SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 1000mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Paracetamol Ph.Eur. 1000mg.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White to off-white, elongated biconvex tablets, with break line & P and 1 debossed on one side and with break line on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of mild to moderate pain and/or fever.

4.2 Posology and method of administration

Paracetamol 1000 mg Tablets are for oral administration.

Adults (including the elderly) and adolescents aged 16 years and over: One tablet up to 4 times daily as required.
The minimum dosing interval is 4 hours and the maximum daily dose is 4000 mg (4 tablets).

Not to be given to children under 16 years.

4.3 Contraindications

Hypersensitivity to paracetamol or any of the other constituents.

4.4 Special warnings and precautions for use

Paracetamol should be administered with caution under the following circumstances (see section 4.2 where relevant):

- Hepatic impairment
- Chronic alcoholism

- Renal impairment (GFR≤50ml/min)
- Gilbert's Syndrome (familial non-haemolytic jaundice)
- Concomitant treatment with medicinal products affecting hepatic function
- Glucose-6-phosphate dehydrogenase deficiency
- Haemolytic anaemia
- Glutathione deficiency
- Dehydration
- Chronic malnutrition
- Weight less than 50kg

Underlying liver disease increases the risk or paracetamol related liver damage. Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication.

Do not exceed the stated dose.

Patients should be advised not to take other paracetamol-containing products concurrently.

This product should only be used by the person for whom it is prescribed when clearly necessary.

Patients should be advised to consult their doctor if their headaches become persistent. Caution should be exercised in patients with glutathione depleted states, as the use of paracetamol may increase the risk of metabolic acidosis (refer also to section 4.9).

Use with caution in patients with glutathione depletion due to metabolic deficiencies.
If symptoms persist, medical advice must be sought.

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.

<u>Pack label:</u>
Immediate medical advice should be sought in the event of an overdose, even if you feel well. Do not take with any other paracetamol-containing products.

Patient Information Leaflet:
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.

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 warfarinand 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 due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4).

4.6 Fertility, pregnancy and lactation

Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results.
A large amount of data on pregnant women (more than 1000 pregnancy outcomes) indicate neither malformative, nor feto/neonatal toxicity.
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.
Paracetamol is excreted in breast milk but not in clinically significant amounts. No undesirable effects on nursing infants have been reported.
Consequently, Paracetamol may be used in breast-feeding women.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Adverse effects 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**	**Frequency**
Blood and lymphatic system disorders	Thrombocytopenia, Agranulocytosis	Very rare

Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angiodema and Stevens Johnson syndrome/toxic epidermal necrolysis. Very rare cases of serious skin reactions have been reported.	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm*	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare

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

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
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 or search for MHRA Yellow Card in the Google Play or Apple App store.

4.9 Overdose

Paracetamol overdose can result in liver damage which may be fatal.
Liver damage is likely in patients who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite become irreversibly bound to liver tissue.

Some patients may be at increased risk of liver damage from paracetamol toxicity:

Risk factors include;
- Patients with liver disease
- Elderly patients
- Young children
- Patients receiving long-term treatment with carbamazepine, phenobarbitone,

- phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver
- enzymes.
- Patients who regularly consume ethanol in excess of recommended amounts
- Patients with glutathione depletion e.g. eating disorders, cystic fibrosis, HIV
  infection, starvation, cachexia.
- Acute renal failure with acute tubular necrosis may also develop.
- Cardiac arrhythmias and pancreatitis have also been reported.

Symptoms
Symptoms generally appear within the first 24 hours and may comprise: nausea, vomiting, anorexia, pallor, and abdominal pain, or patients may be asymptomatic.
Overdose of paracetamol can cause liver cell necrosis likely to induce complete and
irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and
encephalopathy which may lead to coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.

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 Nacetylcysteine, 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

Pharmacotherapeutic group: Analgesics and antipyretics, Anilides ATC code: N02BE01

Paracetamol is an antipyretic analgesic. The mechanism of action is probably similar to that of aspirin and dependent 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. Concentration in plasma reaches a peak in 30 to 60 minutes. Plasma half-life is 1 - 4 hours.

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. Excretion is almost exclusively renal, in the form of conjugated metabolites.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pregelatinized starch

Povidone (K-30)

Stearic Acid

6.2 Incompatibilities

Not applicable

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

White opaque PVC/CR aluminium foil blister packs of 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Noumed Life Sciences Limited

Noumed House

Shoppenhangers Road

Maidenhead

Berkshire SL6 2RB

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 44041/0088

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24/03/2025

10 DATE OF REVISION OF THE TEXT

24/03/2025