Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 500 mg Film-Coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains paracetamol 500 mg.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet
White, capsule shaped, film-coated tablets with a break line on one side. The break line is only to facilitate breaking for ease of swallowing and do not divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Paracetamol tablets are a mild analgesic and antipyretic. The tablets are recommended for use in the short term management of headaches, including migraine and tension headaches, backache, rheumatic and muscle pain, period pains, nerve pains, toothache and for relieving of fever, aches and pains of colds and flu.

4.2 Posology and method of administration

Oral administration only.

Age	How much	How often
Adults and children over 16 years	1 or 2 tablets	Every 4-6 hours, as required. Don't take more than 8 tablets (4 doses) in any 24 hours.
Children 10-15 years	1 tablet	Every 4-6 hours, as required. Don't take more than 4 tablets (4 doses) in any 24 hours.

The recommended daily dosage or the specified number of doses should not be exceeded because of the risk of liver damage (see section 4.4 and 4.9).

Paediatric patients
Paracetamol tablets are not suitable for children under 10 years of age.

These doses should not be repeated more frequently than every 4 hours and not more than 4 doses should be given in any 24 hour period.

The maximum daily dose is 60mg/kg presented in divided doses of 10 - 15 mg/kg body weight every 4–6 hours, maximum 4 times throughout the 24 hour period.

Elderly patients
Elderly patients, especially those who are frail or immobile, may require a reduced dose or frequency of dosing.

Renal impairment
Patients who have been diagnosed with kidney impairment must seek medical advice before taking this medication. It is recommended, when giving paracetamol to patients with renal failure, to reduce the dose and to increase the minimum interval between each administration to at least 6 hours. The restrictions related to the use of paracetamol products in patients with renal impairment are primarily a consequence of the paracetamol content of the drug (see section 4.4).

Hepatic impairment

Patients who have been diagnosed with hepatic impairment or Gilbert's Syndrome must seek medical advice before taking this medication. The restrictions related to the use of paracetamol products in patients with hepatic impairment are primarily a consequence of the paracetamol content of the drug (see section 4.4).

If pain or fever persist for more than 3 days or get worse, or if any other symptoms occur, treatment should be discontinued and a physician consulted.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Hepatic impairment
Underlying liver disease increases the risk of paracetamol-related liver damage. Patients with renal or hepatic impairment should seek medical advice prior to treatment with paracetamol. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

The products should be administered only with particular caution under the following circumstances:

- Hepatocellular insufficiency
- Chronic alcoholism
- Renal failure (GFR≤50ml/min)
- Gilbert's Syndrome (familial non-haemolytic jaundice)
- Concomitant treatment with medicinal products affecting hepatic function
- Glucose-6-phosphate dehydrogenase deficiency
- Haemolytic anaemia
- Glutathione deficiency
- Dehydration
- Chronic malnutrition
- The elderly, adults and adolescents weighing less than 50kg

Precaution should be observed in patients with asthma who are sensitive to acetylsalicylic acid, since mild bronchospasms are reported in association with paracetamol (cross reaction).

Do not exceed the stated dose.

Immediate medical advice should be sought in the event of overdosage even if the patient feels well because the risk of irreversible liver damage (see section 4.9).

Patients should be advised not to take other paracetamol-containing products concurrently. If symptoms persist, consult your doctor. Prolonged use of any type of painkiller for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. The diagnosis of medication overuse headache should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of headache medications

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 malnutrition and 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.

Keep out of the sight and reach of children.

Consult your doctor if you are taking warfarin or have been diagnosed with liver or kidney disease.

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. The rate of paracetamol absorption may be reduced by cholestyramine. Cholestyramine should not be administered within one hour of taking 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.

In case of concomitant treatment with probenecid, the dose of paracetamol should be reduced because the probenecid reduces the clearance of paracetamol by 50% because it prevents the conjugation of paracetamol with glucuronic acid.

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)

Paracetamol is metabolized in the liver and can therefore interact with other medicines that follow the same pathway or may inhibit or induce this route causing hepatotoxicity, particularly in overdose (see Section 4.9).

There is limited evidence to suggesting that paracetamol may affect chloramphenicol pharmacokinetics but its validity has been criticised and evidence of a clinically relevant interaction appears to lack. Although no routine monitoring needed, it is important to bear in mind this potential interaction when these two medications are concomitantly administered, especially in malnourished patients.

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.

Fertility
There are no available data on the effect of paracetamol on fertility.

4.7 Effects on ability to drive and use machines

Paracetamol tablets have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse events associated with paracetamol from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labeled dose and considered attributable are tabulated below by System Organ Class and frequency. The following convention has been utilized for the classification of undesirable effects: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10,000, <1/1000) and very rare (<1/10,000), not known (cannot be estimated from the available data).

