Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

GALPARA IV (Paracetamol Infusion 1% w/v)

2. Qualitative and quantitative composition

Each 100 mL injection contains 1gm of paracetamol

Excipients with known effect:
Mannitol
Sodium Metabisulphite

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Solution for infusion
A clear, colourless to brownish yellow colour solution.

4. Clinical particulars

4.1 Therapeutic indications

- Short-term treatment of moderate pain, especially following surgery,
- Short-term treatment of fever, when the intravenous route is clinically justified by an urgent need to treat pain or hyperthermia and/or when other routes of administration are not possible.

4.2 Posology and method of administration

The 100 ml vial is restricted to adults, adolescents and children weighing more than 33 kg.
The 50 ml vial is adapted to term newborn infants, infants, toddlers and children weighing less than 33 kg.

Posology
Dosing based on patient weight - see the dosing table below.

Patient weight	**Dose per administration**	**Volume per administration**	**Maximum volume per administration based on upper weight limits of group (ml)****	**Maximum daily dose*****
≤ 10 kg*	7.5 mg/kg	0.75 ml/kg	7.5 ml	30 mg/kg
> 10 kg to ≤ 33 kg	15 mg/kg	1.5 ml/kg	49.5 ml	60 mg/kg not exceeding 2 g
> 33 kg to ≤ 50 kg	15 mg/kg	1.5 ml/kg	75 ml	60 mg/kg not

				exceeding 3 g
>50 kg with additional risk factors for hepatotoxicity	1 g	100 ml	100 ml	3 g
> 50 kg and no additional risk factors for hepatotoxicity	1 g	100 ml	100 ml	4 g

*Pre-term newborn infants: No safety and efficacy data are available for pre-term newborn infants (see section 5.2).

** Patients weighing less will require smaller volumes.

*** Maximum daily dose: The maximum daily dose as presented in the table above is for patients that are not receiving other paracetamol containing products and should be adjusted accordingly taking such products into account.

The minimum interval between each administration must be at least 4 hours.

The minimum interval between each administration in patients with severe renal impairment must be at least 6 hours.

No more than 4 doses to be given in 24 hours**.**

Elderly

Dose adjustment is not required in elderly people (see section 5.2).

Severe renal insufficiency:

It is recommended, when giving paracetamol to patients with severe renal impairment (creatinine clearance ≤ 30 ml/min), to reduce the dose and increase the minimum interval between each administration to 6 hours (See section 5.2).

Adults with hepatocellular insufficiency, chronic alcoholism, chronic malnutrition (low reserves of hepatic glutathione), dehydration:

The maximum daily dose must not exceed 3 g (see section 4.4).

Method of administration

Intravenous use.

The paracetamol solution is administered as a 15-minute intravenous infusion.

Take care when prescribing and administering Paracetamol 10 mg/ml solution for infusion to avoid dosing errors due to confusion between milligram (mg) and millilitre (ml), which could result in accidental overdose and death.
Take care to ensure the proper dose is communicated and dispensed.
When writing prescriptions, include both the total dose in mg and the total dose in volume.
Take care to ensure the dose is measured and administered accurately.

Patients weighing < 10 kg:

• The glass vial should not be hung as an infusion due to the small volume of the medicinal product to be administered in this population.

• The volume to be administered should be withdrawn from the vial and could be administered undiluted or diluted (one volume into nine volumes diluent) in a 0.9% sodium chloride solution or 5% glucose solution and administered over 15 minutes. Use the diluted solution within the hour following its preparation (infusion time included). See also section 6.6.

• A 5 or 10 ml syringe should be used to measure the dose as appropriate for the weight of the child and the desired volume. However, this should never exceed 7.5 ml per dose.

• The user should be referred to the product information for dosing guidelines.

For instructions on dilution of the medicinal product before administration, see section 6.6.

For single use only. Any unused solution should be discarded.

Before administration, the product should be visually inspected for any particulate matter and discolouration.

As for all solutions for infusion presented in containers with air space inside, it should be remembered that close monitoring is needed notably at the end of the infusion, regardless of administration route. This monitoring at the end of the infusion applies particularly for central route infusions, in order to avoid air embolism.

50ml vial only

Paracetamol can be diluted in a 0.9% sodium chloride solution or 5% glucose solution (one volume into nine volumes diluent). In this case, use the diluted solution within the hour following its preparation (infusion time included).

4.3 Contraindications

Hypersensitivity to paracetamol, propacetamol hydrochloride (prodrug of paracetamol) or to any of the excipients listed in section 6.1.

