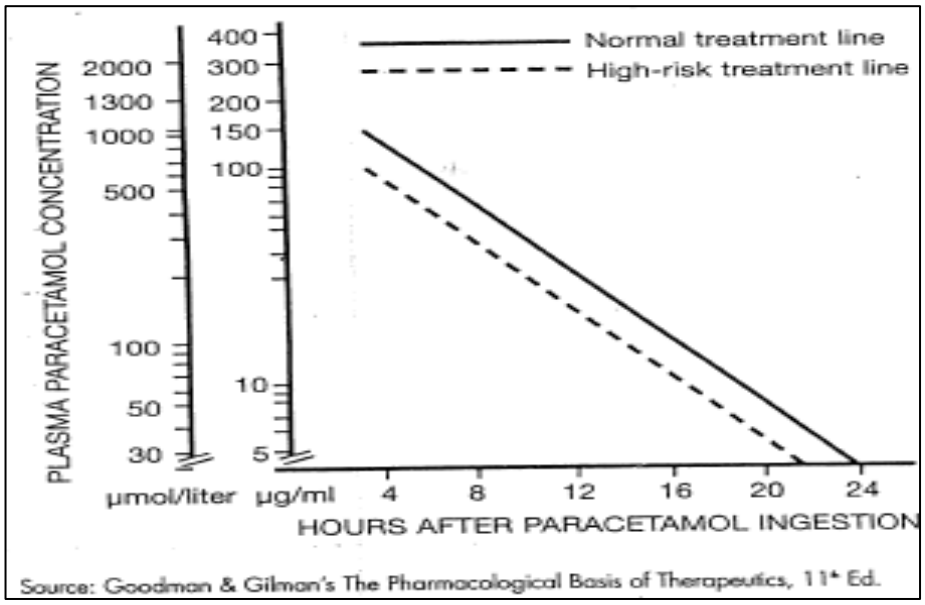
Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias have been reported.

**Treatment for paracetamol overdosage:**

**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 was 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 1000 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, unless high, 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 96 hours.

***Codeine phosphate***

Overdosage produces central stimulation with exhilaration, in children, convulsions, followed by vomiting, drowsiness, respiratory depression and cyanosis, and coma.

Symptoms in decreasing order of frequency included somnolence, rash, miosis, vomiting, itching, ataxia, swelling of the skin and respiratory failure.

Opioid toxicity may occur in adults after overdoses of codeine tablets. Get emergency help immediately if any of the following symptoms occur:

Cold, clammy skin, confusion, convulsions, severe dizziness, low blood pressure, severe nervousness or restlessness, pinpoint pupils of eyes, slow heartbeat, slow or troubled breathing, severe weakness.

In the event of overdosage, consult a doctor or take the patient to the nearest hospital immediately.

Intensive supportive therapy may be necessary to correct respiratory failure and shock. The specific antagonist naloxone may be used to counteract severe respiratory depression.

***Caffeine***

Large doses may cause restlessness, excitement, muscle tremors, tinnitus, scintillating scotoma, tachycardia and extrasystoles.

***Doxylamine succinates***

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 tremors, 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.

In the event of overdosage, consult a doctor or take the patient to the nearest hospital immediately. Respiratory depression will respond to naloxone administration.

Specialized treatment is essential as soon as possible. The latest information regarding the treatment of overdosage can be obtained from the nearest Poison Centre.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacological classification: A 2.9 Other analgesics

Pharmacotherapeutic group: Anilides, Paracetamol combinations

ATC code: N02B E51

**Mechanism of action**

TENSOPYN tablets have analgesic, antipyretic and antihistaminic action.

### 5.2 Pharmacokinetic properties

***Paracetamol***

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 10 to 60 minutes after oral doses. Paracetamol is distributed into most body tissues. It crosses the placenta and is presented in breast milk. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations. The elimination half-life of paracetamol varies from about 1 to 3 hours. Paracetamol is metabolised predominantly in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5 % is excreted as unchanged paracetamol. A minor hydroxylated metabolite (N-acetyl-p-benzoquinoneimine) is usually produced in very small amounts by cytochrome P450 isoenzymes in the liver and kidneys. It is usually detoxified by conjugation with glutathione but may accumulate following paracetamol overdosage and cause tissue damage.

***Codeine phosphate***

Codeine phosphate is absorbed from the gastrointestinal tract. Ingestion of codeine phosphate produces peak plasma-codeine concentrations in about one hour. Codeine phosphate is metabolised by 0 - and N - demethylation in the liver to morphine, norcodeine, and other metabolites including normorphine and hydrocodone. Codeine phosphate and its metabolites are excreted almost entirely by the kidneys, mainly as conjugates with glucuronic acids. The plasma half-life has been reported to be between 3 and 4 hours after an oral dose.

***Caffeine***

Caffeine is absorbed readily after oral doses and is widely distributed throughout the body. Caffeine passes readily into the CNS and into saliva; low concentrations are also present in breast milk. Caffeine crosses the placenta.

In adults, caffeine is metabolised almost completely in the liver via oxidation, demethylation, and acetylation and is excreted in the urine as 1-methyluric acid, 1-methylxanthine, 7-methylxanthine, 1,7-dimethylxanthine (paraxanthine), 5-acetylamino-6-formylamino-3-methyluracil (AFMU), and other metabolites with only about 1 % unchanged. Hepatic cytochrome P450 isoenzyme CYP1A2 is involved in caffeine enzymatic metabolism. Elimination half-lives are about 3 to 7 hours in adults. The metabolism of caffeine has been shown to be dose dependent with clearance decreasing as the dose is increased suggesting saturable metabolism. Four- to five-fold differences in plasma half-lives of caffeine are common among healthy people. The plasma half-life of caffeine is decreased by smoking and by exercise and is increased by liver disease such as cirrhosis and viral hepatitis, and in pregnancy. The plasma half-life of caffeine is not

affected by old age or obesity. Drug interactions also affect the pharmacokinetics of caffeine.

***Doxylamine succinate***

Peak plasma concentrations of doxylamine succinate occur 2 to 3 hours after oral doses. An elimination half-life of about 10 hours has been reported.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

quinoline yellow supra

magnesium stearate

microcrystalline cellulose

povidone

silicon dioxide

sodium croscarmellose

### 6.2 Incompatibilities

Not applicable

### 6.3 Shelf life

24 months

### 6.4 Special precautions for storage

- Store at or below 25 °C.
- Protect from moisture and light. Keep the container closed until ready for use.
- Keep the tablets in the blister strips and outer carton until ready for use.

### 6.5 Nature and contents of container

TENSOPYN is packed in:

- Blister strips of 10 tablets packed in a cardboard carton containing 20 or 40 tablets.
- 40 tablets packed into white plastic containers with white plastic caps.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal and other handling

Not applicable

## 7. HOLDER OF CERTIFICATE OF REGISTRATION

**CIPLA MEDPRO (PTY) LTD.**

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

## 8. REGISTRATION NUMBER(S)

T/2.9/79

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|---|
| Namibia: NS1 11/2.9/0039 |

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorisation: 8 July 1988

Latest renewal: Not applicable.

## 10. DATE OF REVISION OF THE TEXT

16 October 2026.