Summary of Product Characteristics

1. Name of the Medicinal Product.

Curamol-Fizz 500 Tablet.

2. Qualitative and Quantitative Information.

Each Uncoated Effervescent tablet contains Paracetamol 500 mg.

Excipients with known effect:
Each effervescent tablet contains Sodium in the form of sodium carbonate (130mg) and sodium bicarbonate (1398.5mg)
Each effecvescent tablet contains 25mg of Aspartame.

For the full list of excipients, see section 6.1

3. Pharmaceutical Form

Uncoated Effervescent Tablet.
Light Yellow coloured, round shaped, Beveled Edge, flat uncoated tablets and plain on both sides.

4. Clinical Particulars

4.1. Therapeutic Indications

Curamol Fizz tablet is indicated in Symptomatic treatment of mild to moderate pain and/or fever in adults and adolescents aged 12 years and above.

4.2. Posology and method of administration

Paediatric population
Dose depends on body weight and age. A single dose ranges from 10 to 15 mg/kg bodyweight. The maximum total daily dose is 60 mg/kg body weight for total daily dose.
Children below 12 years of age: this product is not recommended in children aged less than 12 years.
Adolescents of 12 to 15 years and weighing 41 to 50 kg: one tablet at a time, every 4-6 hours as needed, the maximum being 4 tablets per day (paracetamol 2000 mg per 24 hours).
Adolescents of 16 to 18 years and weighing more than 50 kg: as adults.

Adults
For adults and adolescents (aged 16 years and older) weighing more than 50 kg the usual single dose is 1-2 tablets at a time, to be repeated every 6 hours as needed, the maximum being 8 tablets per day (paracetamol 4000 mg per 24 hours).
For adults and adolescents (aged 16 years and older) and weighing less than 50 kg the recommended single dose is 1 tablet. The daily effective dose of paracetamol should not exceed 60 mg/kg/day (upto maximum 2g/day).

Renal impairment
In patients with renal insufficiency, the dose should be reduced:

Glomerular filtration rate	Dose
10-50 ml/min	500 mg every 6 hours
< 10 ml/min	500 mg every 8 hours

Hepatic impairment
In patients with impaired hepatic function or Gilbert´s syndrome, the dose must be reduced or the dosing interval prolonged.

Method of administration
For Oral use.
Place the tablets in a full tumbler of water and allow to dissolve completely before swallowing.After dissolving the tablets, a slightly opalescent solution will be produced.

4.3. Contraindications

Hypersensitivity to paracetamol or to any of the excipients.

4.4. Special warnings and Precautions for Use

Prolonged or frequent use is discouraged. Patients should be advised not to take other paracetamol containing products concurrently. Taking multiple daily doses in one administration can severely damage the liver; in such case unconsciousness does not occur. However, medical assistance should be sought immediately. Prolonged use except under medical supervision may be harmful. In adolescents treated with 60mg/kg daily of paracetamol, the combination with another antipyretic is not justified except in the case of ineffectiveness.

Renal and hepatic impairment.
Caution is advised in the administration of paracetamol to patients with moderate and severe renal insufficiency, mild to moderate hepatic insufficiency (including Gilbert's syndrome), severe hepatic insufficiency (**child-pugh>9**), acute hepatitis, concomitant treatment with medicinal products affecting hepatic functions, glucose-6- phosphate dehydrogenase deficiency, hemolytic anemia, alcohol abuse dehydration and chronic malnutrition (see section 4.2).

Alcohol usage
The hazards of overdose are greater in those with non- cirrhotic alcoholic liver disease. Caution should be exercised in cases of chronic alcoholism. The daily dose should not exceed 2000 mg in such case. Alcohol should not be used during the treatment with paracetamol.
“Caution is advised in asthmatic patients sensitive to aspirin (acetylsalicylic acid), because light reaction bronchospasm with paracetamol (cross-reaction) has been reported in less than 5% of the patients tested.”

