SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

EFFERALGAN PAEDIATRIC 3% ORAL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Paracetamol ..... 3 g

Per 100 mL of oral solution.

Excipients with known effect: sucrose (sugar: 0.67 g sucrose in 4 kg graduations on the dosing system) and propylene glycol (E1520) (146 mg propylene glycol per 100 mL of oral solution, equivalent to 3.9 mg/kg/day).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Symptomatic treatment of mild to moderate pain and/or febrile state.

This formulation is **RESERVED FOR CHILDREN from 4 to 32 kg** (aged from around 1 month to 12 years).

4.2. Posology and method of administration

Posology

The lowest effective dose should generally be used for the shortest duration possible.

Paediatric population

In children, it is essential to **observe the posologies defined according to the weight of the child**, and therefore choose an adjusted formulation. The approximate ages based on weight are given for informational purposes.

The recommended daily dose of paracetamol is around 60 mg/kg/day, in 4 doses, i.e. around 15 mg/kg every 6 hours.

The dosing system is graduated in kg, specifying the weights 4-6-8-10-12-14-16 kg. The other scale corresponds to the weights in between 5-7-9-11-13-15 kg. It administers 15 mg/kg/administration. This dose may be repeated after 6 hours if required, **without exceeding 4 doses per day.**

The dose per administration is obtained by filling the dosing system up to the scale marker that matches the weight of the child (see

section 6.6).

- from 4 kg to 16 kg: fill the dosing system up to the scale marker that matches the weight of the child the scale marker closest to that weight. Dose administration can be repeated every 6 hours if required.
  For example, for a child weighing 4 to 4.5 kg: fill the dosing system up to the 4 kg scale marker. For example, for a child weighing 4.5 to 5 kg: fill the dosing system up to the 5 kg scale marker.
- from 16 kg to 32 kg: initially fill up the dosing system, then complete by filling the dosing system a second time until the child's weight is reached. Dose administration can be repeated every 6 hours if required.
  For example, for a child weighing 18 kg: initially fill the dosing system up to the 10 kg scale marker, then fill a second time up to the 8 kg scale marker.

Maximum recommended doses: see section 4.4

Warning: take all medicinal products into account in order to prevent an overdose, including medicines obtained without a prescription (see section 4.4).

Renal impairment

In cases of renal impairment and except medical advice, it is recommended that the dose be reduced, and that the minimum interval between 2 doses be increased, as per the following table:

Creatinine Clearance	Administration interval
>10 mL/min	6 hours
<10 mL/min	8 hours

The total paracetamol dose should not exceed 60 mg/kg/day (no more than 3 g/day).

Hepatic impairment

In patients with hepatocellular impairment or Gilbert's syndrome (non-haemolytic familial jaundice), it is recommended that the dose be reduced and the minimum interval between two administrations be increased. The total paracetamol dose should not exceed 60 mg/kg/day (no more than 3 g/day).

Special clinical situations

The total maximum daily dose of paracetamol should not exceed 60 mg/kg/day (no more than 3 g/day) in the following situations:

- adults under 50 kg,
- chronic alcoholism,
- malnutrition (low reserves of hepatic glutathione),
- dehydration.

Administration

Oral use.

The solution may be consumed as it is or diluted in a small amount of liquid (for example: water, milk, fruit juice).

4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients

listed in section 6.1. Severe hepatocellular impairment.

4.4. Special warnings and precautions for use

Special warnings

In order to prevent a risk of overdose:

- verify the absence of paracetamol in the composition of other medicinal products (medicinal products obtained with or without a prescription),
- observe the maximum

recommended doses. Maximum

recommended doses:

The total maximum daily dose of **paracetamol should not exceed 80 mg/kg/day for children under 37 kg** (see section 4.9). There are special formulations suitable for children weighing over 32 kg which should be used.

For reference, the total maximum daily dose of **paracetamol should not exceed** (see section 4.9):

- 3 g per day in children **from 38 kg to 50 kg**,
- **4 g per day in adults and children over 50 kg**.

Paracetamol may cause serious skin reactions. Patients should be informed of the early signs of these serious skin reactions,and the onset of rash or any other sign of hypersensitivity requires discontinuation of treatment.

Precautions for use

Paracetamol is to be used with caution in the case of:
- mild to moderate hepatocellular impairment (see section 4.2),
- renal impairment (see section 4.2),
- Gilbert syndrome (non-haemolytic familial jaundice) (see section 4.2),
- chronic alcoholism (see section 4.2),
- anorexia or cachexia,
- chronic malnutrition (low reserves of hepatic glutathione) (see section 4.2),
- dehydration (see section 4.2).

In the event of the discovery of acute viral hepatitis, treatment should be discontinued.

In a child treated with paracetamol, the combination of another medicinal product used to lower fever (antipyretic) is only justified in the case of inefficacy. The combination must be initiated and monitored by a doctor without exception.

This medicine contains 0.67 g sucrose in 4 kg graduations on the dosing system. This must be considered within daily intakes in cases of low sugar diets or diabetes. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This medicine contains 146 mg propylene glycol (E1520) in each 100 mL of oral solution which is equivalent to 3.9 mg/kg/day. Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce serious adverse effects in neonates.

