PACKAGE INSERT

SCHEDULING STATUS: S2

PROPRIETARY NAME (AND DOSAGE FORM):

ASTRAPAIN SYRUP(SYRUP)

COMPOSITION:

Each 5 ml of syrup contains:	Paracetamol	120 mg
	Codeine Phosphate	5 mg
	Promethazine hydrochloride	6,5 mg
	Preservatives: Methylparaben	0, 10 % m/v
	Propylparaben	0,01 % m/v
	Alcohol content	12,5 %
	Sugar content	40 % (m/v)

PHARMACOLOGICAL CLASSIFICATION:

A 2.8 Special analgesic combinations.

PHARMACOLOGICAL ACTION:

ASTRAPAIN SYRUP has analgesic, antipyretic and antihistaminic properties.

INDICATIONS:

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

CONTRA-INDICATIONS:

Sensitivity to paracetamol, opiates or phenothiazines. During an attack of bronchial asthma, respiratory depression, especially in the presences of cyanosis and excessive bronchial secretion, heart failure secondary to chronic lung disease, liver or kidney damage, head injuries and where intracranial pressure is raised.

Acute alcoholism. Premature infants or neonates.

WARNINGS:

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.

1. If the patient does not respond, a doctor should be consulted.

2. Do not take continuously for more than 10 days without consulting a doctor.

3. 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.

4 Patients should be examined periodically for abnormal skin pigmentation or eye changes.

5. Should be used with extreme caution in patients receiving monoamine-oxidase inhibitors.

6. Dosages of paracetamol in excess of those recommended may cause severe liver damage.

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

DOSAGE AND DIRECTIONS FOR USE:

DO NOT EXCEED THE RECOMMENDED DOSE.

1 to 5 years: One medicine measurefull (5 ml) three times a day.

6 to 12 years: One to two medicine measurefulls (5 to 10 ml) three times a day.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

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.

Side-effects from codeine that may occur are respiratory depression, bradycardia, circulatory failure, hypotension, orthostatic hypotension, palpitations, deepening coma, confusion, drowsiness, euphoria, mood changes, restlessness, vertigo (dizziness), flushing, hypothermia, increased intracranial pressure, miosis, dry mouth, muscle rigidity, nausea, vomiting, constipation, pruritus, urticaria, sweating, urinary retention, uteric and biliary spasm and an antidiuretic effect.

Should be used with caution or in reduced doses in patients with adrenocortical insufficiency, and hypothyroidism. Should be used with caution in patients with obstructive bowel disorders, liver impairment, myasthenia gravis, impaired renal function or shock.

Dosage should be reduced in debilitated patients. Promethazine and codeine should be used with caution in patients with liver impairment. Prolonged use of high doses of codeine may lead to dependence.

The following side-effects with promethazine have been reported:

Dizziness, lassitude, hypotension, muscular weakness and inco-ordination, nausea, vomiting, diarrhoea or constipation, colic and epigastric pain. It may also produce headache, hallucinations, blurred vision, tinnitus, elation or depression, irritability, anorexia, difficulty in micturition, dryness of the mouth, tightness of the chest and weakness of the hands. Large doses may precipitate fits in epileptics. Blood dyscrasias, including agranulocytosis, leucopenia, haemolytic anaemia and

thrombocytopenic purpura have been reported. Idiosyncrasy and angioedema have been reported.

Other side-effects are polyuria, tiredness and weakness, lowering of temperature (occasionally pyrexia), increase in heart rate, restlessness, insomnia and photosensitivity and skin rash. Extra-pyramidal dysfunction. Deposition of pigment in the eyes, corneal and lens opacities.

Jaundice of the obstructive type and a lupus erythematous-like syndrome has been reported.

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

Interactions:

The anticholinergic effects of agents with anticholinergic properties may be enhanced. The depressant effects are aggravated by alcohol, anaesthetics, hypnotics, sedatives, tricyclic antidepressants 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.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

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:

Although evidence is limited it is recommended that any adult person who has ingested about 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). ln 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 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 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. Death may occur from respiratory failure. Drowsiness and hypotension may occur. Treatment is symptomatic and supportive.

Codeine:

Symptoms of overdosage that may arise include excitement, convulsions and respiratory failure.

Codeine Phosphate:

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 naloxone may be used to counteract severe respiratory depression.

IDENTIFICATION:

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

PRESENTATION:

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

STORAGE INSTRUCTIONS:

Store below 25°C, in a cool place and protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

27/2.8/0139

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