Other medications and withdrawal:
Abrupt discontinuation of long-term use of high-dosed analgesics, taken not as directed, may cause headache, tiredness, muscular pain, nervousness and vegetative symptoms. The withdrawal symptoms subside within a few days. Patients should be advised to consult their doctor if headaches become persistent.

This medicinal product contains 439.46 mg sodium per effervescent tablet, equivalent to 21.97% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

This product also contains aspartame, a source of phenylalanine. May be harmful for people with phenylketonuria.

Do not exceed the stated dose.

If symptoms persist consult a doctor.

Treatment with an antidote is advised if an overdose is suspected.
Immediate medical advice should be sought in the event of overdosage even if the patient feels well, because of the risk of delayed serious liver damage.

This product should not be used for more than 10 consecutive days without a prescription. Liver and kidney damage cannot be excluded with prolonged use or excessive doses (more than 2 gram per day).

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

Pharmacodynamic interactions:

The anticoagulant effect of warfarin and other coumarins may be enhanced by regular use of paracetamol with increased risk of bleeding. The effect may occur already at daily doses of 2000 mg after 3 days. Occasional doses have no significant effect on bleeding tendency. Increased monitoring of INR values should be done during the duration of the combination and after its discontinuation.

Pharmacokinetic interactions:

Use of substances that induce liver enzymes, such as carbamazepine, phenytoin, phenobarbital, rifampicin and St John's wort (Hypericum perforatum) can increase the hepatotoxicity of paracetamol due to increased and more rapid formation of toxic metabolites. Therefore, caution should be taken in case of concomitant use of enzyme inducing substances.
Probenecid nearly halves the clearance of paracetamol by inhibiting its conjugation with glucuronic acid. This probably means that the dose of paracetamol can be halved when being given at the same time as probenecid.
Concurrent intake of medicinal products that accelerate gastric emptying, such as metoclopramide or domperidone, accelerates the absorption and onset of effect of paracetamol.
The absorption of paracetamol is reduced by cholestyramine. Cholestyramine should not be given within one hour if maximum analgesic effect is to be obtained.
Isoniazid affects the pharmacokinetics of paracetamol with possible potentiation of liver toxicity.
Paracetamol may affect the pharmacokinetics of chloramphenicol. Therefore an analysis of chloramphenicol in plasma is recommended in the event of combination treatment with chloramphenicol for injection.

Interference with laboratory tests:

Paracetamol may affect uric acid tests by wolframato phosphoric acid, and blood sugar tests by glucose-oxidase-peroxidase

4.6. Fertility, Pregnancy and breastfeeding.

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.

Breast-feeding

After oral administration, paracetamol is excreted into breast milk in small quantities. 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

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

4.8. Undesirable effects

The frequency using the following convention should be: 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). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Frequency	System	Symptoms
Very Rare	Blood and Lymphatic System disorders	Thrombocytopenia Agranulocytosis
Very Rare	Immune System Disorders	Anaphylaxis, Cutaneous hypersensitivity reactions including skin rashes and angioedema. Very rare cases of serious skin reactions have been reported
Very Rare	Respiratory, thoracic and mediastinal disorders.	Bronchospasm.
Very Rare	Hepatobiliary disorders.	Hepatic Dysfunction.

*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 authorization 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 Pharmacy and Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9. Overdose

There is a risk of poisoning, particularly in elderly subjects, in young adolescents, in patients with liver disease, in cases of chronic alcoholism, in patients with chronic malnutrition. Overdosing may be fatal.

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

- 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, hypoglycemia, 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. 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.
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.
High doses of sodium bicarbonate may be expected to induce gastrointestinal symptoms including belching and nausea. In addition, high doses of sodium bicarbonate may cause hypernatraemia; electrolytes should be monitored and patients managed accordingly.

5. Pharmacological Properties

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: other analgesics and antipyretics; anilides
ATC code: N02BE01.

