PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1 NAME OF THE MEDICINE

ASTRAPAIN SYRUP

2 QUALITIVE AND QUANTITIVE COMPOSITION

Each 5 ml contains:	Paracetamol	120 mg
	Codeine Phosphate	5 mg
	Promethazine hydrochloride	6,5 mg
Preservatives:	Methylparaben	0,10 % m/v
	Propylparaben	0,01 % m/v
Contains alcohol:	Alcohol content	12,5 % v/v
Contains sugar:	Sucrose	2,0 g/ 5 ml
	Liquid glucose	2,0 g/ 5 ml
	Invert syrup	600 mg/ 5 ml
Contains sweetener:	Sodium Saccharin	1,5 mg/ 5 ml
	Sodium Cyclamate	30 mg/ 5 ml

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Syrup.
Mauve to maroon-coloured clear syrup with a distinctive flavour of blackcurrant.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of mild to moderate pain, associated with fever.

4.2 Posology and method of administration

Posology

DO NOT EXCEED THE RECOMMENDED DOSE

2 to 5 years: One medicine measure full (5 ml) three times a day.
6 to 12 years: One to two medicine measure full (5 to 10 ml) three times a day.
Do not use continuously for more than 5 days for pain and 3 days for fever.

Paediatric population

Not recommended for children under the age of 2 years.

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Method of administration

For oral use.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Sensitivity to paracetamol, opiates or phenothiazines.
- Patients sensitive to one antihistamine may be sensitive to others.
- During an attack of bronchial asthma, patients with obstructive airway disease, respiratory depression, especially in the presences of cyanosis and excessive bronchial secretion.
- Heart failure secondary to chronic lung disease and after operations on the biliary tract.
- Patients with severe liver or kidney complications.
- Head injuries and where intracranial pressure is raised.
- Acute alcoholism.
- Convulsive disorder.
- Premature infants or neonates.
- Children under the age of two years.
- Pregnancy and lactation
- Patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.
- ASTRAPAIN SYRUP should not be given during an attack of bronchial asthma or in heart disease secondary to chronic lung disease.
- Promethazine and codeine phosphate, as contained in **ASTRAPAIN SYRUP**, should not be given to comatosed patients.

4.4 Special warnings and precautions for use

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.

- If the patient does not respond, a doctor should be consulted.
- This medicine may cause drowsiness and impaired concentration, which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressant agents. Patients should be warned against performing potentially hazardous activities where loss of concentration may lead to accidents.
- Patients should be examined periodically for abnormal skin pigmentation or eye changes.
- Dosages of paracetamol in excess of those recommended may cause severe liver damage.
- The use of promethazine may be associated with the sudden infant death syndrome.
- Exceeding the described dose, together with prolonged and continuous use of this medication, may lead to dependency and addiction.
- Should be used in caution or in reduced doses in patients with adrenocortical insufficiency and hypothyroidism.
- Should be used with caution in patients with obstructive bowel disorders and myasthenia gravis.

Promethazine hydrochloride

ASTRAPAIN SYRUP may lead to drowsiness and impaired concentration, that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants.

Caution should be used when the following medical conditions exist: prostatic hypertrophy, narrow angle glaucoma, emphysema or chronic bronchitis and porphyria.

Paradoxical hyperexcitability, nervousness and insomnia, may occur in children and the elderly taking antihistamines. Elderly patients are especially susceptible to dizziness, sedation, confusion, hypotension and to anticholinergic effects such as dry mouth and urinary retention.

Promethazine should not be used in patients with pre-existing central nervous system depression, bone marrow depression, phaeochromocytoma or Reye's syndrome. Use with care in patients with epilepsy, jaundice, Parkinsonism, diabetes mellitus, hypothyroidism, and myasthenia gravis.

Risk of severe constipation if used with antidiarrhoeal agents such as diphenoxylate. Increased risk of constipation and urinary retention if used with other anticholinergic agents. Use with caution in patients with obstructive bowel disorders and prostatic hypertrophy.

Promethazine should be used with caution in patients with cardiovascular disease, closed angle glaucoma, asthma and urinary retention. The positive results of skin allergy tests may be suppressed.

Paracetamol

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 systematic (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 ASTRAPAIN SYRUP must immediately be discontinued and appropriate treatment instituted.

