SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 500mg/5ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains 500mg Paracetamol

Excipients with known effect:

Glycerol	1.5 g/5ml
Propylene glycol	1.66 g/5ml
Methylparahydroxybenzoate	9 mg/5ml
Propylparahydroxybenzoate	1 mg/5ml
Sunset yellow	0.15 mg/5ml

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution.

A clear, amber solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of mild to moderate pain in patients who are unable to receive other paracetamol formulations such as lower strength liquid preparations, effervescent tablets or tablets.

4.2 Posology and method of administration

For oral administration only.

Posology

Adults and adolescents over 16 years:

500mg (5ml) to 1000mg (10ml) up to three to four times a day, as required.

Maximum daily dose should not exceed 4g (40ml).

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.

Method of administration

A calibrated oral dosing syringe is supplied with this dosage form for accurate and convenient dose adjustment.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Patients with severe hepatic dysfunction.

Do not use this medicine in children and adolescents under 16 years.

4.4 Special warnings and precautions for use

Care is advised in the administration of paracetamol to patients with renal or hepatic impairment. The hazards of overdose are 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 in patients with 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.

Do not take with any other paracetamol-containing products.

Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed serious or irreversible liver damage.

Do not exceed the recommended dose.

Keep out of the sight and reach of children.

Excipient warnings:

This product contains the following excipients:

Parahydroxybenzoates (E216 and E218): these may cause allergic reactions (possibly delayed).

Sunset yellow (E110): may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

The hepatotoxicity of Paracetamol, particularly after overdosage, may be increased by drugs which induce liver microsomal enzymes such as barbiturates, tricyclic antidepressants and alcohol.

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).

Antivirals: Regular use of Paracetamol possibly reduces metabolism of Zidovudine (increased risk of neutropenia).

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 clinically significant quantities.
Available published data do not contraindicate breast-feeding.

Fertility

There are no fertility data available

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 effects of paracetamol are rare but hypersensitivity including skin rash may occur.
Hepatobiliary disorders: Hepatic dysfunction

Gastrointestinal disorders: Cases of acute pancreatitis have been reported. Paracetamol has been widely used and reports of adverse reactions are rare, and are generally associated with overdosage.

Haematological: There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

Metabolic and nutrition disorders: High anion gap metabolic acidosis (frequency not known)

Immune system: Allergic reactions occur occasionally.

Renal and urinary disorders: Nephrotoxic effects are uncommon and have not been reported in association with therapeutic doses, except after prolonged administration.

Skin and subcutaneous tissue disorders: Very rare cases of serious skin reactions.

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

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 carbmazepine, 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 depleted 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, hypotension, cerebral oedema, coma and death. Prothrombin time may increase with deteriorating liver function. 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 arrythmias 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 one hour. Plasma paracetamol concentration should be measured at four 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 eight 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 dosing schedule. If vomiting is not a problem, oral methionine may be suitable alternative for remote areas, outside hospital. Management of patients who present with serious

hepatic dysfunction beyond 24 hours 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: N02B E01

The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (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 antipyresis by acting centrally on the hypothalamic heat regulating centre to produce peripheral vaso-dilation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

5.2 Pharmacokinetic properties

Oral absorption is rapid and almost complete, it may be decreased if paracetamol is taken following a high carbohydrate meal.

There is no significant protein binding with doses producing plasma concentrations below 60mcg (µg)/ml, but may reach moderate levels with high or toxic doses.

Approximately 90 - 95% of a dose is metabolised in the liver, primarily by conjugation with glucuronic acid, sulphuric acid and cysteine. An intermediate metabolite, which may accumulate in overdosage after primary metabolic pathways become saturated, is hepatotoxic and possibly nephrotoxic.

Half life is 1 to 4 hours; does not change with renal failure but may be prolonged in acute overdosage, in some forms of hepatic disease, in the elderly, and in the neonate; may be somewhat shortened in children.

Time to peak concentration, 0.5 - 2 hours; peak plasma concentrations, 5 - 20mcg (µg)/ml (with doses up to 650mg); time to peak effect, 1 - 3 hours; duration of action, 3 - 4 hours.

Elimination is by the renal route, as metabolites, primarily conjugates, 3% of a dose may be excreted unchanged.

Peak concentrations of 10 - 15mcg (µg)/ml have been measured in breast milk, 1 - 2 hours following maternal ingestion of a single 650mg dose. Half life in breast milk is 1.35 - 3.5 hours.

5.3 Preclinical safety data

There is no pre-clinical data of relevance to the prescriber that are additional to those already included in other sections.
Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

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6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol (E1520)

Glycerol (E422)

Macrogol 400

Citric acid monohydrate

Sodium citrate

Sucralose

Methylparahydroxybenzoate (E218)

Propylparahydroxybenzoate (E216)

Peppermint flavour

Sunset yellow (E110)

Purified water

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Unopened: 3 years

Opened: 3 months

6.4 Special precautions for storage

Store below 25°C. Do not refrigerate or freeze. Store in the original bottle.

6.5 Nature and contents of container

Bottles: Amber (Type III) soda glass 150ml, 200ml and 500ml bottles.

Bottle provided in an outer cardboard carton.

Closure: 28mm white, child-resistant tamper evident caps with expanded polyethylene (EPE) liner.

Syringe: A 5ml dispensing oral syringe and bottle adapter are supplied with this pack.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Wockhardt UK Ltd

Ash Road North

Wrexham

LL13 9UF

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 29831/0593

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

31/01/2022

10 DATE OF REVISION OF THE TEXT

28/07/2025