Mechanism of action

Paracetamol's exact mechanism of action has not been fully established despite this, it is often categorized alongside NSAIDs (nonsteroidal anti-inflammatory drugs) due to its ability to inhibit the cyclooxygenase (COX) pathways.It is thought to exert central actions which ultimately lead to the alleviation of pain symptoms.
One theory is that Paracetamol increases the pain threshold by inhibiting two isoforms of cyclooxygenase, COX-1 and COX-2, which are involved in prostaglandin (PG) synthesis. Prostaglandins are responsible for eliciting

pain sensations. Paracetamol does not inhibit cyclooxygenase in peripheral tissues and, therefore, has no peripheral anti-inflammatory effects. Though acetylsalicylic acid (aspirin) is an irreversible inhibitor of COX and directly blocks the active site of this enzyme, studies have shown that Paracetamol (paracetamol) blocks COX indirectly.Studies also suggest that Paracetamol selectively blocks a variant type of the COX enzyme that is unique from the known variants COX-1 and COX-2.This enzyme has been referred to as *COX-3*. The antipyretic actions of Paracetamol are likely attributed to direct action on heat-regulating centers in the brain, resulting in peripheral vasodilation, sweating, and loss of body heat.The exact mechanism of action of this drug is not fully understood at this time, but future research may contribute to deeper knowledge.

5.2. Pharmacokinetic Properties

The absorption of paracetamol by the oral route is rapid and complete. Maximum plasma concentrations are reached 30 to 60 minutes following ingestion.

Distribution

Paracetamol is distributed rapidly throughout all tissues. Concentrations are comparable in blood, saliva and plasma. Protein binding is low.

Biotransformation

Paracetamol is metabolized mainly in the liver following two major metabolic pathways: glucuronic acid and sulphuric acid conjugates. The latter route is rapidly saturated at doses higher than the therapeutic dose. A minor route, catalyzed by the cytochrome P450, results in the formation of an intermediate reagent (N-acetyl-p- benzoquinoneimine) which under normal conditions of use is rapidly detoxified by glutathione and eliminated in the urine, after conjugation with cystein and mercaptopuric acid. Conversely, when massive intoxication occurs, the quantity of this toxic metabolite is increased.

Elimination

Elimination is essentially through the urine. 90% of the ingested dose is eliminated via the kidneys within 24 hours, principally as glucuronide (60 to 80%) and sulphate conjugates (20 to 30%). Less than 5% is eliminated in unchanged form.

Elimination half life is about 2 hours.

Special patient groups
Renal impairment

In cases of severe renal insufficiency (creatinine clearance lower than 10 ml/min) the elimination of paracetamol
and its metabolites is delayed.

Elderly
The capacity for conjugation is not modified

5.3. Preclinical safety data

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available. 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

Citric acid Anhydrous
Quinoline Yellow Lake
P.V.P.K.30
Tween 80
Methylene Dichloride
Sodium Bicarbonate
Sodium Carbonate
Aspartame
Simeticone (ADIP)

6.2. Incompatibilities

Not Applicable.

6.3. Shelf-life

36 months

6.4. Special Precautions for Storage

Do not store above 30°C. Protect from light and moisture.

6.5. Nature and contents of container

1x4 tablets packed in Alu Strips. 4 such strips are packed in unit carton with a package insert.

6.6. Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization Holder

Dawa Limited,Plot No 7879/9, Baba Dogo Road-Ruaraka.
P.O BOX 16633-00620 -Nairobi, Kenya.

Manufactured by:

Maxtar Bio-Genics,
K. No. 705, Nalagarh road, Malku Majra, (Baddi), Tehsil Nalagarh, Distt. Solan, Himachal Pradesh – 173205, India.

8. Marketing Authorization Number

H2024/CTD10894/23114

9. Date of First Authorization

9th February 2024

10. Date of Revision of the text

November 2024