1.4 PRODUCT INFORMATION.

1.4.1 Prescribing Information (Summary of Product Characteristics): *(Enclosed).*

1. Name of the medicinal product

Paratal Tablets.

2. Qualitative and quantitative composition

Each tablet contains: Paratal BP 500.0mg.

For more information on excipients see section 6.1

3.0 Pharmaceutical form: Tablet for oral administration.

White, circular FFBE tablets embossed "PARATAL" on one side and plain on reverse, packed in Alu/PVC blister packs of 10x10's contained in a unit box and bulk packs of 1000's in HDPE containers along with literature inserts.

4.0 Clinical particulars

4.1 Therapeutic indications

Paratal® tablets are indicated in conditions where analgesic and antipyretic effects are desired. It is used in the management of mild to moderate pain such as headache, dysmenorrhoea, myalgia (muscular pain) and dental pain. The preparation is of value in the reduction of temperature in the treatment of minor febrile conditions, such as colds or influenza and in the symptomatic treatment of local redness, swelling, pain and fever.

4.2 Posology and method of administration:

Method of administration: Oral administration.

Dose:

Adults: 500mg to 1g every 4 to 6 hours up to a maximum of 4g daily. It is recommended that if the preparation is used for long-term therapy, then the daily dose should not exceed 2.6g.

Children: 1 to 5 years: 125-250mg, three to four times daily (about one-quarter to half a tablet, 3 to 4 times daily.

6 to 12 years: 250-500mg, three to four times daily (Half to one tablet 3 to 4 times daily).

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Paediatric population: not recommended for children under the age of 10 years.

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.

Do not exceed the recommended dose.

Do not take for more than 3 days without consulting a doctor.

Do not take with any other paracetamol containing products.

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

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 cholestyramine.

The anticoagulant effect of warfarin and 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, especially in patients with risk factors.

4.6. Pregnancy and lactation

Pregnancy

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. A large amount of data on pregnant women indicates 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 if clinically needed however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Breast-feeding

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

Paracetamol has no influence on the ability to drive and use machines.

4.8 Undesirable effects

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

Skin and subcutaneous disorders

Very rare cases of serious skin reactions have been reported.

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.

Risk factors

If the patient:

- is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St. John's Wort or other drugs that induce liver enzymes, or
- regularly consumes ethanol in excess of recommended amounts, or
- 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, disseminated intravascular coagulation, haemorrhage, hypoglycaemia, cerebral oedema, gastrointestinal bleeding 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.

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.

Further measures will depend on the severity, nature and course of clinical symptoms of paracetamol intoxication and should follow standard intensive care protocols.

5. 0 Pharmacological Properties

5.1 Pharmacodynamic Properties.

Pharmacotherapeutic group: Other analgesics and antipyretics, **ATC code*:* N02B E01**.

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. 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. The time to peak plasma concentration of paracetamol is 0.5 to 2 hours, the time to peak effect 1 to 3 hours and the duration of action 3 to 4 hours.

5.3 Preclinical safety data

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

White cornstarch, Povidone K-30, Potassium Sorbate, Sodium Benzoate, Purified water, Magnesium Stearate & Sodium Starch Glycolate.

6.2 Incompatibilities

None known.

6.3 Shelf-life

36 months (3 years) from the date of manufacture.

6.4 Special precautions for storage

Store in a dry place, below 30°C. Protect from light. Keep all medicines out of reach of children.

6.5 Nature and contents of container

Alu/PVC blister packs of 10 x 10's in a unit box and bulk pack of 1000's in HDPE containers along with a literature insert.

6.6 Special precautions for disposal and other handling

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

6.7 Distribution Category

General Sales Drug (GS).

7. Marketing authorization holder/Registrant.

Laboratory & Allied Limited
Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa Road
P.O Box 42875 GPO 00100, Nairobi –Kenya.

8. Manufacturer

Laboratory & Allied Limited
Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa Road
P.O.BOX 42875 GPO 00100, Nairobi –Kenya
Email: info@laballied.com

9. Marketing Authorisation Number(s)

Registration No(s).: Kenya: H82098.
Botswana: BOT1803500 (10x10's).
BOT1803500A (1000's).
Malawi: PMPB/PL108/18.

Date of registration: Kenya: 12th November 1982.
Retention: Retained annually.

10. Date of revision of the text:

September 2023.