28800
Ref. No: B2128800/23.08

Costapyn® (Tablets)

Paracetamol / Codeine Phosphate / Caffeine Anhydrous / Doxylamine Succinate

Anilides / Paracetamol Combinations

COSTAPYN® TABLETS

PRESENTATION:
Costapyn® Tablets: Yellow, circular, flat bevelled tablet plain on one side and 'breakline' on the other side. Each tablet contains Paracetamol 450mg, Codeine Phosphate 10mg, Caffeine Anhydrous 50mg, Doxylamine Succinate 5mg and other excipients.

CLINICAL PHARMACOLOGY:
Paracetamol is an analgesic that acts peripherally, probably by blocking impulse generation at the bradykinin-sensitive chemo-receptors that evoke pain. Although it is a prostaglandin synthetase inhibitor, the synthetase system in the CNS rather than the periphery appears to be more sensitive to it. This may explain paracetamol's lack of appreciable anti-inflammatory activity. Paracetamol also exhibits antipyretic activity.
Codeine is a centrally-acting weak analgesic. Codeine exerts its effect through μ opioid receptors, although codeine has a low affinity for these receptors, and its analgesic effect is due to its conversion to morphine. Codeine, particularly in combination with other analgesics such as paracetamol, has been shown to be effective in acute nociceptive pain.

PHARMACOKINETICS:
The pharmacokinetics of Paracetamol, Codeine Phosphate and Caffeine are widely published (see Goodman and Gilman's Pharmacological Basis of Therapeutics, Seventh Edition pgs. 693, 505 and 596 respectively. Doxylamine Succinate is readily absorbed from the gastrointestinal tract. Following oral administration, the effects start within 15 to 30 minutes and peak within one hour. In humans, 60 - 80% of Doxylamine given has been recovered in urine at 24 hours post-dose.
The bioavailabilities of Paracetamol and Codeine Phosphate when given as a combination are similar to those when they are given separately.
Codeine is mainly metabolized by glucuronidation to codeine-6-glucuronide. Minor routes of metabolism include O- O-demethylation leading to morphine, N-demethylation to norcodeine and both O- and N-demethylation to normorphine. Morphine and norcodeine are further transformed into glucuronide conjugates. Unchanged Codeine and its metabolites are mainly excreted by the urinary route within 48h (84.4±15.9%). The O-demethylation of codeine to morphine is catalyzed by the cytochrome P450 isozyme 2D6 (CYP2D6) which shows genetic polymorphism that may affect the efficacy and toxicity of Codeine.
Genetic polymorphism in CYP2D6 leads to ultra-rapid, extensive and poor metabolizer phenotypes.

USES:
For the short-term treatment of acute moderate pain that is not relieved by Paracetamol, Ibuprofen or Aspirin alone such as headache, tension headache, migraine, neuralgia, toothache, dysmenorrhea, muscular and rheumatic aches and pains and post-operative analgesia following surgical or dental procedures.

DOSAGE AND ADMINISTRATION:
The duration of treatment should be limited to 3 days and if no effective pain relief is achieved the patients/carers should be advised to seek the views of a physician. Do not take continuously for more than 3 days without consulting your doctor as the prolonged use of high doses of Codeine has produced dependence on the morphine type.
Adults
One or two tablets every four to six hours as needed for relief. The total dosage over a 24-hour period should not normally exceed eight tablets.
Elderly and Debilitated
Codeine should be used with caution in the elderly and debilitated patients as they may be more susceptible to the respiratory depressant effects.
Paediatric population
Children aged less than 12 years:
Codeine should not be used in children below the age of 12 years because of the risk of opioid toxicity due to the variable and unpredictable metabolism of codeine to morphine
Children aged 16 years to 18 years:
One to two tablets every 6 hours, up to a maximum of 8 tablets in 24 hours.
Children aged 12 years to 15 years:
One tablet every six hours when necessary to a maximum of 4 tablets in 24 hours

CONTRA-INDICATIONS:
Hypersensitivity to the active substance or to any of the excipients.

