SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 500mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Tablet contains: 500mg Paracetamol.
Excipient(s) with known effect:
• Lactose-16.670mg of lactose per tablet.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Paracetamol is a mild analgesic and antipyretic, and is recommended for the treatment of most painful and febrile conditions, for example, headache, including migraine, toothache, neuralgia, colds and influenza, sore throat, backache, rheumatic pain and dysmenorrhoea.

4.2 Posology and method of administration

Method of administration:
For oral administration

Posology:
Adults, the elderly and children 16 years and over: take one or two tablets up to 4 times a day. Maximum dose of 8 tablets in 24 hours.

Children 10 to 15 years of age: take one tablet up to 4 times a day. Maximum dose of 4 tablets in 24 hours.

Not recommended for children under 10 years of age.

Dosage instruction
1. 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.
2. Dosage should not be continued for more than 3 days without consulting a doctor.

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

Paediatric population

Not recommended for children under 10 years of age.
Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Do not exceed the recommended dose.
Do not take paracetamol for more than 3 days without consulting a doctor.
Do not take with any other paracetamol-containing products.

If symptoms persist, consult your doctor.
Keep out of the reach of children.

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.

Immediate medical advice should be sought in the event of an overdose even if you feel well, because of the risk of delayed, serious liver damage.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 cholestyramine.

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).

4.6 Fertility, pregnancy and lactation

Pregnancy
Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use.

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 if clinically needed 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

Paracetamol has no influence on the ability to drive and use machines.

4.8 Undesirable effects

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).

Immune system disorders
Hypersensitivity including skin rash may occur.
Not known: anaphylactic shock, angioedema

Blood and lymphatic system disorders
Not known: blood dyscrasias including thrombocytopenia and agranulocytosis.

Skin and subcutaneous disorders
Very rare cases of serious skin reactions such as Toxic Epidermal Necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute generalized exanthematous pustulosis, fixed drug eruption have been reported.

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

- is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes, or
- regularly consumes ethanol in excess of recommended amounts, or
- 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, disseminated intravascular coagulation, 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.

Further measures will depend on the severity, nature and course of clinical symptoms of paracetamol intoxication and should follow standard intensive care protocols.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N02BE01, Other analgesics and antipyretics

Paracetamol is an effective analgesic and antipyretic agent, but has only weak anti-inflammatory properties. Its mechanism of action is not fully understood. It has been suggested that it may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (CNS) and to a lesser extent, through a peripheral action by blocking pain-impulse generation.

The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation.

Antipyretic – paracetamol probably produces an antipyretic action by a central effect on the hypothalamic heat-regulation centre to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss.

The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus. The drug has no effect on the cardiovascular and respiratory systems, and unlike salicylates it does not cause gastric irritation or bleeding.

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolised in the liver (90-95%) and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours. Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite (N-acetyl-p-benzoquinoneimine) which is usually produced in very small amounts by mixed function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause liver damage. The time to peak plasma concentration of paracetamol is 0.5 to 2 hours, the time to peak effect 1 to 3 hours and the duration of action 3 to 4 hours.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

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

Povidone BP

Lactose BP

Starch (Maize) BP

Magnesium Stearate BP

Sodium Starch Glycollate BP

Colloidal Anhydrous Silica BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 Years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

Child-resistant blister packs of 48, 60, 96 and 100 tablets.
PVC/aluminium IPVC 250/20/15 micron Glassine paper 35g/sqm/Adehesive lacquer 2.5g/sqm/Aluminium foil (9 micron)/ Heat seal coating 7.0g/sqm/PVC 250 micron
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None stated.

7 MARKETING AUTHORISATION HOLDER

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