

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Panadol Cold and Flu Relief 500mg/65mg Film-Coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Paracetamol 500.0 mg and Caffeine 65 mg.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

White, film-coated capsule-shaped tablets with flat edges, with a triangular logo and a '+' symbol debossed on one side and blank on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The tablets are recommended for use as an analgesic in the relief of mild to moderate pain such as is associated with rheumatism, neuralgia, musculoskeletal disorders, headache and of discomfort associated with influenza, feverishness and feverish colds, toothache and dysmenorrhoea.

4.2 Posology and method of administration

For oral administration.

Adults (including the elderly) and children 16 years and over:
2 tablets up to four times daily. Do not exceed 8 tablets in 24 hours.

Children aged 12 – 15 years:
1 tablet up to four times daily. Do not exceed 4 tablets in 24 hours.

Not recommended for children under 12 years of age.

Minimum dosing interval: 4 hours.

The lowest dose necessary to achieve efficacy should be used.
Should not be used with other paracetamol-containing products.

Renal Impairment

Patients who have been diagnosed with renal impairment must seek medical advice before taking this medication. The restrictions related to the use of paracetamol and caffeine products in patients with renal impairment are primarily a consequence of the paracetamol content of the drug.

Hepatic Impairment

Patients who have been diagnosed with liver impairment must seek medical advice before taking this medication. The restrictions related to the use of paracetamol and caffeine products in patients with hepatic impairment are primarily a consequence of the paracetamol content of the drug.

The maximum daily dose of paracetamol should not exceed 60mg/kg/day (up to a maximum of 2g per day) in the following situations, unless directed by a physician:

- Weight less than 50kg
- Chronic alcoholism

- Dehydration
- Chronic malnutrition

4.3 Contraindications

Known hypersensitivity to paracetamol.

4.4 Special warnings and precautions for use

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 can lead to liver transplant or death.

Cases of paracetamol induced hepatotoxicity, including fatal cases, have been reported in patients taking paracetamol at doses within the therapeutic range. These cases were reported in patients with one or more risk factors for hepatotoxicity including low body weight (<50 Kg), renal and hepatic impairment, chronic alcoholism, concomitant intake of hepatotoxic drugs, sepsis and in acute and chronic malnutrition (low reserves of hepatic glutathione). Paracetamol should be administered with caution to patients with these risk factors.

Caution is also advised in patients on concomitant treatment that induce hepatic enzymes and in conditions which may predispose to glutathione deficiency (see sections 4.2 and 4.9).

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism), who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Doses of paracetamol should be reviewed at clinically appropriate intervals and patients should be monitored for emergence of new risk factors for hepatotoxicity which may warrant dosage adjustment.

Underlying liver disease increases the risk of paracetamol related liver damage. Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication.

Excessive intake of caffeine (e.g. coffee, tea and some canned drinks) should be avoided while taking this product. Prolonged use except under medical supervision may be harmful. In general, medicinal products containing paracetamol should be taken for only a few days without the advice of a doctor or dentist and not at high doses.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

Do not exceed the stated dose.
Take only when necessary.

If high fever or signs of secondary infection occur or if symptoms persist for longer than 3 days, consult your doctor.

Keep out of the sight and reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

Paracetamol

Paracetamol may increase the elimination half-life of chloramphenicol. The absorption of paracetamol may be increased by metoclopramide and decreased by cholestyramine. Oral contraceptives may increase the rate of clearance of paracetamol.

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.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4)

Caffeine

Caffeine can increase the elimination of lithium from the body. Concomitant use is therefore not recommended.

4.6 Fertility, pregnancy and lactation

Pregnancy

Paracetamol

A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results.

Caffeine

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

Lactation

Paracetamol and caffeine are excreted in breast milk.

Not recommended for use during breastfeeding.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by System organ Class and frequency.

Frequencies are defined as: very common ($\geq 1/10$), common ($\geq 1/100, < 1/10$), uncommon ($\geq 1/1,000, < 1/100$), rare ($\geq 1/10,000, < 1/1000$), very rare ($< 1/10,000$), not known (cannot be estimated from available data).

Adverse event frequencies have been estimated from spontaneous reports received through post marketing data.

