

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol Tablets 500mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 500 mg of paracetamol. Each tablet also contains sodium metabisulphite 0.56 mg.

For a list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

White to off white, circular flat bevelled edge tablet with breakline on one side and plain on other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Paracetamol Tablets is a mild analgesic and antipyretic, and is recommended for the treatment of most painful and febrile conditions, for example, headache including migraine and tension headaches, toothache, backache, rheumatic and muscle pains, dysmenorrhoea, sore throat, and for relieving the fever, aches and pains of colds and flu. Also recommended for the symptomatic relief of pain due to non-serious arthritis.

4.2 Posology and Method of Administration

Adults, the elderly, and children aged 16 years and over:

One or two tablets up to four times daily as required.

Children:

Aged 10 - 15 years: One tablet up to four times daily as required.

Not suitable for children under 10 years of age.

Children should not be given Paracetamol Tablets for more than 3 days without consulting a doctor.

Dosage instruction:

Do not take more frequently than every 4 hours. Not more than 4 doses should be administered in any 24-hour period.

Oral administration only.

4.3 Contraindications

Hypersensitivity to paracetamol or any other ingredients. Alcoholics could be at risk in taking paracetamol.

4.4 Special warnings and precautions for use

- i) Do not exceed the stated dose.
- ii) Patients should be advised to consult their doctor if their headaches become persistent.
- iii) Consult a doctor if symptoms persist or worsen. Do not continue to use for longer than 3 days except on the advice of a doctor.
- iv) Ask the doctor or pharmacist about taking the tablets if pregnant or already on a course of medication.
- v) This product contains paracetamol.
- vi) Patients should be advised to consult a doctor if they suffer from non-serious arthritis and need to take painkillers every day.
- vii) *The label shall say:* “Talk to a doctor at once if you take too much of this medicine, even if you feel well.”,
“Do not take anything else containing paracetamol while taking this medicine.”
“Do not take more medicine than the label tells you to. If you do not get better, talk to your doctor.”
- viii) *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.”.
- ix) 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.
- x) Contains sodium metabisulphite which may rarely cause severe hypersensitivity reactions and bronchospasm.
- xi) Keep out of the sight and reach of children.

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 in patients with malnutrition or 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.

4.5 Interaction with other medicinal products and other forms of interaction

Alcohol reduces liver capacity to deal with paracetamol.

Chronic use of paracetamol enhances effect of warfarin and other coumarins with increased risk of bleeding; occasional doses have no significant effect. Colestyramine reduces absorption of paracetamol. Therefore, the colestyramine should not be taken within one hour if maximal analgesia is required.

Metoclopramide and Domperidone accelerate absorption of paracetamol. However concurrent use need not be avoided

May interact with Chloramphenicol causing increased plasma levels of Chloramphenicol.

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

Paracetamol is excreted in breast milk but not in clinically significant quantities. Available published data do not contraindicate breast-feeding.

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.

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 postmarketing 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 postmarketing experience indicates that adverse reactions to paracetamol are rare and serious reactions are very rare.

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.

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.

Gastrointestinal

Not known: acute pancreatitis

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.

Metabolism and nutrition disorders

Not known: High anion gap metabolic acidosis

Description of selected adverse reactions

High anion gap metabolic acidosis

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 10 g or more of paracetamol. Ingestion of 5 g 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 overdose 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.

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.

5.1 Pharmacodynamic Properties

ATC code: N02BE01, Other analgesics and antipyretics

Paracetamol is an antipyretic analgesic. The mechanism of action is probably similar to that of aspirin and dependant on the inhibition of prostaglandin synthesis. This inhibition appears, however, to be on a selective basis.

5.2 Pharmacokinetic Properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract with peak plasma concentrations occurring 30 minutes to 1 hour and the plasma half-life is 1 - 4 hours after therapeutic doses.

Paracetamol is relatively uniformly distributed throughout most body fluids.

Binding of the drug to plasma proteins is variable; 20 to 30 % may be bound at the concentrations encountered during acute intoxication. Following therapeutic doses 90 - 100% of the drug may be recovered in the urine within the first day. However, practically no paracetamol is excreted unchanged and the bulk is excreted after hepatic conjugation.

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

Pregelatinised starch (maize)

Sodium metabisulphite

Stearic acid (E570)

Magnesium stearate (E572)

6.2 Incompatibilities

None stated.

6.3 Shelf life

5 years.

6.4 Special Precautions for Storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Paracetamol 500mg Tablets are available in child-resistant packs (Glassine paper foil/ Aluminium or PVC / Aluminium foil) of 4,6,12 and 16tablets.

Specification details of blister packs:

PVC/Aluminium foil

- PVC (white, rigid, opaque): 250 microns
- PVC/Aluminium foil (hard tempered): 15/20 microns
- Primer (nitrocellulose): 1.5 to 2.5 gsm
- Heat seal lacquer: 6.5 to 8.5 gsm

PVC/Glassine paper – Aluminium foil

- PVC (white, rigid, opaque): 250 microns
- Glassine paper/Aluminium foil : $35\pm 3.50/25\pm 2.0$ gsm

6.6 Special precautions for disposal

No special precautions required.

7 MARKETING AUTHORISATION HOLDER

Flamingo Pharma UK Ltd
1st Floor, Kirkland House,
11-15 Peterborough Road,
Harrow, Middlesex,
HA1 2AX,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 43461/0006

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22/10/2024

10 DATE OF REVISION OF THE TEXT

22/01/2025