

1. NAME OF THE MEDICINAL PRODUCT

Copaz or Codipar caplet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each caplet contains Paracetamol 500mg and Codeine Phosphate 15mg.

3. PHARMACEUTICAL FORM

Coated tablet

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

For the relief of moderate pain.

4.2. Posology and method of administration

Adults The usual dose is one or two caplets every four hours as required. The total daily dose of paracetamol should not exceed 4g (8 caplets in a day).

Elderly A reduced dosage may be necessary.

Children Not recommended in children below the age of 12 years.

Dosage needs to be adjusted according to the severity of pain and the response of the patient.

Method of administration: Oral.

4.3. Contraindications

Hypersensitivity to either Paracetamol or codeine, or any of the excipients of Copaz caplets.

Children under 12 years of age.

Patients who have taken MAOIs within 14 days.

Severe renal or hepatic impairment.

Copaz is contraindicated in patients for whom opiate medications are contraindicated.

This will include some patients with acute asthma, obstructive airway disease, respiratory depression, acute alcoholism, head injuries, raised intracranial pressure and following biliary surgery.

4.4 Special warnings and precautions for use

The efficacy and safety of Copaz caplets in children below the age of 12 years has not been established, and use in such children is contraindicated.

Copaz caplets must be used with caution in patients with increased intracranial pressure, acute abdominal conditions, the elderly, the debilitated, impaired hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy and urethral stricture.

The increased hazard of paracetamol overdosage in patients with alcoholic liver disease.

Patients should be advised not to exceed the recommended dose and not to take other products containing paracetamol or opiate derivatives.

Patients should be advised to consult their doctor if symptoms persist.

Tolerance to Codeine can develop with continued use. The incidence of unwanted effects is dose related.

The risk-benefit of continued use should be assessed regularly by the prescriber.

The leaflet will state in a prominent position in the 'before taking' section

- Do not take for longer than directed by your prescriber
- Taking codeine/dihydrocodeine (DHC) regularly for a long time can lead to addiction, which might cause you to feel restless and irritable when you stop taking the tablets.
- Taking a painkiller for headaches too often or for too long can make them worse.

The label will state (To be displayed prominently on outer pack- not boxed):

- Do not take for longer than directed by you prescriber as taking codeine/DHC regularly for a long time can lead to addiction.

4.5 Interaction with other medicinal products and other forms of interaction

The hypotensive effects of antihypertensive agents, including diuretics, may be potentiated by codeine.

Quinine or quinidine may inhibit the analgesic actions of codeine.

The CNS depressant action of Zapaain may be enhanced by coadministration with any other drug which has a CNS depressant effect (eg. anxiolytics, hypnotics, antidepressants, antipsychotics and alcohol). Concomitant use of any drug with a CNS depressant action should be avoided. If combined therapy is necessary, the dose of one or both agents should be reduced.

Concomitant administration of Copaz and MAOIs or tricyclic antidepressants may increase the effect of either the antidepressant or codeine.

Concomitant administration of codeine and anticholinergics may cause paralytic ileus. Concomitant administration of codeine with an anti-diarrhoeal agent increases the risk of severe constipation, and coadministration with an antimuscarine drug may cause urinary retention.

The absorption of paracetamol is speeded by metaclopramide or domperidone, and absorption is reduced by cholestyramine.

Codeine may delay the absorption of mexilitine, and cimetidine may inhibit codeine metabolism.

Opioids may interfere with the results of plasma amylase, lipase, bilirubin, ALP, LDH, AST, and ALT tests

The effects of codeine on the gut may interfere with diagnostic tests of gastrointestinal functions.

The anticoagulant effect of warfarin and other coumarins may be increased by long term regular daily use of paracetamol, with increased risk of bleeding.

Occasional doses of paracetamol do not have a significant effect on these anticoagulants.

4.6. Pregnancy and lactation

Copaz is not recommended during pregnancy or lactation.

Codeine crosses the placenta and is found in breast milk.

Use during pregnancy may lead to withdrawal syndromes in neonates, and use during labour may cause neonatal respiratory depression.

4.7. Effects on ability to drive and use machines

Patients should be advised not to drive or operate machinery if Copaz causes dizziness or sedation. Codeine may cause visual disturbances.