Cases of severe hepatocellular insufficiency.

4.4 Special warnings and precautions for use

RISK OF MEDICATION ERRORS

Take care to avoid dosing errors due to confusion between milligram (mg) and millilitre (ml), which could result in accidental overdose and death (see section 4.2).

Appropriate oral analgesia is recommended as soon as this route of administration can be used.

To avoid any risk of overdose, the absence of paracetamol or propacetamol from the composition of other concomitant medicinal products must be checked.

Doses higher than those recommended cause a risk of very severe liver damage. The symptoms and clinical signs of liver damage (including fulminant hepatitis, hepatic insufficiency, cholestatic hepatitis, cytolytic hepatitis) are generally observed after 2 days and normally reach their peak within 4 to 6 days. Treatment with an antidote should be administered as soon as possible (see section 4.9).

Paracetamol can cause serious skin reactions. Patients should be informed about the early signs of serious skin reactions, and the use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

As for all solutions for infusion presented in glass vials, a close monitoring is needed notably at the end of the infusion (see section 4.2).

Paracetamol should be used with caution in cases of:

• hepatocellular insufficiency

• severe renal insufficiency (creatinine clearance ≤ 30 ml/min) (see sections 4.2 and 5.2)

• chronic alcoholism

• chronic malnutrition (low reserves of hepatic glutathione)

• dehydration

• patients suffering from a genetically caused G-6-PD deficiency (favism), the occurrence of a haemolytic anaemia is possible due to the reduced allocation of glutathione following the administration of paracetamol.

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of

paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per container, i.e. essentially 'sodium- free'.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid

Causes an almost two-fold reduction in clearance of paracetamol by inhibiting its conjugation with glucuronic acid. A reduction in the paracetamol dose should be considered if it is to be used concomitantly with probenecid.

Salicylamide

May prolong the elimination half-life of paracetamol.
Caution should be paid to the concomitant intake of **enzyme-inducing substances.** These substances include, but are not limited to, barbiturates, isoniazid, carbamazepine, rifampicin and ethanol (see section 4.9).

Oral anticoagulants

Concomitant use of paracetamol (4 000 mg per day for at least 4 days) with oral anticoagulants may lead to slight variations of INR values. In this case, increased monitoring of INR values should be conducted during the period of concomitant use as well as for 1 week after paracetamol treatment has been discontinued.

Flucloxacillin

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with high risk factors (see section 4.4).

4.6 Pregnancy and Lactation

Pregnancy

Clinical experience of intravenous administration of paracetamol is limited. However, epidemiological data from the use of oral therapeutic doses of paracetamol indicate no undesirable effects on the pregnancy or on the health of the foetus / newborn infant.
Prospective data on pregnancies exposed to overdoses did not show an increase in malformation risk.
Reproductive studies with the intravenous form of paracetamol have not been performed in animals. However, studies with the oral route did not show any malformation of foetotoxic effects.

Nevertheless, paracetamol should only be used during pregnancy after a careful benefit-risk assessment. In this case, the recommended posology and duration must be strictly observed

Lactation

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

Not relevant.

4.8 Undesirable effects

The frequency of adverse events listed below is defined using the following convention:

System Organ Class	Common	Rare	Very rare	Not known
Blood and lymphatic system disorders			Thrombocytopenia, Leucopenia, Neutropenia	
Immune system disorders			Hypersensitivity reaction (1) Anaphylactic shock (1)	
Metabolism and nutrition disorders			High anion gap metabolic acidosis (HAGMA) (4)	
Cardiac disorders				Tachycardia (2)
Vascular disorders		Hypotension		Flushing (2)
Hepatobiliary disorders		Increased levels of hepatic transaminases		

Skin and subcutaneous tissue disorders			Rash (1), Urticaria (1), Serious skin reactions (3)	Pruritus (2), Erythema (2)
lisorders and ration site ns	Administration site reaction (pain and burning sensation)	Malaise		

Common (≥1/100 to <1/10); Rare (≥ 1/10,000 to < 1/1,000); Very rare (< 1/10,000), Not known (cannot be estimated from the available data).
(1) Very rare cases of hypersensitivity reactions ranging from simple skin rash or urticaria to anaphylactic shock have been reported and require discontinuation of treatment.
(2) Isolated cases
(3) Very rare cases of serious skin reactions have been reported and required discontinuation of treatment.
(4) Post marketing experience when paracetamol is used concomitantly with flucloxacillin; generally in the presence of risk factors (see section 4.4).
Frequent adverse reactions at injection site have been reported during clinical trials (pain and burning sensation).