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

Combinations requiring precautions for use

- Vitamin K antagonists

Risk of increase of the Vitamin K antagonist effect and of the risk of haemorrhage in the event that paracetamol is taken at maximum doses (4 g/day) for at least 4 days.

More frequent monitoring of INR. Potential adjustment of the Vitamin K antagonist dosage during treatment with paracetamol and after its discontinuation.

+ Flucloxacillin

Caution is advised when paracetamol is administered concomitantly with flucloxacillin due to the increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with a risk factor for glutathione deficiency, such as severe renal impairment, sepsis, malnutrition, or chronic alcoholism. Close monitoring is recommended in order to detect the

onset of HAGMA, via the testing for urinary 5-oxoproline.

Interactions with paraclinical testing

Administration of paracetamol can cause errors in blood glucose tests using the glucose oxidase- peroxidase method in the case of abnormally high concentrations.

Administration of paracetamol can cause errors in blood uric acid assays using the phosphotungstic acid method.

4.6. Fertility, pregnancy and lactation

Pregnancy

Studies in animals did not show evidence of a teratogenic or foetotoxic effect from paracetamol.

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

In therapeutic doses, the administration of this medicinal product is possible during breast-feeding.

Fertility

Due to the potential mechanism of action on cyclooxygenase and prostaglandin synthesis, paracetamol may impair fertility in women, affecting ovulation. This is reversible upon discontinuation of therapy.

Effects on male fertility were observed in one animal study. The relevance of these effects in humans is not known.

4.7. Effects on ability to drive and use machines

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

4.8. Undesirable effects

Adverse reactions are classified by organ system. Their frequencies are defined as follows:

- 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)
- Unknown frequency (cannot be estimated from the available data)

Immune system disorders

Rare: hypersensitivity reactions, such as anaphylactic shock, angioedema (Quincke's oedema), erythema, urticaria, skin rash. Their occurrence requires permanent discontinuation of this drug and related drugs.

Skin and subcutaneous tissue disorders

Very rare: serious skin reactions. Their occurrence requires discontinuation of treatment.

Blood and lymphatic system disorders

Very rare: thrombocytopenia, leukopenia and neutropenia.

A risk of imbalance of INR can occur in combination with VKA and paracetamol at maximum dose (4g/day) for a minimum duration of 4 days (see section 4.5).

Reporting of suspected adverse reactions

Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9. Overdose

The risk of severe intoxication (therapeutic overdose or accidental intoxication) may be particularly high in elderly subjects, young children, patients with hepatic impairment, cases of chronic alcoholism, and patients suffering from chronic malnutrition. In these cases, intoxication can be fatal.

Symptoms

Nausea, vomiting, anorexia, paleness, malaise, sweating, abdominal pain usually appearing within the first 24 hours.

An overdose, starting at 10 g of paracetamol in a single administration in adults, and 150 mg/kg of body weight in a single administration in children, causes hepatic cytolysis that could lead to complete and irreversible necrosis, resulting in hepatocellular impairment, metabolic acidosis, encephalopathy, which could lead to coma and death.

At the same time, there is an increase in hepatic transaminases, lactic dehydrogenase, bilirubin, and a decrease in prothrombin levels that may occur 12 to 48 hours after ingestion. The clinical symptoms of hepatic involvement are usually observed after 1 to 2 days and reach a maximum after 3 to 4 days.

Emergency procedure

- Discontinue treatment.
- Immediate transfer to hospital setting.
- Collect a tube of blood to measure the initial plasma dose of paracetamol as soon as possible from the fourth hour after ingestion.
- Rapid elimination of the ingested product by gastric lavage.
- The treatment of paracetamol overdose typically includes administration of the antidote N-acetyl cysteine intravenously or orally as early as possible, preferably before the tenth hour.
- Symptomatic treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: OTHER ANALGESICS AND

ANTIPYRETICS, ANILIDES, **ATC code: N02BE01.**

N: Central nervous system.

Mechanism of action

Paracetamol has a central and peripheral mechanism of action.

5.2. Pharmacokinetic properties

Absorption

The absorption of paracetamol for oral use is complete and fast. Maximum plasma concentrations are obtained 30 to 60 minutes after ingestion.

Distribution

Paracetamol is distributed rapidly throughout all tissues. The concentrations are comparable in the blood, saliva, and plasma. Plasma protein binding is low.

Biotransformation

Paracetamol is metabolised primarily by the liver. The two major metabolic routes are conjugation with glucuronic acid and sulphate. The latter route can be rapidly saturated at posologies that exceed the therapeutic doses. A

minor pathway, catalysed by cytochrome P 450, is the formation of a reactive intermediate (N-acetyl benzoquinoneimine), which, under normal conditions of use, is rapidly detoxified by reduced glutathione and eliminated in the urine after conjugation with cysteine and mercapturic acid.

In contrast, during massive intoxications, the quantity of this toxic metabolite is increased.

Elimination

Elimination is primarily urinary. 90% of the ingested dose is eliminated by the kidney in 24 hours, mainly in the form of glucuronide (60 to 80%) and sulphate (20 to 30%) conjugates. Less than 5% is eliminated unchanged.

