SCHEDULING STATUS: S2

PROPRIETARY NAME: **PROPAIN®**

(AND DOSAGE FORM) **(TABLET)**

COMPOSITION:

Each tablet contains:

Codeine phosphate	10 mg
Diphenhydramine hydrochloride	5 mg
Paracetamol	400 mg
Caffeine anhydrous	50 mg
Preservative:	
Total parabens (Nipastat/Salistat)	0,1 % *m/m*

Sugar free

Contains no tartrazine

List of excipients: colour yellow anstead 18900, Polyvinylpyrrolidone (PVP K25), magnesium stearate, Pregelatinized starch, Purified Talc.

CATEGORY AND CLASS:

A 2.8 Analgesic combinations

PHARMACOLOGICAL ACTION:

Paracetamol has analgesic and antipyretic actions. Codeine phosphate is an analgesic. Diphenhydramine HCl has sedative and antihistaminic properties and, in combination with the above analgesics is of value, especially in tension states.

Note: **PROPAIN** tablets may be used to advantage by people who cannot tolerate aspirin e.g. aspirin sensitivity, peptic ulcer patients, acute and chronic gastritis patients on steroid therapy.

INDICATIONS:

Headaches, including those due to sustained muscle contraction - tension headaches. Pain and stiffness in muscle joints - low back pain. Dysmenorrhoea, premenstrual tension, period pain. Toothache and dental pain. Neuralgia.

CONTRAINDICATIONS:

Hypersensitivity to paracetamol or any of the other components.

Codeine should not be given during an attack of bronchial asthma or in heart failure secondary to chronic lung disease. It is contraindicated in the presence of acute alcoholism, head injuries and conditions in which intracranial pressure is raised.

Codeine should be administered with extreme caution to patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.

WARNINGS AND SPECIAL PRECAUTIONS:

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

Consult your doctor if no relief is obtained with the recommended dosage. Do not use continuously for longer than 10 days without consulting your doctor.

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

Do not administer to children under 12 years of age.

This medicine may lead to drowsiness and impaired concentration which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants.

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

Diphenhydramine hydrochloride should be used with care in patients suffering from conditions such as closed angle glaucoma, urinary retention, prostatic hypertrophy and pyloroduodenal obstruction.

Caution should be taken in patients with epilepsy or severe cardiovascular disorders.

Diphenhydramine hydrochloride may mask the warning signs of damage caused by ototoxic drugs such as aminoglycoside antibiotics; and may suppress positive skin test results and should be stopped several days before the test.

Codeine should be used with extreme caution in patients with decreased respiratory reserve. Codeine should be used with caution in patients with obstructive bowel disorders, liver impairment, myasthenia

gravis, prostatic hypertrophy, impaired renal function or shock. It should be used with caution or in reduced doses in patients with adrenocortical insufficiency and hypothyroidism.

Caffeine should be administered with caution to patients with a history of peptic ulceration or hyperacidity, hyperthyroidism, hypertension, cardiac arrhythmias or other cardiovascular disease or uncontrolled seizure disorders as these conditions may be exacerbated.

INTERACTIONS:

Paracetamol should be given with care to patients taking other drugs that effect the liver.

Diphenhydramine hydrochloride may enhance the sedative effects of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillisers. Monoamine oxidase inhibitors may enhance the effects of antihistamines and diphenhydramine hydrochloride may have an additive antimuscarinic action with other antimuscarinics such as atropine and tricyclic antidepressants.

Codeine may affect the activity of other medicines by delaying their absorption. The depressant effects are aggravated by alcohol, anaesthetics, hypnotics, sedatives, tricyclic antidepressants and phenothiazines.

HUMAN REPRODUCTION:

Safety has not been proven in pregnancy.

DOSAGE AND DIRECTIONS FOR USE:

Adults and children over 12 years: One or two tablets repeated 4 hourly if necessary. Do not exceed 8 tablets per day.

SIDE EFFECTS:

Paracetamol:

Side effects of paracetamol are usually mild, though haematological reactions including thrombocytopenia, leucopenia, pancytopenia, neutropenia and agranulocytosis have been reported. Pancreatitis, skin rashes and other allergic reactions occur occasionally.

Diphenhydramine hydrochloride:

Diphenhydramine hydrochloride may give rise to sedation, varying from slight drowsiness to deep sleep, and including lassitude, dizziness and inco-ordination. Sedative effects when they occur, may diminish after a few days of treatment.

