SOUTH AFRICAN PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S2

PROPRIETARY NAME AND DOSAGE FORM

LENAPAIN (tablet)

COMPOSITION

Each tablet of LENAPAIN contains:

Codeine phosphate	10,00 mg
Doxylamine succinate	5,00 mg
Paracetamol	450,00 mg
Caffeine anhydrous	30,00 mg

Excipients:

Colloidal silicone dioxide, colour spectracol quinolone yellow, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, povidone, starch maize

Sugar free

CATEGORY AND CLASS

A 2.9 Other analgesics

PHARMACOLOGICAL ACTION

LENAPAIN has analgesic, antipyretic and antihistaminic action.

INDICATIONS

Relief of mild to moderate pain associated with tension.

CONTRAINDICATIONS

- Sensitivity to any of the ingredients.
- The dosage in renal functional impairment must be reduced.
- LENAPAIN should be taken only with caution by asthmatics.
- Severe liver function impairment.
- LENAPAIN should not be administered to patients with acute intermittent porphyria.
- Asthma, respiratory depression especially in the presence of cyanosis and excessive bronchial secretion.
- Head injuries and conditions in which intracranial pressure is raised.
- Heart failure secondary to chronic lung disease, a history of cardiac disease.
- Epilepsy and all convulsive states.
- Patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.
- Acute alcoholism.
- LENAPAIN should not be taken during pregnancy, nor whilst breastfeeding (see HUMAN REPRODUCTION).

WARNINGS AND SPECIAL PRECAUTIONS

Dosages in excess of those recommended may cause severe liver damage. Patients suffering from liver or kidney disease should take paracetamol under medical supervision. Consult your doctor if no relief is obtained with the recommended dosage. Taking LENAPAIN may lead to drowsiness and impaired concentration, which may be aggravated by simultaneous intake of alcohol or other central nervous system depressants. Do not use LENAPAIN continuously for longer than 10 days without consulting your doctor. Exceeding the prescribed dose, together with prolonged and

continuous use of LENAPAIN, may lead to dependency and addiction.

Doxylamine, as contained in LENAPAIN, should be used with care in the elderly, and in conditions such as closed-angle glaucoma, urinary retention, liver impairment, prostatic hypertrophy or pyloroduodenal obstruction. Use with care in cardiac failure, hypertension, oedema and cardiovascular disease.

Effects on ability to drive and use machines

Patients should be warned against taking charge of a vehicle or machinery and performing potentially hazardous tasks where loss of concentration may lead to accidents.

INTERACTIONS

Doxylamine succinate

Doxylamine succinate, as contained in LENAPAIN, may enhance the sedative effects of central nervous system depressants including alcohol, tricyclic antidepressants, barbiturates, hypnotics, narcotics analgesics, sedatives and tranquillisers. Monoamine oxidase inhibitors may enhance the antimuscarinic effects of doxylamine succinate, and it has additive effects with other antimuscarinic agents, such as atropine and tricyclic antidepressants. It has been suggested that doxylamine succinate could mask the warning signs of damage caused by ototoxic medicines such as aminoglycoside antibiotics.

Codeine phosphate

Do not take monoamine oxidase inhibitors with LENAPAIN or within 14 days of taking such a treatment (see CONTRAINDICATIONS). The depressant effects of codeine, as contained in LENAPAIN, are enhanced by depressants such as alcohol, anaesthetics, hypnotics, sedatives, tricyclic antidepressants and phenothiazines. The gastrointestinal effects may delay absorption as with mexiletine or may be counteractive as with metoclopramide.

HUMAN REPRODUCTION

LENAPAIN is contraindicated in pregnancy and lactation (see CONTRAINDICATIONS).

DOSAGE AND DIRECTIONS FOR USE

Adults:

Take one to two tablets every 4 to 6 hours. Do not exceed 8 tablets per day.

SIDE EFFECTS

Doxylamine succinate

Blood and lymphatic system disorders

Agranulocytosis, leucopenia and haemolytic anaemia have been reported.

