SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 500 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 500.00 mg of Paracetamol BP

3 PHARMACEUTICAL FORM

White, capsule shaped tablets, plain on one side and with a breakline on the other side.

The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Paracetamol is indicated for the relief of headaches, migraine, neuralgia, rheumatic aches and pains.
For the relief of colds and influenza.

4.2 Posology and method of administration

Posology
Unless otherwise directed by the doctor:

Adults, the elderly and children 16 years and over: One or two tablets every 4 – 6 hours when necessary to a maximum of 4 doses in 24 hours.

Paediatric population
Children 12 to 15 years: One to one and a half tablets every 4 – 6 hours when necessary to a maximum of 4 doses in 24 hours.

Children 10 to 12 years: One tablet every 4 – 6 hours when necessary to a maximum of 4 doses in 24 hours.

Children 6 to 10 years: Half a tablet every 4 – 6 hours when necessary to a maximum of 4 doses in 24 hours.

Not recommended for children under 6 years.

The dose should not be repeated more frequently than every 4 hours and not more than 4 doses should be taken in any 24 hour period.

Method of administration
For oral use. To be swallowed with some water.

4.3 Contraindications

Hypersensitivity to paracetamol or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Care is advised in the administration of paracetamol to patients with renal or hepatic impairment; patients must seek medical advice before taking this medicine. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

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, 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.

Patients should be advised to consult their doctor if their headaches become persistent.

Caution should be exercised in patients with glutathione depleted states, as the use of paracetamol may increase the risk of metabolic acidosis in overdose (see section 4.9). Use with caution in patients with glutathione depletion due to metabolic deficiencies.

Caution is advised in asthmatic patients sensitive to aspirin, because light reaction bronchospasm with paracetamol (cross-reaction) has been reported in less than 5% of the patients tested.

In case of high fever, or signs of secondary infections or persistence of symptoms a doctor should be consulted.

Label states:
Do not take more medicine than the label tells you to. If you do not get better talk to your doctor.

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

Leaflet states:
Do not take anything else containing paracetamol while taking this medicine. 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.

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

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 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).

Imatinib - restriction or avoidance of regular concomitant paracetamol use should be taken.

Paracetamol may decrease busulfan clearance when used in combination.

Alcohol reduces liver capacity to deal with paracetamol.
Chronic alcohol intake could enhance hepatotoxicity of paracetamol overdose.
Acute alcohol intake may diminish an individual's ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

The risk of liver damage in those taking the maximum recommended doses of paracetamol will be higher in patients being treated with enzyme-inducing agents such as carbamazepine, phenytoin, phenobarbital, primidone and rifampicin, and also in those taking St. John's wort (hypericum perforatum).

4.6 Fertility, pregnancy and lactation

Pregnancy

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. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Breast-feeding

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

4.7 Effects on ability to drive and use machines

No or negligible influence.

4.8 Undesirable effects

Adverse events of paracetamol 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 system class and frequency (very rare: may affect up to 1 in 10,000 people; not known: frequency cannot be estimated from the available data).

Body system class	**Undesirable effect**	**Frequency**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis	Very rare
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angioedema	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm*	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare
Skin and subcutaneous tissue disorders	Very rare cases of serious skin reactions have been reported	Very rare
Metabolism and nutrition disorders	High anion gap metabolic acidosis	Not known

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

Description of selected adverse reactions

High anion gap metabolic acidosis

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.

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 the Yellow Card Scheme website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App store.

4.9 Overdose symptoms, emergency procedures, antidotes

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, phenobarbital, 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 24 h from ingestion should be discussed with the NPIS or a liver unit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol is an analgesic with antipyretic properties. The mechanism of action is probably similar to that of aspirin and dependant on the inhibition of prostaglandin synthesis. This inhibition appears, however, to be on a selective basis.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract following oral administration. The concentration in plasma reaches a peak in 30 to 60 minutes and the plasma half-life is 1 - 4 hours after therapeutic doses. Paracetamol is relatively uniformly distributed throughout most body fluids. Binding of the drug to plasma proteins is variable; 20 to 30 % may be bound at the concentrations encountered during acute intoxication. Following therapeutic doses 90 - 100% of the drug may be recovered in the urine within the first day. However, practically no paracetamol is excreted unchanged and the bulk is excreted after hepatic conjugation

5.3 Preclinical safety data

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Povidone

Pregelatinised maize starch
Sodium starch glycollate
Magnesium stearate

6.2. Incompatibilities

None reported.

6.3. Shelf Life

5 years.

6.4 Special precautions for storage

Keep out of the reach and sight of children

Protect from heat, light and moisture.

6.5 Nature and Contents of Container

1) Opaque plastic containers with tamper-evident or tamper-evident child resistant closures.

2) Blister Packs of 20 µm hard aluminium foil laminated to 15 µm rigid PVC film, and 250 µm white opaque PVC.

Contents: 25, 100, 250, 500, 1000 tablets.

6.6. Instruction for Use/Handling

No special instructions for use/handling.

7 MARKETING AUTHORISATION HOLDER

Crescent Pharma Limited,
Key House
Sarum Hill, Basingstoke
RG21 8SR
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 20416/0123

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03/03/2009

10 DATE OF REVISION OF THE TEXT

05/03/2025