System Organ Class	Undesirable effect	Frequency
Blood and lymphatic system disorders	Thrombocytopaenia	Very rare
Immune system disorders	Allergies (not including angioedema)	Rare
	Anaphylaxis	Very rare
Respiratory system disorders	Aggravation of bronchospasm has been reported in asthmatic patients known to be sensitive to aspirin and other non-steroidal anti-inflammatory drugs	Very rare
Hepatobiliary disorders	Liver dysfunction	Very rare
Skin and subcutaneous tissue disorders	Cutaneous hypersensitivity reactions, including skin rashes, pruritus, sweating, purpura, urticaria and angioedema	Very rare
	Very rare cases of serious skin reactions have been reported, such as	Very rare

	Toxic epidermal necrolysis (TEN), drug- induced dermatitis, Stevens Johnson syndrome, acute generalized exanthematous pustulosis (AGEP).	
Renal and urinary disorders	Sterile pyuria (cloudy urine)	Very rare
Metabolismand nutrition disorders	Highanion gap metabolic acidosis*	Notknown

*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 HPRA Website: www.hpra.ie.

4.9 Overdose

Paracetamol overdose can result in liver damage which can be fatal. Liver damage is possible in patients who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite become irreversibly bond to liver tissue. Some patients may be increased risk of liver damage from paracetamol toxicity:

Risk factors include:

1. patients with liver disease;
2. elderly patients;
3. young children;
4. patients receiving long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St. John's Wort or other drugs that induce liver enzymes;
5. patients who regularly consume ethanol in excess of recommended amounts;
6. patients with glutathione depletion e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia. SymptomsSymptoms of paracetamol overdose generally appear in the first 24 hours and may comprise: pallor, nausea, vomiting, anorexia and abdominal pain, or patients may be asymptomatic. Liver damage, e.g. increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin, together with increased prothrombin levels may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. Paracetamol overdose may cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficient, which may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, coma and death. On initial presentation, the patient's symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. 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. ManagementImmediate 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 and any patient who has ingested around 7.5g or more of paracetamol in the preceding 4 hours should undergo gastric lavage. Administration of oral methionine or intravenous N-acetylcysteine which may have a beneficial effect up to at least 48 hours after the overdose, may be required.General supportive measures must be available.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N02BE01
Pharmacotherapeutic group: Analgesics, Anilides

Paracetamol is an analgesic and antipyretic. Its mechanism of action is believed to include inhibition of prostaglandin synthesis, primarily within the central nervous system. The lack of peripheral prostaglandin inhibition confers important pharmacological properties such as the maintenance of the protective prostaglandins within the gastrointestinal tract.

5.2 Pharmacokinetic properties

Absorption
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Concentration in plasma reaches a peak in 30-60 minutes.

Distribution
Paracetamol is relatively uniformly distributed throughout most body fluids. Plasma protein binding is variable.

Biotransformation
Plasma half-life is 1-4 hours.
Paracetamol is metabolised mainly in the liver, following two major metabolic pathways, glucuronic acid and sulphuric acid conjugates. The latter route is rapidly saturated at doses higher than the therapeutic dosages. A minor route, catalysed by the Cytochrome P 450 (mostly CYP2E1), results in the formation of an intermediate reagent (N-acetyl-p-benzoquinoneimine) which under normal conditions of use, is rapidly detoxified by glutathione and eliminated in the urine, after conjugation with cysteine and mercapturic acid.
Conversely, when massive intoxication occurs, the quantity of this toxic metabolite is increased.

Elimination
Less than 5% is excreted as unmodified paracetamol; the elimination half-life varies from 1 to 4 hours. Elimination is essentially through the urine. 90% of the ingested dose is eliminated via the kidneys within 24 hours, principally as glucuronide (60-80%) and sulphate conjugates (20-30%).
In cases of renal failure (GFR≤50ml/min), the elimination of paracetamol is slightly delayed, the elimination half-life ranging from 2 to 5.3 hours. For the glucuronide and sulfate conjugates, the elimination rate is 3 times slower in subjects with severe renal impairment than in healthy subjects

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

- Pregeletanised starch
- Povidone
- Stearic acid
- Hypromellose
- Polyethylene Glycol
- Carnauba Wax

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Opaque PVC/aluminium foil blister strips packed into cardboard boxes containing 16 or 24 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Chefaro Ireland DAC
The Sharp Building
Hogan Place
Dublin 2
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1186/009/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 August 1992

Date of last renewal: 20 August 2007

10 DATE OF REVISION OF THE TEXT

January 2025