Paradoxical central nervous system stimulation may occur especially in children. Symptoms of cerebral stimulation with insomnia, nervousness, euphoria, irritability, tremors and rarely nightmares, hallucinations and convulsions. In high doses CNS stimulation may be attributed to antimuscarinic activity.

Diphenhydramine hydrochloride possesses antimuscarinic properties and may give rise to side effects including dry mouth, thickened respiratory tract secretions and tightness of chest, blurred vision, urinary difficulty and retention, constipation and increased gastric reflux. In high doses transient bradycardia followed by tachycardia with palpitations and arrhythmias. Gastrointestinal disturbances such as nausea, vomiting, diarrhoea or epigastric pain has occurred with antihistamines.

Hypersensitivity reactions particularly of the skin and cross sensitivity to related drugs may occur.

Blood disorders including agranulocytosis, leucopenia, haemolytic anaemia, thrombocytopenia and jaundice, although rare, have been reported.

Other side effects that have been reported with antihistamines, although rarely, include hypotension, tinnitus, headache and paraesthesia.

Elderly patients are susceptible to many adverse effects of diphenhydramine hydrochloride including antimuscarinic effects, sedation and hypotension.

Codeine phosphate:

Codeine may cause nausea, vomiting, constipation, drowsiness and confusion; urinary retention, ureteric and biliary spasm, and an antidiuretic effect. Dry mouth, sweating, flushing, vertigo, bradycardia, palpitations, orthostatic hypotension, hypothermia, restlessness, mood changes, euphoria and miosis can occur. Raised intracranial pressure and muscle rigidity have been reported following high doses.

Caffeine:

Caffeine may cause insomnia, headache, nausea, gastrointestinal irritation, stimulation of the CNS and palpitations.

KNOWN SYMPTOMS OF OVER-DOSAGE AND PARTICULARS OF ITS TREATMENT:

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 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 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 non-specific myocardial depression have also occurred.

In the event of an 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. Any patient who has ingested about 7,5 g of paracetamol in the preceding 4 hours should undergo gastric lavage. Specific therapy with an antidote such as acetylcysteine should be administered IV as soon as possible.

Acetylcysteine:

Acetylcysteine should be administered as soon as possible, preferably within 8 hours of overdosage.

IV: An initial dose of 150 mg/kg in 200 ml glucose injection, given intravenously over 15 minutes, followed by an intravenous infusion of 50 mg/kg in 500 ml of glucose 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. Acetylcysteine is effective if administered within 8 hours of overdosage.

Overdosage of antihistamines may be fatal especially in children. Overdosage with diphenhydramine hydrochloride is associated with antimuscarinic, extrapyrimidal, gastrointestinal and CNS effects. In children CNS stimulation predominates. In adults CNS depression is more common with drowsiness, coma and convulsions, progressing to respiratory failure or possible cardiovascular collapse.

In severe overdosage with antihistamines or caffeine the stomach should be emptied. Activated charcoal has been given, as have saline laxatives. Convulsions may be controlled with diazepam although it has

been suggested that CNS depressants should be avoided with overdose of antihistamines. Cerebral stimulants may increase the risk of convulsions and should be avoided.

Large doses of codeine produce respiratory depression and hypotension, with circulatory failure and deepening coma. Convulsions may occur especially in children. Rhabdomyolysis, progressive renal failure has been reported in overdose. Coma, pinpoint pupils and respiratory depression are considered indicative of overdosage.

Codeine phosphate: In acute poisoning the stomach should be emptied by aspiration and lavage.

Severe overdosage of caffeine or idiosyncrasy may lead to maniac behaviour, diuresis and repeated vomiting with extreme thirst, tremor, delirium, hyperthermia, tachycardia, tachypnoea, electrolyte disturbances, convulsions and death.

See also '**SIDE EFFECTS'**

Other treatment is symptomatic and supportive.

IDENTIFICATION:

Round, yellow, flat, bisected tablets.

PRESENTATION:

Blister packs of 4, 18, 20, 40, 54, 100 using PVC film and printed aluminium foil. White HDPE (high density polyethylene) securitainers with LDPE (low density polyethylene) closures containing 100 tablets. Brown HDPE bottles with black, screw on caps containing 1 000 tablets. All pack sizes may not be marketed simultaneously.

STORAGE INSTRUCTIONS:

Store at or below 25 ºC.

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

Store in a safe place.

KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBER:

F/2.8/8

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

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand,1685

Private Bag X69

Bryanston, 2021

www.adcock.com

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION:

Date of registration: 06/05/1974

Date of Revision : 12 February 1980

Zimbabwe: 77/2.2/909 P

Namibia: NS2 90/2.8/00165

Botswana: B9323340 S3