ADVERSE EFFECTS:
Feeling sick (nausea) • Being sick (vomiting) • Low blood pressure (causing light-headedness or fainting when standing up) • Confusion • Depression • Difficulties sleeping • Shaking, fits • Irregular heartbeat • Stomach pain • Sweating • Facial flushing • General discomfort • Loss of appetite • Very slow or shallow breathing • Shortness of breath • Hallucinations, nightmares • Cramps or stiffness • Becoming dependent on codeine.

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OVERDOSAGE:
Signs of overdose may include unusually pale skin, nausea, vomiting, loss of appetite, abdominal pain, pupils that may be pinpoint in size, difficulty in breathing, an increased or irregular heart rate, and loin (kidney) pain.

- Talk to a doctor at once if you take too much of this medicine even if you feel well. This is because too much Paracetamol can cause delayed, serious liver damage.
- Remember to take any remaining tablets and the pack with you. This is so the doctor knows what you have taken.

DRUG INTERACTIONS:
Benzodiazepines
The concomitant use of opioids with sedative medicines such as benzodiazepines or related drugs increases the risk of sedation, respiratory depression, coma and death because of the additive CNS depressant effect. The dosage and duration of concomitant use should be limited.
Alcohol and Opioids
The concomitant use of alcohol and opioids increases the risk of sedation, respiratory depression, coma, and death because of the additive CNS depressant effect. Concomitant use with alcohol is not recommended.
The hypotensive actions of diuretics and anti-hypertensive agents 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.
The respiratory depressant effect caused by neuromuscular blocking agents may be additive to the central respiratory depressant effects of opioid analgesics. Quinidine can inhibit the analgesic effect of codeine.
Concurrent use of Codeine with antidiarrheal and ant-peristaltic agents such as loperamide and kaolin may increase the risk of severe constipation. Concomitant use of antimuscarinics or medications 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 antagonize the gastrointestinal effects of metoclopramide, cisapride and domperidone. Cimetidine inhibits the metabolism of opioid analgesics resulting in increased plasma concentrations.

SPECIAL WARNINGS AND PRECAUTIONS:
Talk to your doctor or pharmacist before taking Costapyn® if:

- You have liver, kidney, thyroid or heart problems and/or are elderly or in a weakened state.
- You have high blood pressure, problems with the prostate gland, obstructive bowel problems, acute abdominal conditions (e.g. peptic ulcer), hormonal problems, problems passing urine or have had recent gastrointestinal surgery;
- You are in shock, have gallstones, glaucoma, or a disease called myasthenia gravis (a condition which weakens muscles) or a history of fits.
- You have a history of mood swings, alcohol or drug abuse or are under psychiatric treatment.
- You are taking a benzodiazepine (used for the treatment of anxiety or sleep disorders), e.g. diazepam, clobazam, lorazepam, chlordiazepoxide, oxazepam, temazepam, nitrazepam, loprazolam, lormetazepam or clonazepam.

Codeine is transformed into morphine in the liver by an enzyme. Morphine is a substance that produces pain relief. Some people have a variation of this enzyme, which can affect people differently. In some people, morphine is not produced or produced in very small quantities, and it will not provide enough pain relief. Other people are more likely to get serious side effects because a very high amount of morphine is produced. If you notice any of the following side effects, you must stop taking this medicine and seek immediate medical advice: slow or shallow breathing, confusion, sleepiness, small pupils, feeling or being sick, constipation, and lack of appetite.

Pregnancy and Breastfeeding:
The safety of Costapyn® Tablets during fertility, pregnancy and lactation has not been established therefore consult a physician before use.

PHARMACEUTICAL PRECAUTIONS:
Store in a dry place below 30ºC. Protect from light. Keep all medicines out of the reach of children.

LEGAL CATEGORY:
Prescription Only Medicine (POM)

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