Summary of product characteristics

1. Name of the medicinal product:
CETALSyrup

2. Qualitative and quantitative composition:
Each 5 ml contains:
Paracetamol Microfined …….120 mg

3. Pharmaceutical form:
A clear syrupy liquid.

4. Clinical particulars:
4.1 Therapeutic indications:
As an antipyretic: Symptomatic treatment of febrile conditions such as influenza, exanthematous diseases, acute respiratory tract diseases, etc.
As an analgesic: Headaches, neuralgia, myalgia and other painful manifestations of medium entity, of various origins.

4.2 Posology and method of administration
For children it is essential to respect the dosage defined according to their body weight, and therefore to choose the suitable formulation. Approximate ages as a function of body weight are given for information.
Below three months, in case of jaundice, it is advisable to reduce the single dose by mouth.
In adults, the maximum oral dose is 3000 mg per day (see section "**Overdose**").
The dosage schedule of **Cetal** in relation to age, weight and route of administration is as follows:
A measuring cup is attached to the package with level marks.
Children weighing between 7 and 10 kg (approximately between 6 and 18 months): 5 ml at a time (corresponding to 120 mg of paracetamol), to be repeated if necessary, after 6 hours, without exceeding 4 doses per day.
Children weighing between 11 and 12 kg (approximately between 18 and 24 months): 5 ml at a time (corresponding to 120 mg of paracetamol), to be repeated if necessary, after 4 hours, without exceeding 6 doses per day.
Children weighing between 13 and 20 kg (approximately between 2 and 7 years): 7.5-10 ml at a time (corresponding respectively to 180 mg and 240 mg of paracetamol), to be repeated if necessary, after 6 hours, without exceed 4 administrations per day.
Children weighing between 21 and 25 kg (approximately between 6 and 10 years): 10 ml at a time (corresponding to 240 mg of paracetamol), to be repeated if necessary, after 4 hours, without exceeding 6 doses per day.
Children weighing between 26 and 40 kg (approximately between 8 and 13 years): 15-20 ml at a time (corresponding respectively to 360 mg and 480 mg of paracetamol), to be repeated if necessary, after 6 hours, without exceeding the 4 administrations per day.
Adolescents weighing between 41 and 50 kg (approximately between 12 and 15 years): 20 ml at a time (corresponding to 480 mg of paracetamol), to be repeated if necessary, after 4 hours, without exceeding 6 doses per day.
Adolescents weighing more than 50 kg (approximately over 15 years): 20 ml at a time (corresponding to 480 mg of paracetamol), to be repeated if necessary, after 4 hours, without exceeding 6 doses per day.
Adults: 20 ml at a time (corresponding to 480 mg of paracetamol), to be repeated if necessary, after 4 hours, without exceeding 6 doses per day.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients.
Patients with severe hemolytic anemia.
Severe hepatocellular insufficiency.

4.4 Special warnings and precautions for use
In rare cases of allergic reactions, administration should be discontinued and appropriate treatment instituted.
Paracetamol should be administered with caution to patients with mild to moderate hepatocellular insufficiency (including Gilbert's syndrome), severe hepatic insufficiency (Child-Pugh> 9), acute hepatitis, concomitant treatment with drugs that impair liver function, deficiency of glucose-6-phosphate dehydrogenase, hemolytic anemia. High or prolonged doses of the product can cause and even serious alterations in the kidney and blood, therefore administration in subjects with renal insufficiency must be carried out only if actually necessary and under direct medical supervision.
During treatment with paracetamol, before taking any other drug, check that it does not contain the same active ingredient, as if paracetamol is taken in high doses, serious adverse reactions can occur.
Instruct the patient to contact the doctor before combining any other medication.
Cetal syrup contains:
Sucrose and Sorbitol: Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption, or sucrase isomaltase insufficiency, should not take this medicine.
In patients with diabetes, it should be borne in mind that a dose of 15 milliliters of this medicine contains 3.96 mg of sucrose and a dose of 20 milliliters contains 5.28 mg of sucrose.
Sorbitol May cause softening of the stool
Propylene Glycol: Co-administration with any alcohol dehydrogenase substrate such as ethanol can induce severe adverse effects in infants and children less than 5 years of age. Although propylene glycol has not shown toxic effects on reproduction and development in animals or humans, it can reach the fetus and was found in breast milk. As a consequence, the administration of propylene glycol to pregnant or lactating patients should be considered on a case-by-case basis. Clinical monitoring is required for patients with hepatic or renal insufficiency due to various adverse events attributed to propylene glycol such as renal dysfunction (acute tubular necrosis), acute renal injury and hepatic dysfunction.
Do not administer for more than 3 consecutive days without consulting your doctor.