ASTRAPAIN SYRUP contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdosage 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 function damage. Patients suffering from hepatitis or alcoholism, or recovering from any form of liver disease, should not take paracetamol.

Codeine phosphate

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

Potentiates the effect of alcohol and other sedatives.

Prolonged use of high doses of codeine may lead to dependence.

There is a risk of severe constipation if used with antidiarrhoeal agents such as diphenoxylate. There is also an increased risk of constipation and urinary retention if used with other anticholinergic agents.

Codeine phosphate, as contained in ASTRAPAIN SYRUP, should be given with caution or in reduced doses to patients with hypotension, hypothyroidism, compromised respiratory function, adrenocortical insufficiency, prostatic hypertrophy, shock or head injury. It should be used with caution in patients with inflammatory or

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obstructive bowel syndrome. It should be given with caution to patients with myasthenia gravis. The administration during labour may cause respiratory depression in the newborn infant.

The dosage should be reduced in elderly and debilitated patients.

ASTRAPAIN SYRUP contains sucrose:

Patients with rare hereditary problems such as fructose intolerance, glucose-galactose mal-absorption or sucrase-isomaltase insufficiency should not take this medicine.

ASTRAPAIN SYRUP contains liquid glucose:

Patients with rare glucose-galactose malabsorption should not take this medicine.

ASTRAPAIN SYRUP contains invert syrup:

Patients with rare hereditary problems of fructose intolerance or glucose-galactose malabsorption should not take this medicine.

ASTRAPAIN SYRUP contains propylene glycol:

Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce adverse effects in children less than 5 years old.
While propylene glycol has not been shown to cause reproductive or development toxicity in animals or humans, it may reach the foetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case to case basis.
Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

ASTRAPAIN SYRUP contains ethanol

Co-administration with medicines containing e.g. propylene glycol or ethanol may lead to accumulation of ethanol and induce adverse effects, in particular in young children with low or immature metabolic capacity.

4.5 Interaction with other medicines and other forms of interaction

The anticholinergic effects of agents with anticholinergic properties may be enhanced. The depressant effects are aggravated by alcohol, anaesthetics, hypnotics, sedatives, tricyclic antidepressants, maprotiline and phenothiazines. Monoamine oxidase inhibitors may enhance the anticholinergic effects.

The warning signs of damage caused by ototoxic agents may be masked. May affect the activity of the other medicines by delaying their absorption.

Promethazine may potentiate the hypotensive effect of some antihypertensives. False negative and positive results have been reported with some pregnancy tests.

All sedatives, including alcohol, will potentiate depressant effects on the central nervous system if taken with antihistamines. The antiparkinsonian effects of levodopa may be inhibited

Antihistamines may suppress positive skin test results and should be stopped several days before the test.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/ Contraception in males and females
No information available.

Pregnancy
ASTRAPAIN SYRUP is contraindicated in pregnancy (see section 4.3)

Breastfeeding
ASTRAPAIN SYRUP is contraindicated in lactation (see section 4.3).

Fertility
No information available.

4.7 Effects on ability to drive and use machines

This medicine may cause drowsiness and impaired concentration, which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressant agents. Patients should be warned against performing potentially hazardous activities where loss of concentration may lead to accidents.

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4.8 Undesirable effects

Tabulated list of adverse reactions

Body System	**Undesirable effect**		
	Frequent	Less frequent	Frequency not known
PARACETAMOL			
Blood and the lymphatic system disorders:		Neutropenia Pancytopenia Leucopenia Thrombocytopenia Agranulocytosis Anaemia	
Skin and subcutaneous tissue disorders:		Skin rashes and other allergic reactions may occur. This rash is usually erythematous or urticarial, but sometimes more serious and may be accompanied by fever and mucosal lesions. The use of paracetamol has been associated with the occurrence of dermatitis.	Fixed dug eruptions (FDE) Drug-induced hypersensitivity syndrome (DIHS) have been reported in patients treated with paracetamol containing medicines.
Psychiatric disorders	Confusion Hallucinations A central effect include euphoria.		
Nervous system disorders	Sedation (varying from slight drowsiness to deep sleep, including dizziness and incoordination) Paradoxical central nervous system stimulation may occur especially in children, with insomnia, nervousness, tachycardia, tremors, ataxia, irritability and consvulsions. A central effect includes occasional headache.		
Ear and labyrinth disorders		Tinnitus	
Vascular disorders		Hypotension	
Gastrointestinal disorders		Side effects include gastrointestinal disturbances such as nausea, vomiting, diarrhoea or constipation, anorexia or increased	

