SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol Tablets BP 500mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains: Paracetamol BP 500mg.

3 PHARMACEUTICAL FORM

Compressed tablet.

4.1 Therapeutic indications

Paracetamol is a mild analgesic and antipyretic.

It is indicated in the treatment of most painful and febrile conditions, for example, relief of headache, toothache, colds, influenza, rheumatic pain, dysmenorrhoea, sore throat, migraine, rheumatic aches and pains and neuralgia.
For the relief of colds and influenza. Also recommended for the symptomatic relief of pain due to non-serious arthritis.

4.2 Posology and method of administration

Posology
Adults, Elderly and Children over 16 years:
Two tablets every four hours as required. Not more than eight tablets in 24 hours. Do not take for more than 3 days without consulting your doctor.

These doses should not be repeated more frequently than every four hours nor should more than four doses be given in any 24 hour period.

Paediatric population
Children under 10 years:
Not recommended for children under 10 years of age.

Children aged 10 to 15 years:
One tablet every four to six hours when necessary to a maximum of four doses in 24 hours. Do not take for more than 3 days without consulting your doctor.

These doses should not be repeated more frequently than every four to six hours nor should more than four doses be given in any 24 hour period .

Method of administration
For oral administration

4.3 Contraindications

Hypersensitivity to paracetamol and/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.

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.

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.

<u>The Pack Label will state:</u>

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

<u>The Patient Information Leaflet will state:</u>
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.

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, 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.
Breastfeeding

Paracetamol is excreted in breast milk but not in clinically significant amount. Available published data do not contra-indicate 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.

The information below lists reported adverse reactions, ranked using the following frequency classification:

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (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

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

4.9 Overdose

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, gastrointestinal bleeding 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.

5.1 Pharmacodynamic properties

ATC code: N02B E01, Other analgesics and antipyretics
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. Less than 5% 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

Each tablet contains Maize Starch, Colloidal Anhydrous Silica, Magnesium Stearate and Potassium Sorbate

6.2 Incompatibilities

This product is designed for oral administration.

Admixture with other medicines prior to ingestion is not intended or desirable.

6.3 Shelf life

The shelf life of the product is 3 years when stored in cartoned blister packs, 2 years in paper strips, and 5 years in all other packs, assuming the precautions stated below are taken.

In the case of tubs, provided the pack is re-sealed after each use there should be no reduction in shelf life.

Re-packing into any other pack may affect the shelf life and appropriate pharmaceutical judgement should be exercised.

6.4 Special precautions for storage

Store below 25°C.
Store in the original container in order to protect the capsules from light and moisture.

6.5 Nature and contents of container

Blister strips of 0.25mm PVC/0.02mm aluminium enclosed in a cardboard carton containing 2, 4, 6, 8, 10, 12, 15, 16, 20, 24, 30, 32, 45, 48, 50, 56, 60, 75, 84, 96 or 100 tablets.

HDPE or polypropylene tub or vial fitted with a plastic cap, child resistant and/or tamper-evident as appropriate, containing 16, 25, 32, 50, 56, 84, 100, 250, 500 or 1000 tablets.

An amber glass bottle fitted with a child-resistant screw-cap, containing 16, 25, 32, 50, 56 or 100 tablets.

HDPE bucket lined with a polythene bag and fitted with a HDPE lid, containing 5000, 20000, 25000 or 30000 tablets.

A corrugated cardboard box lined with a polythene bag, containing 5000, 20000, 25000 or 30000 tablets.

PVDC coated paper strips enclosed in a cardboard carton, containing 16, 24, 32, tablets.

Amber Polystyrene bottles fitted with a child-resistant screw-cap, containing 16, 25, 32, 50, 56 or 100 tablets.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER(S)

PL 20416/0719

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

14/02/2024