Immune system disorders

Allergic reaction and cross-sensitivity to related medicine may occur.

Psychiatric disorders

Other central effects include euphoria or depression, irritability and nightmares.

Nervous system disorders

The most common side effect is sedation, varying from slight drowsiness to deep sleep, and including lassitude, dizziness and in-coordination. Paradoxical central nervous system stimulation may occur with insomnia, nervousness, tachycardia, tremors and convulsion. Doxylamine succinate may precipitate epileptiform seizures in patients with focal lesion of cerebral cortex. Other central effects include headache.

Eye disorders

Doxylamine succinate may also produce antimuscarinic effects including blurred vision.

Ear and labyrinth disorders

Other central effects including tinnitus.

Vascular disorders

Other central effects include hypotension.

Respiratory, thoracic and mediastinal disorders

Doxylamine succinate may also produce antimuscarinic effects including tightness of the chest.

Gastrointestinal disorders

Other side effects include gastrointestinal disturbances such as nausea, vomiting, diarrhoea or constipation, anorexia or increased appetite and epigastric pain. Doxylamine succinate may also produce antimuscarinic effects including dryness of the mouth.

Musculoskeletal, connective tissue and bone disorders

Other central effects include muscular weakness.

Renal and urinary disorders

Doxylamine succinate may also produce antimuscarinic effects including difficulty in micturition and dysuria.

Codeine phosphate

Immune system disorders

A dose-related histamine-releasing effect which may be responsible in part for reactions such as urticaria, pruritus as well as hypotension and flushing may occur.

Psychiatric disorders

Its euphoric activity has led to abuse. The most common side effect is confusion*. Restlessness, changes of mood and hallucinations may occur, these effects are more common in ambulant patients and in those without severe pain.

Nervous system disorders

The most common side effect is drowsiness*. Raised intracranial pressure occurs in some patients. Vertigo may occur, this effect is more common in ambulant patients and in those without severe pain.

Eye disorders

Miosis may occur, this effect is more common in ambulant patients and in those without severe pain.

Cardiac disorders

Bradycardia and palpitations may occur, these effects are more common in ambulant patients and in those without severe pain.

Vascular disorders

Facial flushing and orthostatic hypotension may occur, these effects are more common in ambulant patients and in those without severe pain.

Gastrointestinal disorders

The most common side effects are nausea*, vomiting* and constipation*. Dry mouth may occur, this effect is more common in ambulant patients and in those without severe pain.

Hepato-biliary disorders

There may be biliary spasm.

Renal and urinary disorders

Micturition may be difficult and there may be ureteric spasm as well as an antidiuretic effect.

General disorders and administrative site conditions

Hypothermia may occur, this effect is more common in ambulant patients and in those without severe pain.

*Tolerance usually develops to nausea, vomiting, drowsiness and confusion, but not to constipation.

Caffeine anhydrous

Psychiatric disorders

Insomnia, anxiety, restlessness.

Nervous system disorders

Headache, dizziness.

Cardiac disorders

Palpitations.

Gastrointestinal disorders

Gastrointestinal irritation, nausea, vomiting, abdominal pain, diarrhoea and gastrointestinal bleeding.

Paracetamol

Blood and lymphatic system disorders

Haematological reactions including thrombocytopenia, leucopenia, pancytopenia, neutropenia, agranulocytosis, anaemia have been reported.

Immune system disorders

Skin rashes and allergic reactions occur occasionally.

Gastrointestinal disorders

Pancreatitis occurs occasionally.

Hepato-biliary disorders

Hepatitis occurs occasionally.

Renal and urinary disorders

Renal colic, renal failure, sterile pyuria occur occasionally.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Doxylamine succinate

Symptoms

In children central nervous system stimulation, resulting in ataxia, excitement, tremors, psychoses, hallucinations and convulsions occurs. Hyperpyrexia may occur. Deepening coma and cardiorespiratory collapse may follow. Death may occur from respiratory failure. In adults, central nervous system depression is more common, with drowsiness, coma and convulsions, progressing to respiratory failure or possible cardiovascular collapse.