		appetite, and epigastric pain. Pancreatitis may occur.	
Hepato-biliary disorders		This medicine can cause liver damage which may be fatal, if taken in excess.	The use of paracetamol has been associated with the occurrence of hepatitis.
Musculoskeletal, connective tissue and bone disorders		Other central effects include muscular weakness.	
Renal and urinary disorders		Prolonged excessive use may cause irreversible kidney damage. The use of paracetamol has been associated with the occurrence of renal colic, renal failure, sterile pyuria.	
General disorders and administrative site conditions	Lassitude		
CODEINE			
Cardiac disorders		Hypotension Orthostatic hypotension Circulatory failure	Bradycardia Palpitation
Gastrointestinal disorders	Constipation Nausea Vomiting		Dry mouth
Nervous system disorders:	Drowsiness Confusion	Hypothermia Deepening coma Euphoria Muscle rigidity Dry mouth Sweating Facial flushing Dizziness Restlessness Changes of mood	Raised intracranial pressure occurs in some patients.
Skin and subcutaneous tissue disorders			Pruritis Urticaria Contact dermatitis
Other disorders		Respiratory depression Raised intracranial pressure and miosis	
Psychiatric disorders	Confusion		Mood changes Restlessness
Vascular disorders			Facial flushing Orthostatic hypotension

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Eye disordrer		Miosis	
Ear and labyrinth disorders			Vertigo (dizziness)
Hepato-biliary disorders			Biliary spasm and antidiuretic effect.
Musculoskeletal, connective tissue and bone disorders			Muscle rigidity
Renal and urinary disorders	Micturition Ureteric spasm and an antidiuretic effect These effects occur more commonly in ambulant patients than in those at rest in bed.		
General disorders and administrative site conditions	Sweating		Hypothermia
PROMETHAZINE HYDROCHLORIDE			
Nervous system disorders	Sedation Lassitude Dizziness Hypertension Muscular weakness and in-coordination	Headache Tinnitus Elation or depression Irritability Halluciantion Dryness of the mouth Tightness of the chest and tingling Dissiness and weakness of the hands may occur In infants and children it may act as a cerebral stimulant. Symptoms of stimulation include insomnia, nervoursness, tachycardia, tremors, muscle twitching and convulsions. Large doses may precipitate fits in epileptics.	Extrapyramidal dysfunction
Cardiac disorders		Increase in heart rate.	Hypotension In high doses, transient bradycardia followed by tachycardia with palpitations and dysrhythmias can occur.
Gastrointestinal disorders:		Nausea Vomiting Constipation Diarrhoea Colic Epigastric pain	

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Blood and lymphatic system disorders		Blood dyscrasias including, Agranulocytosis, Leucopenia, Haemolytic anaemia Thrombocytopenic purpura	
Eye disorders			Blurred vision Depostiton of pigment in the eyes, corneal and lens opacities.
Renal and urinary disorders:		Difficulty in micturition and dysuria.	Polyuria
Immune system disorders			Idiosyncrasy Angioedema Lupus erythematous-like syndrome
Metabolism and nutrition disorders		Anorexia, or increased appetite.	
General disorders and administration site conditions			Lowering of blood temperature (occasionally pyrexia)
Psychiatric disorders		Irritability and restlessness.	Depression Hallucinations Insomnia
Vascular disorder		Dizziness	May also produce antimuscurinic effects including flushing.
Respiratory, thoracic and mediastinal disorders			May also produce antimuscarinic effects including thickened respiratory tract secretions, dryness of the nose, tightness of the chest.
Hepato-biliary disorders			Jaundice of the obstructive type
Skin and subcutaneous tissue disorders		Photosensitivity reactions and skin rash may ocuur.	Allergic dermatitis and thrombocytopaenic purpura have also been reported.
Musculoskeletal and connective tissue disorders			Weakness of hands

Post Marketing Experience:

Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicine. If a patient develops SCAR (Severe cutaneous adverse reactions), treatment with ASTRAPAIN SYRUP must immediately be discontinued and appropriate treatment instituted (see section 4.4).

