Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Panadol Extra 500mg/65mg Soluble Effervescent Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Paracetamol 500.0 mg and Caffeine 65 mg.

Excipients: Also contains 425mg sodium per tablet.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Soluble Effervescent tablets.
Flat, white tablets with beveled edges, plain on one side, breakline on the other.
The tablet can be divided into equal halves.

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.

Panadol Extra Soluble should be dissolved in at least half a tumbler full of water.

Adults (including the elderly) and children aged 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.

Do not exceed the stated dose.

Should not be used with other paracetamol-containing products.

Renal Impairment

Patients who have been diagnosed with liver or kidney 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 or kidney 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 drugs.

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, caffeine or any of the other ingredients.

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 patient on concomitant treatment with drugs that induce hepatic enzymes and in conditions which may predispose to glutathione deficiency (see sections 4.2 and 4.9). In patients with glutathione depleted states such as sepsis; the use of paracetamol may increase the risk of metabolic acidosis.

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

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

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

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.

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, a physician should be consulted.

Each tablet contains 427 mg of sodium. This is equivalent to 21% of the WHO recommended maximum daily intake for sodium. The maximum daily dose of this product is 171% of the WHO recommended maximum daily intake for sodium. Panadol Extra Soluble is considered high in sodium. This should be taken into consideration by patients on a controlled sodium diet.

Each tablet contains sorbitol powder (E 420) at 50 mg per tablet. Patients with rare hereditary problems of fructose intolerance should not take this medicine

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, 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. The following convention has been utilised for the classification of undesirable effects: very common (≥ 1/10), common (≥ 1/100, < 1/10), uncommon (≥ 1/1,000, < 1/100), rare (≥ 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	Thrombocytopaenia	Very rare
Immune System disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angiodema, and Stevens Johnson syndrome and toxic epidermal necrolysis. Very rare cases of serious skin reactions have been reported	Very rare
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	Not known
	Dizziness	Not known
Cardiac disorders	Palpitation	Not known
Psychiatric disorders	Insomnia, restlessness, anxiety and irritability	Not known
Gastrointestinal disorders	Gastrointestinal disturbances	Not known

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.

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 l-methyluric acid and l-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

Sorbitol
Saccharin sodium
Sodium hydrogen carbonate
Povidone
Sodium laurilsulfate
Dimeticone
Citric acid (anhydrous)
Sodium carbonate (anhydrous)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Do not store above 25ºC.

6.5 Nature and contents of container

Panadol extra soluble tablets are foil-packed into either standard laminate strips comprising 40 g/m2 paper/12 g/m2 polyethylene (PE)/ 8 µm or 12 µm Aluminium foil/ 23 g/m2 PE, or child resistant laminate strips comprising 19 µm polyethylene terephthalate (PET)/ 12 g/m2 PE/ 12 µm Aluminium foil/ 30 g/m2 PE.

The laminate strips are further packed into cardboard cartons. These are available in packs of 12 and 24 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Haleon Ireland Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0678/039/010

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 02 November 2001

Date of last renewal: 02 November 2006

10 DATE OF REVISION OF THE TEXT

November 2023