Body System	Undesirable Effect	Frequency
Paracetamol		
Blood and lymphatic system disorders	Thrombocytopenia	Very rare
Immune System disorders	Anaphylaxis Cutaneous hypersensitivity reactions, including skin reactions, angioedema and Stevens Johnson syndrome and toxic epidermal necrolysis. Very rare cases of serious skin reactions have been reported	Very rare
Metabolism and nutrition acidosis	High anion gap metabolic acidosis*	Not known
Respiratory, thoracic and mediastinal disorders	Bronchospasm in patients sensitive to aspirin and other NSAIDs	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare
Caffeine		
Central Nervous System	Nervousness, Dizziness	Not known
Cardiac disorders	Palpitation	Not known

Psychiatric disorders	Insomnia, restlessness, anxiety and irritability	Not known
Gastrointestinal disorders	Gastrointestinal disturbances	Not known

*Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

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 such as insomnia, restlessness, anxiety, irritability, headaches, gastrointestinal disturbances and palpitations.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance website: www.hpra.ie.

4.9 Overdose

Paracetamol

Paracetamol overdose may cause liver failure which can lead to liver transplant or death. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity.

There is a risk of poisoning with paracetamol particularly in elderly subjects, young children, patients with liver disease, cases of chronic alcoholism and in patients with chronic malnutrition. Overdosing may be fatal in these cases. Symptoms generally appear within the first 24 hours and may comprise: nausea, vomiting, anorexia, pallor, and abdominal pain, or patients may be asymptomatic.

Overdose of paracetamol in a single administration in adults or in children can cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration. Liver damage is likely in adults who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested), become irreversibly bound to liver tissue.

Some patients may be at increased risk of liver damage from paracetamol toxicity. Risk Factors include: If the patient;

- Is on long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
- Regularly consumes ethanol in excess of recommended amounts
- Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia

Emergency Procedure:

Immediate transfer to hospital.

Blood sampling to determine initial paracetamol plasma concentration. In the case of a single acute overdose, paracetamol plasma concentration should be measured 4 hours post ingestion.

Administration of activated charcoal should be considered if >150mg/kg paracetamol has been taken within 1 hour. The antidote N-acetylcysteine, should be administered as soon as possible in accordance with National treatment guidelines.

Symptomatic treatment should be implemented. Caffeine

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 liver toxicity.

No specific antidote is available, but supportive measures such as beta adrenoreceptor antagonists to reverse the cardiotoxic effects may be used.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

5.2 Pharmacokinetic properties

Paracetamol is well absorbed from the gastrointestinal tract, peak plasma concentrations occurring 0.5 – 2 hours after ingestion. It is metabolised in the liver and excreted in the urine mainly as glucuronide and sulphate conjugates – less than 5% is excreted as unmodified paracetamol. The half-life is 1 to 4 hours. Binding to the plasma proteins is minimal at therapeutic concentrations.

Caffeine is absorbed readily after oral administration, maximal plasma concentrations are achieved after approximately 20 – 60 minutes and the plasma half-life is about 4 hours. Over 48 hours, 45% of a dose is excreted in the urine as 1-methyluric acid and 1-methylxanthine.

5.3 Preclinical safety data

Preclinical safety data on paracetamol in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use of the product and which have not been mentioned elsewhere in this Summary.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core

Pregelatinised starch

Maize starch

Povidone

Potassium sorbate

Purified talc

Stearic acid

Croscarmellose sodium

Film-coating

Hypromellose

Triacetin

6.2 Incompatibilities

Not applicable

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Panadol Cold and Flu Relief Film Coated Tablets are packed in blister strips packed into cardboard cartons containing 4, 6, 12, 24, 30, 48, 60 and 96 tablets, or into cardboard wallets containing 12 tablets.

These blister strips are either:

- Blister strips comprising a PVC laminate heat sealed with hard tempered aluminium foil
- Child resistant blister strips comprising PVC laminate heat sealed to a bilayer of aluminium and polyethylene terephthalate

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Haleon Ireland Limited
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8 MARKETING AUTHORISATION NUMBER

PA0678/105/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 25th May 2012

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July 2025