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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 "Report Drug Reaction Process", found online under SAHPRA's safety publications: https://www.sahpra.org.za/

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 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 medicines that include 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 prothrombin time. The liver damage may lead to encephalopathy, coma and death.

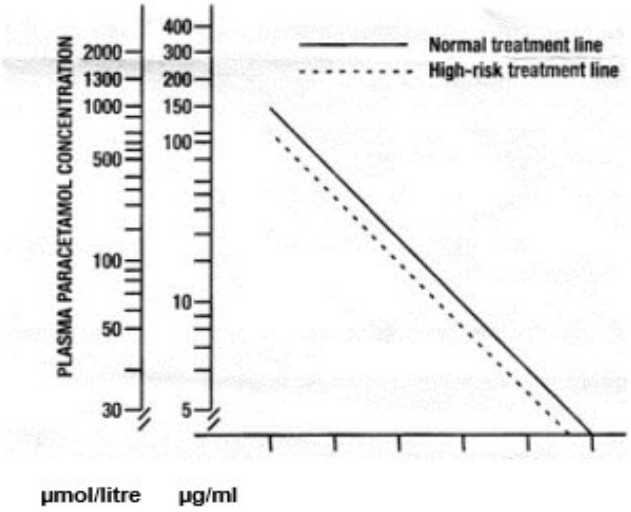
Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias have been reported.

Treatment for paracetamol overdosage:

N-acetylcysteine should be administered to all cases of suspected overdosage as soon as possible, preferably within 8 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 4 hours, and then 100 mg/kg in 1000 ml dextrose injection over the next 16 hours. **The volume of intravenous fluids should be modified for children.**

Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water as a 5% solution may be administered initially, followed by 70 mg/kg every 4 hours for 17 doses.

A plasma paracetamol level should be determined 4 hours after ingestion in all cases of suspected overdosage. Levels done before 4 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 plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the normogram.



Those whose plasma paracetamol levels are above the "normal treatment line", should continue N-acetylcysteine treatment with 100 mg/kg IV over 16 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 ingestion for at least 96 hours.

Promethazine:
Overdosage may be fatal, especially in infants and children in whom 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, respiratory collapse. Children and the elderly are more likely to exhibit anticholinergic and central nervous system stimulant effects. The elderly are prone to hypotension. Death may occur from respiratory failure. Drowsiness and hypotension may occur.

There is no specific antidote and ~~T~~treatment is symptomatic and supportive. It may be necessary to treat extrapyramidal reactions with barbiturates or diphenhydramine.

Codeine:
Symptoms of overdosage that may arise include excitement, consulsions and respiratory failure. Respiratory depression is the most important feature of overdosage with codeine containing preparations and it occurs with circulatory failure and a deepening coma. Pinpoint pupils, hypotension and hypothermia, excitement and convulsions, especially in children, and non-cardiogenic pulmonary oedema occur. Immediate attention should be given to maintaining adequate respiration.

Death may occur from respiratory failure. Naloxone should be given intravenously in a dose of 0,4 mg to 2 mg every 2 to 3 minutes until improvement occurs to a maximum of 10 mg. Children may be given 0,01 mg/kg initially followed by a dose of 0,1 mg/kg.

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

5 PHARMACOLOGICAL PROPERTIES

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5.1 Pharmacodynamic properties

Category and class: A 2.8 Analgesic combinations

ASTRAPAIN SYRUP has analgesic (relief of pain), antipyretic (reduces fever) and antihistaminic (prevention or relief of symptoms associated with some types of allergies such as hayfever and runny nose) properties.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Blackcurrant colour
- Citric Acid
- Essence Blackcurrent
- Ethanol 96 % v/v
- Invert Syrup
- Liquid Glucose
- Methylparaben
- Propylparaben
- Propylene Glycol
- Raspberry Red
- Sodium Cyclamate
- Sodium Saccharin
- Sucrose
- Vanilla Flavour

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 light.
Store in the original container.

6.5 Nature and contents of container

Amber, plastic or glass bottles containing 100 ml of syrup.

Not all pack sizes may be marketed.

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6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

No special requirements.

7 THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Astral Pharma (Pty) Ltd
125 Meade Street
George
6529
South Africa

8 REGISTRATION NUMBER

27/2.8/0139

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14 January 1995

10 DATE OF REVISION OF TEXT

31 December 2023

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