Treatment

Treatment is supportive and symptomatic.

Codeine phosphate

Symptoms

Large doses may cause excitement and convulsions, respiratory depression and hypotension with circulatory failure and deepening coma. Rhabdomyolysis progressing to renal failure has been reported in overdosage. Death may occur from respiratory failure. Toxic doses vary considerably with the individual and regular users may tolerate larger doses. The threat of coma, pinpoint pupils and respiratory depression is considered indicative of overdosage, dilation of pupils occurs as hypoxia develops. Pulmonary oedema after overdosage is a common cause of fatalities among addicts.

Treatment

In acute poisoning, the stomach should be emptied. A laxative may be given to aid peristalsis. Intensive supportive therapy may be required to correct respiratory failure and shock. In addition a specific antagonist, naloxone hydrochloride, is used to very rapidly counteract the severe respiratory depression and coma produced by excessive doses of opioid analgesics. A dose of 0,4 mg to 2 mg is given by intravenous injection, repeated at intervals of 2 to 3 minutes if necessary, up to 10 mg. Naloxone may also be given by subcutaneous injection, intra-muscular injection or by intravenous infusion. The effect of naloxone may be of shorter duration than that of the opioid analgesic and additional doses may be required to prevent relapses. Nalorphine and levallorphan have also been used to antagonise adverse effects of opioid analgesics. These antagonists may induce withdrawal symptoms in persons physically dependent on morphine related analgesics.

Caffeine anhydrous

Symptoms

Severe overdosage or idiosyncrasy may lead to maniacal behaviour, diuresis and repeated vomiting with extreme thirst, tremor, delirium, hyperthermia, tachycardia, tachypnoea, electrolyte disturbances, convulsions and death. Severe toxicity may not be preceded by milder symptoms.

Treatment

In cases of overdosage, consult a doctor immediately. Treatment is supportive and symptomatic.

Paracetamol

Symptoms

Symptoms of paracetamol overdosage in the first 24 hours are pallor, increased sweating, nausea, vomiting, diarrhoea, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, convulsions, respiratory depression, coma, cerebral oedema, coagulation defects, gastrointestinal bleeding, disseminated intravascular coagulation, hypoglycaemia, metabolic acidosis, cardiac dysrhythmia and cardiovascular collapse may occur. Acute renal failure with tubular necrosis may develop even in the absence of severe liver damage.

Treatment

Prompt treatment is essential in the management of paracetamol overdosage. Any patient who has ingested about 7,5 g or more in the preceding 4 hours should undergo gastric lavage. The plasma or serum-paracetamol concentration should be determined as soon as possible, but no sooner than 4 hours after ingestion. Generally, treatment is required if the paracetamol concentration is higher than a line [the ‘200’ line] drawn on semi-log/linear paper joining the

points 200 mg per litre [1,32 mmol per litre] at 4 hours and 30 mg per litre [0,20 mmol per litre] at 15 hours.

Acetylcysteine is given either intravenously or by mouth and tends to be preferred to methionine which is given by mouth to increase glutathione stores and stimulate the nontoxic metabolism of paracetamol.

Acetylcysteine should be started as soon as possible, preferably within 8 hours of overdosage. Oral treatment is usually given for 72 hours and intravenous therapy for 20 hours [up to 48 hours]. It has been suggested that the 72 hour oral regimen may be more effective than the 20 hour IV regimen if the treatment is delayed.

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 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.

IDENTIFICATION

A yellow, flat, circular, bevelled-edged tablet, bisected on one side and imprinted “C54” on the other side.

PRESENTATION

18 or 36 tablets packed in clear PVC/Aluminium foil blister strips. Each blister sheet contains 18 tablets, and is packed in an outer cardboard carton.

Not all pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C. Protect from light.

Exposure to air should be MINIMUM.

Keep the blisters in the carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

Q/2.9/301

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

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

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