1. NAME OF THE MEDICINAL PRODUCT

Paracetamol 500mg Caplets
Paracetamol 500mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Paracetamol 500 mg

Excipients with known effect:

Each Paracetamol 500mg tablet contains 0.560mg Sodium Metabisulphite.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablets for oral administration

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of mild to moderate pain including headache, migraine, neuralgia, toothache, sore throat and dysmenorrhoea.

For the symptomatic relief of rheumatic and muscular aches and pains, sciatica, fibrositis, lumbago, joint swelling and stiffness.

For the symptomatic relief of influenza, feverish colds and feverishness.

4.2 Posology and method of administration

For all indications:

Adults and children aged 16 years and over:
One or two tablets up to four times a day, as required.
Maximum daily dose is 4 g in divided doses.

Children aged 12 to 15 years:
One to one and a half tablets up to four times a day, as required,

Children ages 10 to 12 years:
One tablet up to four times a day, as required,

Children 6 to 10 years:
Half a tablet up to four times a day, as required.

Children under 6 years:
Do not give to children under 6.

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

Dosage should not be continued for longer than 3 days without consulting a doctor.

4.3 Contraindications

Hypersensitivity to paracetamol or 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 severe renal or severe hepatic impairment. The hazard of overdose is 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, 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.

The leaflet will state: 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.

Keep this medicine out of sight and reach of children.

The label will state: 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.

Keep all medicines out of the sight and reach of children.

Sodium content: This medicine contains less than 1 mmol sodium (23 mg) per 2 caplets, that is to say essentially ‘sodium-free’.

Sodium metabisulphite (E223) may rarely cause severe hypersensitivity reactions

and bronchospasm.

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).

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 a clinically significant amount. Available published data do not contra-indicate breast-feeding.

4.7 Effects on ability to drive and use machines

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

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. Due to limited clinical trial data, the frequency of these adverse events is not known (cannot be estimated from available data), but post-marketing experience indicates that adverse reactions to paracetamol are rare and serious reactions are very rare.

Post marketing data

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angiodema and Stevens Johnson syndrome/toxic epidermal necrolysis
Respiratory, thoracic and mediastinal disorders	Bronchospasm*
Hepatobiliary disorders	Hepatic dysfunction
Skin and subcutaneous tissues disorders	Very rare cases of serious skin reactions have been reported.
Metabolism and nutrition disorders	**High anion gap metabolic acidosis with frequency “Not known” (cannot be estimated from the available data)

Description of selected adverse reactions

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

** 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 at: www.mhra.gov.uk/yellowcard.

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, 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

Pharmacotherapeutic group: Other Analgesics and Antipyretics
ATC code: N02BE01

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 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.

Paracetamol probably produces an antipyretic action by a central effect on the hypothalamic heat-regulating 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 gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion; the time to peak effect 1 to 3 hours and the duration of action 3 to 4 hours. It is metabolised in the liver (90 - 95%) and excreted in the urine mainly as the glucuronide and sulfate 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.

5.3 Preclinical safety data

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

6.1 List of excipients

Pregelatinised Maize Starch
Sodium Metabisulfite
Magnesium Stearate

6.2 Incompatibilities

None

6.3 Shelf life

3 years

6.4 Special precautions for storage

None

6.5 Nature and contents of container

Polypropylene or HDPE containers with polypropylene or HDPE lids containing 8, 10, 12 or 16 tablets.
or
Blister strips comprised of 20 micron Aluminium/15 micron PVC lidding foil with 250 – 300 micron PVC base material.
or
Blister strips comprised of 20 micron Aluminium/6 micron PET lidding foil with 250 – 300 micron PVC base material.
or
Blister strips comprised of 20 micron Aluminium/23 micron PVC lidding foil with 256.5– 283.5 micron PVC base material.

Blister pack sizes of 8, 10, 12 or 16 tablets.

6.6 Special precautions for disposal

No special requirements for disposal.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Galpharm Healthcare Limited
Wrafton
Braunton
Devon
EX33 2DL
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 16028/0012

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/06/1997 / 11/06/2001

10 DATE OF REVISION OF THE TEXT

26/03/2025