4.8. Undesirable effects

The commonest side effects of codeine are nausea, vomiting, light headaches, dizziness, sedation, shortness of breath and constipation. Some of these side effects appear more common in ambulatory: rather than non-ambulatory patients. Lying down may alleviate these effects they occur. In addition, miosis, visual disturbances, headache, bradycardia, respiratory depression, difficult micturition and urinary retention, and allergic reactions (including skin rash) can occur.

Codeine can cause respiratory depression particularly in overdosage and in patients with compromised respiratory function.

Euphoria, dysphoria, abdominal pain, and pruritus can occur as reactions to Copaz.

Liver damage in association with therapeutic use of paracetamol has been documented; most cases have occurred in conjunction with chronic alcohol abuse.

There have been some reports of blood dyscrasias – thrombocytopenia and agranulocytosis, with the use of paracetamol-containing products, but the causal relationship has not been established.

Regular prolonged use of codeine/DHC is known to lead to addiction and symptoms of restlessness and irritability may result when treatment is then stopped.

Prolonged use of a pain killer for headaches can make them worse.

4.9. Overdose

Paracetamol

Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk Factors:

If the patient

a, Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

Or

b, Regularly consumes ethanol in excess of recommended amounts.

Or

c, Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms:

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 metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Management:

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable) but results should not delay initiation of treatment beyond 8 hours after ingestion, as the effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital.

Codeine

The effects in overdosage will be potentiated by simultaneous ingestion of alcohol and psychotropic drugs.

Symptoms:

Central nervous system depression, including respiratory depression, may develop but is unlikely to be severe unless other sedative agents have been co-ingested, including alcohol, or the overdose is very large. The pupils may be pin-point in size; nausea and vomiting are common. Hypotension and tachycardia are possible but unlikely.

Management:

This should include general symptomatic and supportive measures including a clear airway and monitoring of vital signs until stable. Consider activated charcoal if an adult presents within one hour of ingestion of more than 350 mg or a child more than 5 mg/kg.

Give naloxone if coma or respiratory depression is present. Naloxone is a competitive antagonist and has a short half-life so large and repeated doses may be required in a seriously poisoned patient. Observe for at least four hours after ingestion, or eight hours if a sustained release preparation has been taken.

Pharmacological Properties

5.1. Pharmacodynamic Properties

Paracetamol (N02B E51) has analgesic and antipyretic actions. It is a weak inhibitor of prostaglandin biosynthesis. Single or repeated therapeutic doses of paracetamol do not affect the cardiovascular or respiratory systems. Gastric irritation, erosion, or bleeding is not produced by paracetamol. There is minimal effect on platelets, no effect on bleeding time or excretion of uric acid.

Codeine (N02A A59) is an analgesic with similar uses to morphine, but only mild sedative effects. Codeine affects the CNS and the gut, including analgesia, drowsiness, mood changes, respiratory depression, reduced gastrointestinal motility, nausea or vomiting, changes in the endocrine and autonomic nervous system. Codeine's effect on pain relief is selective, and it does not affect other sensations such as touch, vibration, vision, or hearing.

5.2. Pharmacokinetic Properties

Paracetamol is readily absorbed from the gastro-intestinal tract. It is metabolised in the liver and undergoes extensive biotransformation. The major metabolites are inactive phenolic sulphate and glucuronide conjugates. An adequate supply of SH groups can prevent hepatic toxicity. Paracetamol is excreted in the urine. The elimination half-life varies from about 1 to 4 hours.

Codeine is absorbed from the gastro-intestinal tract and peak plasma concentrations are produced in about 1 hour. It is metabolised in the liver to morphine and norcodeines. Codeine and its metabolites are excreted almost entirely by the kidney. The plasma half-life is between 3 and 4 hours

5.3. Preclinical Safety Data

None stated.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Maize Starch sifted
Methylcellulose
Talc
Calcium Stearate
Povidone
Purified Water
Hypromellose
Macrogol 3350

6.2. Incompatibilities

None relevant

6.3. Shelf-Life

36 months

6.4. Special Precautions for Storage

Do not store above 25°C

6.5. Nature and Content of Container

Polyethylene capsule container with low density polyethylene child resistant closure.

Or

Aluminium foil over PVC/PVDC or ACLAR film blisters.

In pack sizes of 28, 30, 56, 100 or 112 caplets.

6.6. Instruction for Use, Handling and Disposal

None

7. MARKETING AUTHORISATION HOLDER

Goldshield Pharmaceuticals Limited

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CR0 0XT

United Kingdom

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