Summary of product characteristics

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1. Name of the medicinal product

Cadimol 500mg tablet

2. Qualitative and quantitative composition

Each tablet contains Paracetamol 500mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Tablet.

White to off white, flat, round, bevelled edged, uncoated tablets with break line on one side and plain on the other side.

4. Clinical particulars

4.1. Therapeutic indications

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 Paracetmol 500mg tablets for more than 3 days without consulting a doctor.

These doses should not be repeated more frequently than every four hours nor should more than four doses be given in any 24 hour period.

Method of Administration

Oral administration only.

4.3. Contra-indications

Hypersensitivity to paracetamol or any of the constituents.

4.4. Special warnings and special precautions for use

Caution should be exercised in asthma patients who are sensitive to acetylsalicylic acid, since mild reactions of bronchospasm have been reported with paracetamol (cross-reaction).

In patients with glutathione-depleted conditions such as sepsis, the use of paracetamol may increase the risk of metabolic acidosis.

Caution in liver disease. Do not combine with other analgesic drugs containing paracetamol (eg combination medicine). Higher doses than recommended may result in very severe liver damage. Clinical signs of liver injury usually start after a couple of days and usually culminate in 4-6 days. Antidote should be given as early as possible. See also section 4.9 Overdose. In case of high fever, signs of secondary infection or if the symptoms last longer than 3 days, treatment should be reassessed.

4.5. Interaction with other medicinal products and other forms of interaction

Studies have shown that the effect of warfarin may be enhanced during treatment with paracetamol. The effect appears to increase with the dose of paracetamol but may occur at doses of 1.5-2.0 g of paracetamol per day for at least 5-7 days. Single doses of paracetamol in normal dosage are considered to have no effect.

Pharmacokinetic interactions

Enzyme-inducing drugs, such as certain antiepileptics (phenytoin, phenobarbital, carbamazepine) have been shown to decrease to approximately 60% of plasma AUC of paracetamol in pharmacokinetic studies. Other substances with enzyme inducing properties, eg rifampicin and St. John's Wort (Hypericum) are also suspected of lowering paracetamol concentrations. In addition, the risk may be greater for liver injury when treated with the maximum recommended dose of paracetamol in patients on enzyme inducing drugs.

Probenecid almost halves the clearance of paracetamol by inhibiting its conjugation with glucuronic acid. This would mean that the dose of paracetamol may be halved when co-administered with probenecid.

The absorption rate of paracetamol may be increased by metoclopramide, but the substances can be given in combination. The absorption of paracetamol is reduced by cholestyramine. Colestyramine should not be given within one hour if maximum analgesic effect is to be achieved.

Paracetamol may affect the pharmacokinetics of chloramphenicol. Therefore, plasma-based chloramphenicol is recommended for combination therapy.

4.6. Use during pregnancy and lactation

Pregnancy

Cadimol has no known risks during pregnancy. A large amount of data from pregnant women indicates neither malformations, fetal toxicity nor neonatal toxicity. Paracetamol may be used during pregnancy if clinically motivated, but it should be used with the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Lactation

Paracetamol passes into breast milk but the risk of affecting the child seems unlikely with therapeutic doses.

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

Adverse effects of paracetamol are rare. Very rare cases of serious skin reactions have been reported. There have been reports of blood dyscrasias including thrombocytopenia purpura, methaemoglobenaemia and agranulocytosis, but these were not necessarily causality related to paracetamol.

Blood and lymphatic system disorders Very rare (<1/10 000)	Thrombocytopenia Agranulocytosis
Immune system disorders Very rare (<1/10 000)	Anaphylaxis
Respiratory, thoracic and mediastinal disorders Very rare (<1/10 000)	Bronchospasm
Kidney and urinary tract Very rare (<1/10 000)	renal effects
Skin and subcutaneous tissue Rare (> 1/10 000 to <1/1 000) Very rare (<1/10 000)	Exanthem, urticaria, angioedema Allergic dermatitis
Hepatobiliary disorders Rare (> 1/10 000 to <1/1 000) Very rare (<1/10 000)	Hepatic dysfunction Liver damage

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 EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA).

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 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 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.

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.

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.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics, antipyretic, ATC code: N02BE01

Paracetamol is an anilide derivative with corresponding analgesic and antipyretic properties such as acetylsalicylic acid. However, paracetamol does not cause gastrointestinal irritation and is also well tolerated by patients with ulcer. Paracetamol does not affect platelet aggregation or bleeding time. Paracetamol is generally tolerated by patients with hypersensitivity to acetylsalicylic acid.

The antipyretic effect is obtained by the influence of heat regulating centers in the CNS, thereby increasing heat output.

The latency of the analgesic effect is about ½ hour, maximum power is reached within 1-2 hours and the duration is 4-5 hours. The progress of the antipyretic effect is somewhat slower: Thus, latency is about ½- 1 hour, maximal fever reduction is noted after 2-3 hours and the effect duration is approx. 8 hours.

5.2. Pharmacokinetic properties

Paracetamol is well absorbed by oral administration. Maximum plasma concentrations of paracetamol are achieved within ½-1 hour.

Plasma half-life is approximately 2 hours. Paracetamol is metabolised in the liver primarily by conjugation to glucuronide and sulphate. A minor proportion (in therapeutic dose about 3-10%) is oxidatively metabolized by cytochrome P450 and the resulting reactive intermediate metabolite is preferentially bound to the glutathione of the liver and excreted as cysteine and mercaptic acid conjugate. The secretion is via the kidneys. From a therapeutic dose, approximately 2-3% unchanged, approx. 80- 90% as glucuronide and sulfate and a minor amount of cysteine and mercapturic acid derivatives.

5.3. Preclinical safety data

There are no preclinical data relevant to the safety assessment beyond what has already been taken into account in the Summary of Product Characteristics.

6. Pharmaceutical particulars

6.1. List of Excipients

Maize starch,Polyvinyl pyrolidon K-30, Magnesium Stearate, microcrystalline cellulose, sodium starch glycolate, colloidal anhydrous silica.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

48 Months.

6.4. Special precautions for storage

Store below 30°C. Protect from light & moisture.

6.5. Nature and content of container

Cadimol tablets are packed in blister packs of 0.02mm Printed Aluminum foil and .025mm non-toxic transparent PVC film.

Pack size: 10 tablets in blister

6.6. Instructions for use and handling, and disposal (if appropriate)

No specific instructions for use/handling.

7. Marketing authorization holder

CADILA PHARMACEUTICALS (ETHIOPIA) PLC
GELAN CITY, OROMIA REGION
ETHIOPIA

8. NUMBER (S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS :

Certificate No: 3513/5025/REN/2017

9. Date of first authorization / renewal of the authorization:

Nov 1, 2017

10. Date of revision of the text:

August 2023