The elimination half-life is around 2 hours.

Physiopathological variations

Renal impairment: in the case of renal impairment (see section 4.2), the elimination of paracetamol and its metabolites is delayed.

5.3. Preclinical safety data

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

Conventional preclinical studies of safety pharmacology, genotoxicity, repeated dose toxicity and carcinogenic potential did not reveal any special risk for humans at therapeutic doses.

In hepatotoxic doses, paracetamol has demonstrated genotoxic and carcinogenic potential (tumours in the liver and bladder) in mice and rats. However, this genotoxic and carcinogenic activity is considered to be linked to changes of the metabolism of paracetamol when administered at high doses or concentrations and does not present a risk for clinical use.

In rats, effects on male fertility (oligospermia, abnormal sperm motility and decrease in the fertilising potential of sperm) at high doses (500 and 1000 mg/kg of body weight per day) have been observed.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Macrogol 6000, sucrose solution, sodium saccharin, potassium sorbate, anhydrous citric acid, caramel-vanilla flavouring (including propylene glycol (E1520), colouring (E150d), purified water.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

After first opening the bottle: 3 months.

6.4. Special precautions for storage

Do not store above 25°C.

6.5. Nature and contents of container

90 mL bottle with dosing spoon:

90 mL brown bottle made of polyethylene terephthalate with a child proof cap made of low density polyethylene.

Dosing system (dosing spoon) made of polystyrene with a scale in kg representing the weight of the child at 4 kg, 6 kg, 8 kg, 10 kg, 12 kg, 14 kg and 16 kg, corresponding to a dose of 15 mg of paracetamol per kg weight

of the child.

A 90 mL bottle administers 180 doses of 15 mg

(see section 4.2). 90 mL bottle with oral dosing

syringe:

90 mL brown bottle made of polyethylene terephthalate with a child proof cap made of low density polyethylene.

Dosing system (oral dosing syringe), consisting of polyethylene housing and a polystyrene plunger, with a scale in kg representing the weight of the child at 4 kg, 6 kg, 8 kg, 10 kg, 12 kg, 14 kg
and 16 kg, corresponding to a dose of 15 mg of paracetamol

per kg weight of child. A 90 mL bottle administers 180 doses

of 15 mg (see section 4.2).

150 mL bottle with dosing spoon:

150 mL brown bottle made of polyethylene terephthalate with a child proof cap made of low density polyethylene.

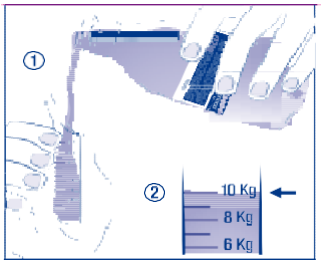
Dosing system (dosing spoon) made of polystyrene with a scale in kg representing the weight of the child at 4 kg, 6 kg, 8 kg, 10 kg, 12 kg, 14 kg and 16 kg, corresponding to a dose of 15 mg of paracetamol per kg weight of the child.

A 150 mL bottle administers 300 doses of 15 mg (see section 4.2).

6.6. Special precautions for disposal and other handling

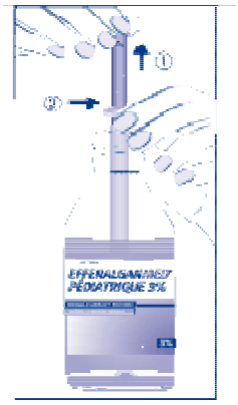
90 mL bottle with dosing spoon:

The dose per administration is obtained by filling the dosing spoon (1) up to the scale marker that matches the weight of the child (2), according to the diagram below (see section 4.2):



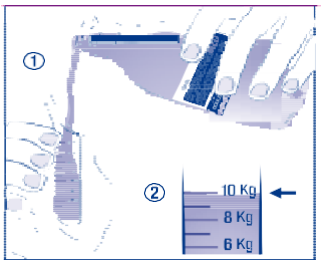
90 mL bottle with oral dosing syringe:

The dose per administration is obtained by pulling the plunger (1) up to the scale marker that matches the weight of the child (2), according to the diagram below (see section 4.2):



150 mL bottle with dosing spoon:

The dose per administration is obtained by filling the dosing spoon (1) up to the scale marker that matches the weight of the child (2), according to the diagram below (see section 4.2):



To open the bottle, you must press down and twist the child proof cap.

After each use, close the bottle of oral solution, rinse the dosing system well with water and dry. Then immediately store the dosing system in its box, in a location that is inaccessible to children. Never separate the dosing system from the rest of the medicinal product's packaging (bottle, box, leaflet)**.**

Use of the dosing system is strictly reserved for the administration of EFFERALGANMED PAEDIATRIC 30 mg/mL, oral solution.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. The dosing system should be discarded at the same time as the medicinal product's container.

7. MARKETING AUTHORISATION HOLDER

LABOREX KENYA

8. MARKETING AUTHORISATION NUMBER(S)

CTD10628

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/04/2024

10. DATE OF REVISION OF THE TEXT

17/5/2025