SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 500mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

500mg Paracetamol B.P.

3 PHARMACEUTICAL FORM

Uncoated Tablets
White, flat bevelled edge tablets break line on one face

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- For the treatment of mild to moderate pain, including headache, migraine, neuralgia, pain of teething, toothache sore throat and dysmenorrhoea.
- Symptomatic relief of rheumatic aches and pains, muscular aches and pains, sciatica, fibrositis, lumbago, joints swelling and stiffness.
- Symptomatic relief of influenza, feverish colds and feverishness associated with Childhood infections such as chicken pox, whooping cough, measles and mumps.
- Symptomatic relief of febrile reaction due to vaccination and immunisation.

4.2 Posology and method of administration

Adult including elderly and children aged 16 years or over:
Single dose: 1 or 2 tablets every 4-6 hours
Maximum daily dose: 8 tablets in a 24-hour period

Children dosage:

Age	Dose (number of tablet)	Frequency
6-10 years	half	Every 4-6 hours when necessary to a maximum of 4 doses in 24 hours
10-12 years	one	
12-15 years	one – one & half	

Not recommended for children for children aged under 6 years.

Dosage Instruction:

Take every 4 to 6 hours, as required. Do not take more frequently than every 4 hours. Dosage should not be continued for more than 3 days without consulting a doctor. Refer to contraindications when administering paracetamol to patients with renal or hepatic disorders.

Method Of administration:
Oral

4.3 Contra-indication:

Hypersenstivity to paracetamol and/or other ingredients. Alcoholics could be at risk in taking paracetamol.

4.4 Special warnings and precautions for use

Paracetamol should be given with care to patients with impaired liver function, and to patients taking other drugs that effect the liver. Liver function tests may be required at periodic intervals during high dose or long-term therapy, especially in patients with pre-existing hepatic disease. Plasma concentrations of the metabolites of paracetamol are increased in patients with moderate renal failure and paracetamol may be regenerated from these metabolites care should be taken in giving paracetamol to patients with alcohol dependence. Care should be taken giving paracetamol to patients with glucose-6 phosphate dehydrogenase deficiency.

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease

Do not exceed the recommended dose.

If symptoms persist consult your doctor. Do not continue to use for longer than 3 days without consulting your doctor or pharmacist

Ask the doctor or pharmacist about taking the tablets if pregnant or already on a course of medication.

Keep out of the sight and reach of children.

The label shall say:
“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” and “Talk to a doctor at once if you take too much of this medicine, even if you feel well”.

The leaflet shall say: “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

Alcohol and hepatotoxic medications reduce the capacity of the liver to metabolise paracetamol.

Chronic use of paracetamol enhances the effects of anticoagulants. 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.

Cholestyramine reduces absorption of paracetamol.

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine.

Paracetamol may decrease busulfan clearance when used in combination.

Plasma levels of chloramphenicol may increase with concurrent administration of paracetamol. However, the clinical relevance of this interaction is uncertain.

Concurrent use of paracetamol with NSAID may increase the risk of adverse renal effects. Prolonged concurrent use of paracetamol and aspirin or other salicylate may increase the risk of renal damage (such as analgesic nephropathy and renal papillary necrosis).

Patients receiving enzyme inducing drugs such as carbamazepine are considered at high risk of overdose. In cases of overdose an antidote should be administered even if their plasma-paracetamol concentrations are up to 50% below the standard reference line.

Interactions with laboratory tests: paracetamol may interfere with a number of test results; blood glucose, urate, bilirubin, lactate dehydrogenase and trasaminase concentrate, urine 5-hydroxyindoleacetic acid determination, prothrombin function using benitromide.

4.6 Fertility, pregnancy and lactation

Pregnancy

Paracetamol crosses the placenta. There is no known hazard in normal dosage, but like all non-essential medications paracetamol should be avoided especially during the first trimester unless considered essential by the physician. 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.

Lactation
Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breastfeeding.

4.7. Effects on ability to drive and use machines

None.

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, but these were not necessarily causality related to Paracetamol.
There are isolated reports of thrombocytopenia purpura, methaemoglobinaemia, and agranulocytosis.

Skin and subcutaneous disorders
Very rare cases of serious skin reactions such as Toxic Epidermal Necrolysis (TEN), Stevens- Johnson syndrome (SJS), acute generalised exanthematous pustulosis, fixed drug eruption have been reported.
Not known: purpura

Renal and urinary disorders
Rare: uraemia, azotaemia, renal colic, sterile pyuria

Hepato-biliary disorders
Rare: hepatitis

Gastrointestinal disorders
Rare: acute pancreatitis

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 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, phenobarbitone, 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 over dosage in first 24 hours are pallor, nausea, vomiting, diarrhoea, anorexia and abdominal pain and increased sweating. 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, coma 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.

It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are employed) become irreversibly bound to liver tissue.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: N02BE01

Paracetamol is 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 chemical stimulation. Paracetamol probably produces an antipyretic action by a central effect on the hypothalamic heat-regulating centre to produce peripheral vasodilatation 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 dose 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 2hours 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 form about 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 concentrations of paracetamol is 0.5 to2 hours, the time of peak effects 1 to 3 hours and the duration of action 3 to 4 hours.

5.3 Preclinical safety data:

There is no pre-clinical data of relevance to a prescriber, which is additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Starch	B.P	70.00	mg
Povidone	B.P	1.00	mg
Talc	B.P	6.00	mg

Stearic acid	B.P	4.00	mg
Aerosil	B.P	2.00	mg
Sodium starch glycollate	B.P	2.00	mg

6.2. Incompatibilities

None known.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

Will be stored in a cool and dry place, protected from light.

6.5. Nature and contents of container

Securitainer with polypropylene lids containing paracetamol tablets.(material of the container complies to EEC directives for plastic in contact with drugs and food stuff). In the packs of 25's, 50's, 100's, 1000's, 5000's, 10,000's.

6.6 Special precaution for disposal and other handling:
No special precautions required.

7. MARKETING AUTHORISATION HOLDER

Pharmvit Limited
177 Bilton Road, Perivale
Greenford, Middlesex,
UB6 7HQ

8. MARKETING AUTHORISATION NUMBER

PL: 04556/0004.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09/02/1983.

10 DATE OF REVISION OF THE TEXT

09/02/2017