
SmPC

S3

1. NAME OF THE MEDICINAL PRODUCT

Acetaminophen 500mg and Caffeine 65mg soft gelatin Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft gelatin capsule contains:

Acetaminophen USP 500 mg

Caffeine BP 65 mg

Full list of excipients, section 6.1

3. PHARMACEUTICAL FORM

White to off-white coloured, oblong shaped, opaque, soft gelatin capsules containing white coloured oily mass.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

A mild analgesic and antipyretic formulated to give extra pain relief. The capsules are recommended for the treatment of most painful and febrile conditions, for example, headache, including migraine, backache, toothache, rheumatic pain and dysmenorrhoea, and the relief of the symptoms of colds, influenza and sore throat.

4.2 Posology and method of administration

Oral use.

Adults (including the elderly), and children aged 16 years and over:

Two capsules up to four times daily. The dose should not be repeated more frequently than every 4 hours. Do not exceed 8 capsules in 24 hours.

Children aged 12-15 years:

One capsule up to four times daily. The dose should not be repeated more frequently than every 4 hours. Do not exceed 4 capsules in 24 hours.

Not recommended for children under 12 years.

4.3 Contraindications

Hypersensitivity to paracetamol, caffeine or any of the other constituents.

4.4 Special warnings and precautions for use

Do not exceed stated dose.

Contains paracetamol. Do not use with any other paracetamol containing products. The concomitant use with other products containing paracetamol may lead to an overdose.

Paracetamol overdose may cause liver failure, which may require liver transplant or lead to death.

Care is advised in the administration of paracetamol to patients with renal or hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Caution should be exercised in patients with glutathione depleted states, as the use of paracetamol may increase the risk of metabolic acidosis (see section 4.9).

Excessive intake of caffeine (e.g. coffee, tea and some canned drinks) should be avoided while taking this product.

If symptoms persist, medical advice must be sought.

Keep out of the sight and reach of children.

Pack Label:

Talk to a doctor at once if you take too much of this medicine, even if you feel well. Do not take anything else containing paracetamol while taking this medicine.

Patient Information Leaflet:

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.

4.5 Interaction with other medicinal products and other forms of interaction

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Caffeine may increase clearance of lithium. Concomitant use is therefore not recommended.

4.6 Pregnancy and lactation

Paracetamol-caffeine is not recommended for use during pregnancy due to the possible increased risk of lower birth weight and spontaneous abortion associated with caffeine consumption.

Caffeine in breast milk may potentially have a stimulating effect on breast fed infants.

Due to the caffeine content of this product it should not be used if you are pregnant or breast feeding.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Adverse events from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by MedDRA System Organ Class. Adverse reactions identified during post-marketing use are reported voluntarily from a population of uncertain size, the frequency of these reactions is unknown but likely to be very rare (<1/10,000).

Post marketing data

PARACETAMOL

Body System	Undesirable effect
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis
Immune system disorders	Very rare cases of serious skin reactions have been reported. Anaphylaxis Cutaneous hypersensitivity reactions including (amongst others) skin rashes and angioedema.
Respiratory, thoracic and mediastinal disorders	Bronchospasm – more likely in patients sensitive to aspirin and other NSAIDs
Hepatobiliary disorders	Hepatic dysfunction

CAFFEINE

When the recommended paracetamol-caffeine dosing regimen is combined with dietary caffeine intake, the resulting higher dose of caffeine may increase the potential for caffeine-related adverse effects.

Body System	Undesirable effect
Central nervous system	Dizziness Headache
Cardiac disorders	Palpitation
Psychiatric disorders	Insomnia Restlessness Anxiety and irritability
Gastrointestinal disorders	Gastrointestinal disturbances

4.9 Overdose

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g 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 deplete 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). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. 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. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit.

Caffeine

Symptoms

Overdose of caffeine may result in epigastric pain, vomiting, diuresis, tachycardia or cardiac arrhythmia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, tremors and convulsions).

It must be noted that for clinically significant symptoms of caffeine overdose to occur with this product, the amount ingested would be associated with serious paracetamol-related toxicity.

Management

Patients should receive general supportive care (e.g. hydration and maintenance of vital signs). The administration of activated charcoal may be beneficial when performed within one hour of the overdose, but can be considered for up to four hours after the overdose. The CNS effects of overdose may be treated with intravenous sedatives.

Summary

Treatment of overdose requires assessment of plasma paracetamol levels for antidote treatment, with signs and symptoms of caffeine toxicity being managed symptomatically.

5. Pharmacological properties

5.1 Pharmacodynamic properties

ATC code: N02BE51

Pharmacological Classification: 2.1 – Analgesics and Antipyretics: Compound Products

The combination of paracetamol and caffeine is a well established analgesic combination.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastro-intestinal tract. It is relatively uniformly distributed throughout most body fluids and exhibits variable protein binding. Excretion is almost exclusively renal, in the form of conjugated metabolites. Caffeine is absorbed readily after oral administration. Maximal plasma concentrations are achieved within one hour and the plasma half-life is about 3.5 hours. 65 - 80% of administered caffeine is excreted in the urine as 1-methyluric acid and 1-methylxanthine.

Panadol Extra Advance 500 mg/65 mg Tablets contain a disintegrant system which accelerates tablet dissolution compared to standard paracetamol and caffeine tablets.

Human pharmacokinetic data demonstrate that the time taken to reach plasma paracetamol threshold (4-7 mcg/ml) is at least 44% faster with Panadol Extra Advance 500 mg/65 mg Tablets compared with standard paracetamol and caffeine tablets.

Total extent of absorption of paracetamol and caffeine from Panadol Extra Advance 500 mg/65 mg Tablets is equivalent to that from standard paracetamol and caffeine tablets.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. Pharmaceutical particulars

6.1 List of excipients

Ingredients	Specifications
Povidone (Poly Vinyl Pyrrolidone K30)	BP
Propylene Glycol	BP
Macrogol 4000 (Poly ethylene glycol 4000)	BP
Macrogol 400 (Poly ethylene glycol 400)	BP
Gelatin	BP
Partially dehydrated liquid sorbitol (Polysorb 85/70/00)	BP
Fumaric acid	USP
Iron oxide yellow (Ferric oxide)	USP
Titanium dioxide	BP
Purified water	BP

6.2 Incompatibilities

None.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container

Acetaminophen 500mg and Caffeine 65mg Soft Gelatin Capsules is available in 2x10's and 4x10's Blister Pack

6.6 Special precautions for disposal and other handling

None.

7. Marketing authorisation holder:

Cospharm Investments (Pty) Ltd

No.2 Concourse Crescent

Lonehill

Johannesburg

2191

8. Registration Number:

9. Category for distribution of the product – Pharmacy Medicine

10. Name and Address of the Manufacturer:

Softgel Healthcare Private Limited

Survey No. 20/1,

Vandalur-Kelambakkam Road,

Pudupakkam Village,

Chengalpattu District, Tamilnadu - 603 103

11. Name and Address of the Principal:

Softgel Healthcare Private Limited

Survey No. 20/1,

Vandalur-Kelambakkam Road,

Pudupakkam Village,

Chengalpattu District, Tamilnadu - 603 103