SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 500mg Caplets
Paracetamol 500mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Paracetamol BP 500 mg

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

Contra-indicated in patients with a known hypersensitivity to Paracetamol and / or any other constituents.

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.

Leaflet: 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.

Label: 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 symptoms persist consult your doctor.
Keep all medicines out of the sight and reach of children.

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 use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6 Pregnancy and lactation

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.

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

None

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

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

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 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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 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.

5.3 Preclinical safety data

None stated

6.1 List of excipients

Wet mix formulation: Pregelatinised Maize Starch BP; Sodium Metabisulfite BP; Magnesium Stearate BP.

Dry mix formulation: Maize Starch BP, Stearic Acid BPC, Magnesium Stearate BP; Talc BP.

6.2 Incompatibilities

None

6.3 Shelf life

Wet Mix Formulation:
3 years - Polypropylene or HDPE containers.
3 years - Blister packs.
3 years - Polypropylene blister packs.

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, 16, 32, 25, 50, 100, 500, 1000, or 5000 tablets.

or

Blister strips comprised of 30micron hard temper Aluminium lidding foil with 250 – 300micron PVC base material.

or

Blister strips comprised of 30micron hard temper Aluminium lidding foil with 250 micron PVC/PVdC (40-90gsm) base material.

or

Blister strips comprised of 20micron Aluminium/15micron PVC lidding foil with 250 – 300micron PVC base material.

or

Blister strips comprised of 20micron Aluminium/15micron PVC lidding material with 250micron PVC/PVdC (40-90gsm) base material.

or

Blister strips comprised of 35-41gsm Glassine paper/9micron Aluminium lidding foil with 250 – 300micron PVC base material.

or

Blister strips comprised of 35-41gsm Glassine paper/9micron Aluminium lidding foil with 250micron PVC/PVdC (40-90gsm) base material.

Blister pack sizes of 8, 10, 12, 16, 24, 32, 48 or 96 tablets.

6.6 Special precautions for disposal

Not applicable.

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

27/01/2017