4.5 Interaction with other medicinal products
The oral absorption of paracetamol depends on the rate of gastric emptying. Therefore, concomitant administration of drugs that slow (e.g. anticholinergics, opioids) or increase (e.g. prokinetics) the rate of gastric emptying may result in a decrease or increase in the bioavailability of the product, respectively.
Concomitant administration of cholestyramine reduces the absorption of paracetamol. The simultaneous intake of paracetamol and chloramphenicol can induce an increase in the half-life of chloramphenicol, with the risk of elevating its toxicity.
The concomitant use of paracetamol (4 g per day for at least 4 days) with oral anticoagulants can induce slight variations in the INR values. In these cases, more frequent monitoring of INR values must be conducted during concomitant use and after its discontinuation.
Use with extreme caution and under strict control during chronic treatment with drugs that can determine the induction of hepatic monooxygenases or in case of exposure to substances that can have this effect (for example rifampicin, cimetidine, antiepileptics such as glutethimide, phenobarbital, carbamazepine) . The same is true in cases of alcoholism and in patients treated with zidovudine.
The administration of paracetamol can interfere with the determination of uricemia (by the phospho-tungstic acid method) and with that of blood sugar (by the glucose-oxidase-peroxidase method)

4.6 Pregnancy, fertility and Lactation

A large amount of data on pregnant women indicates neither malformative nor fetal / neonatal toxicity. Epidemiological studies of neuro-developmental in children exposed to paracetamol in utero show inconclusive results. If clinically necessary, paracetamol can be used during pregnancy; however it should be used at the lowest effective dose for the shortest possible time and with the lowest possible frequency.
It is advisable to administer the medicine during pregnancy and breastfeeding only in cases of real need and under the direct supervision of the doctor.

4.7 Effects on ability to drive and use machines
Cetal does not affect the ability to drive or to use machines.

4.8 Undesirable effects
The following symptoms have been reported with the use of paracetamol:
MedDRA System Organ Classification and its frequency (not known: (frequency cannot be estimated from the available data):
Blood and Lymphatic system disorders: Thrombocytopenia, leukopenia, anemia, agranulocytosis.
Immune system disorders: Hypersensitivity reactions (urticaria, laryngeal edema, angioedema, anaphylactic shock).
Nervous system disorders: Dizziness.
Gastrointestinal disorders: Gastrointestinal reaction.
Hepatobiliary disorders: Abnormal liver function, hepatitis.
Skin and Subcutaneous tissue disorders*: Erythema multiforme, Stevens Johnson syndrome, epidermal necrolysis, rash.
Renal and Urinary disorders: Acute renal failure, interstitial nephritis, hematuria, anuria.
***** Very rare cases of severe skin reactions have been reported.

4.9 Overdose
In case of accidental intake of very high doses of paracetamol, acute intoxication is manifested by anorexia, nausea and vomiting, followed by a profound deterioration of the general condition, these symptoms usually appear within the first 24 hours. In case of overdose, paracetamol can cause hepatic cytolysis which can evolve towards massive and irreversible necrosis, with consequent hepatocellular insufficiency, metabolic acidosis and encephalopathy, which can lead to coma and death. Simultaneously, an increase in the levels of hepatic transaminases, lactic-dehydrogenase, and bilirubinemia, and a reduction in prothrombin levels are observed, which can occur in the 12-48 hours following ingestion.
The measures to be taken consist of early gastric emptying and hospitalization for appropriate treatment, by administering, as early as possible, N-acetylcysteine as an antidote: the dosage is 150 mg / kg i.v. in glucose solution in 15 minutes, then 50 mg / kg in the following 4 hours and 100 mg / kg in the following 16 hours, for a total of 300 mg / kg in 20 hours.

5. Pharmacological properties
5.1 Pharmacodynamics properties
Pharmacotherapeutic group: Analgesics and antipyretics, anilides.
The analgesic effect of paracetamol is attributable to a direct action at the level of the Central Nervous System, probably mediated by the opioid and serotonergic system, as well as by an action of inhibition of the synthesis of prostaglandins at a central level. Furthermore, paracetamol has a marked antipyretic activity.

5.2 Pharmacokinetics properties
Absorption:
Absorption of paracetamol by mouth is complete and rapid. The maximum concentrations in plasma are reached between 30 and 60 minutes after ingestion.
Distribution:

Paracetamol is evenly distributed in all tissues. Concentrations in blood, saliva and plasma are comparable. Binding to plasma proteins is weak.

Metabolism:

Paracetamol is mainly metabolized in the liver. There are two main metabolic pathways: conjugation with glucuronic acid and sulfo-conjugation. The latter route is rapidly saturable at doses higher than therapeutic doses. A minor pathway, catalyzed by cytochrome P450 (particularly CYP2E1), leads to the formation of a reactive intermediate, N-acetyl-p-benzoquinoneimine, which, under normal conditions of use, is rapidly detoxified from glutathione and eliminated in the urine. after conjugation with cysteine and mercapturic acid. Conversely, during severe poisoning, the amount of this toxic metabolite is increased

Elimination:

It is essentially urinary. 90% of the ingested dose is eliminated by the kidneys in 24 hours, mainly as glucuronide (60 to 80%) and as sulfur conjugates (20 to 30%). Less than 5% is eliminated unchanged.
The elimination half-life is about 2 hours

Renal failure:

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

6. Pharmaceutical particulars:

6.1 List of excipients:

Sorbitol 70%, Citric acid anhydrous, Propylene glycol, Glycerin, Orange yellow EII0, Orange oil, Sodium benzoate, Sucrose, Purified water.

6.2 Incompatibilities:

None known

6.3 Shelf life:

3 years

6.4 Special precautions for storage:

Do not store above 30°C.

6.5 Nature and contents of container:

A carton box containing bottles of 60, 100, 125 mland an inner leaflet.

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

7. Marketing authorization holder:

Egyptian international pharmaceutical industries company (EIPICO)

8. MARKETING AUTHORISATION NUMBER(S)

2452/NMR/LD

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10.Date of revision of the text:

December2022.