1. NAME OF THE MEDICINAL PRODUCT

Cipladon -500

Cipladon -1000

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains:

Paracetamol BP..... 500mg in the 500mg tablet

Paracetamol BP..... 1000mg in the 1000mg tablet

Excipient with known effect: Sodium, aspartame

3. PHARMACEUTICAL FORM

Tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Paracetamol 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.

4.2 Method of administration

Adults and the elderly:

1 -2 tablets in at least half a tumbler of water, up to 4 times daily as required.

Children:

6 - 12 years: ½ - 1 tablet dissolved in water up to 4 times daily. Not recommended for children under the age of 6 years.

Doses of paracetamol should not be given more frequently than every 4 hours, and not more than 4 doses should be given in any 24 hour period.

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

Oral administration only.

4.3 Contraindications

Hypersensitivity to paracetamol or any of the other constituents.

4.4 Special warnings and precautions for use

Contains paracetamol. Do not use with any other paracetamol-containing products.

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 to consult their doctor if their headaches become persistent.

Patients should be advised to consult a doctor if they suffer from non-serious arthritis and need to take painkillers every day.

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.

Cipladon-500 contains 439 mg sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

Cipladon-500 contains a source of phenylalanine. May be harmful for people with phenylketonuria.

If symptoms persist, medical advice must be sought.

Keep out of the sight and reach of children.

<u>Pack Label:</u>

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.

<u>Patient Information Leaflet:</u>

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

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 daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6 Pregnancy and lactation

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, as with any medicine it should be used at the lowest effective dose for the shortest possible time.

Paracetamol is excreted in breast milk but not in a clinically significant amount in recommended dosage. Available published data do not contraindicate breast feeding. **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 post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by system class and frequency.

The following convention has been utilised for the classification of the undesirable effects: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000) and very rare (<1/10,000), not known (cannot be estimated from available data).

Adverse event frequencies have been estimated from spontaneous reports received through post-marketing data.

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, among others, skin rashes and angiodema. Very rare cases of serious skin reactions have been reported.	Very rare
Respiratory, thoracic and	Bronchospasm*	Very rare
mediastinal disorders		
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.

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 local reporting system.

4.9 Overdose

Paracetamol overdose may cause liver failure which may require liver transplant or lead to death.

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

- 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, 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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.

Clinical Efficacy

In two dental pain studies, pain relief was observed at a median time of 15 minutes following administration of the 1000 mg dose of paracetamol (new formula).

Paracetamol (new formula) demonstrated superior pain relief at 1000 mg dose compared to placebo and to paracetamol (new formula) at 500 mg dose. Paracetamol (new formula) at the 500 mg dose also demonstrated superior efficacy compared to placebo.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastro-intestinal tract. The concentration in plasma reaches a peak in 30 to 60 minutes 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

Citric acid

Povidone

Sodium saccharin

Sodium bicarbonate

Sodium carbonate anhydrous

Simethicone

Polysorbate 80

Methylene chloride

Aspartame

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a cool and dry place below 25° C. Protect from moisture.

6.5 Nature and contents of container

Cartons having 4 strips of 4 tablets each.

6.6 Instructions for use, handling and disposal

NA

7. MARKETING AUTHORISATION HOLDER

Cipla Ltd

8. MARKETING AUTHORISATION NUMBER(S)

Kenya Reg no.: H2001/0427

Uganda Reg No.: NDA/MAL/HDP/2175

Mauritius Reg no.: R3950/02/14

Zambia Reg no.: 099/190

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Kenya:25/10/2001

Uganda: 4/8/2010

Mauritius: 01/01/1995

Zambia:30/5/2008

10. DATE OF REVISION OF TEXT

April 2021