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

There is a risk of liver injury (including fulminant hepatitis, hepatic failure, cholestatic hepatitis, cytolytic hepatitis), particularly in elderly subjects, in young children, in patients with liver disease, in cases of chronic alcoholism, in patients with chronic malnutrition and in patients receiving enzyme inducers.

Overdosing may be fatal in these cases. Symptoms generally appear within the first 24 hours and comprise: nausea, vomiting, anorexia, pallor and abdominal pain. Immediate emergency measures are necessary in case of paracetamol overdose, even when no symptoms are present.

Overdose, 7.5 g or more of paracetamol in a single administration in adults or 140 mg/kg of body weight in a single administration in children, causes hepatic cytolysis likely to induce complete and

irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death.

Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with decreased prothrombin levels that may appear 12 to 48 hours after administration. Clinical symptoms of liver damage are usually evident initially after two days, and reach a maximum after 4 to 6 days.

Treatment
• Immediate hospitalisation.
• Before beginning treatment, take a blood sample for plasma paracetamol assay, as soon as possible after the overdose.
• The treatment includes administration of the antidote, N-acetylcysteine (NAC) by the intravenous or oral route, if possible before the 10th hour. NAC can, however, give some degree of protection even after 10 hours, but in these cases prolonged treatment is given.

Symptomatic treatment
Hepatic tests must be carried out at the beginning of treatment and repeated every 24 hours. In most cases hepatic transaminases restitution to normal in one to two weeks with full return of normal liver function. In very severe cases, however, liver transplantation may be necessary.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics; Other analgesics and antipyretics; Anilides.
ATC Code: N02BE01

Mechanism of action
The precise mechanism of the analgesic and antipyretic properties of paracetamol has still to be established; it may involve central and peripheral actions.

Pharmacodynamic effects
Paracetamol provides onset of pain relief within 5 to 10 minutes after the start of administration. The peak analgesic effect is obtained in 1 hour and the duration of this effect is usually 4 to 6 hours.
Paracetamol reduces fever within 30 minutes after the start of administration with a duration of the antipyretic effect of at least 6 hours.

5.2 Pharmacokinetic properties

Adults
Absorption

• Paracetamol pharmacokinetics is linear up to 2 g after single administration and after repeated administration during 24 hours.
• The bioavailability of paracetamol following infusion of 500 mg and 1 g of Paracetamol is similar to that observed following infusion of 1 g and 2 g propacetamol (containing 500mg and 1 g paracetamol respectively). The maximal plasma concentration (Cmax) of paracetamol observed at the end of 15-minutes intravenous infusion of 500 mg and 1 g of Paracetamol is about 15 µg/ml and 30 µg/ml respectively.
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Distribution:

• The volume of distribution of paracetamol is approximately 1 l/kg.
• Paracetamol is not extensively bound to plasma proteins.
• Following infusion of 1 g paracetamol, significant concentrations of paracetamol (about 1.5 µg/ml) were observed in the cerebrospinal fluid at and after the 20th minute following infusion.
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Biotransformation

• Paracetamol is metabolised mainly in the liver following two major hepatic pathways: glucuronic acid conjugation and sulphuric acid conjugation. The latter route is rapidly saturable at doses that exceed the therapeutic doses. A small fraction (less than 4 %) is metabolised by cytochrome P450 to a reactive intermediate (N-acetyl benzoquinone imine) which, under normal conditions of use, is rapidly detoxified by reduced glutathione and eliminated in the urine after conjugation with cysteine and mercapturic acid. However, during massive overdosing, the quantity of this toxic metabolite is increased.

Elimination

• The metabolites of paracetamol are mainly excreted in the urine. 90 % of the dose administered is excreted within 24 hours, mainly as glucuronide (60 – 80%) and sulphate (20 – 30 %) conjugates. Less than 5 % is eliminated unchanged. Plasma half-life is 2.7 hours and total body clearance is 18 l/h.
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Newborn infants, infants and children:

• The pharmacokinetic parameters of paracetamol observed in infants and children are similar to those observed in adults, except for the plasma half-life that is slightly shorter (1.5 to 2 h) than in adults. In newborn infants, the plasma half-life is longer than in infants i.e. around 3.5 hours. Newborn infants, infants and children up to 10 years excrete significantly less glucuronide and more sulphate conjugates than adults.

Table - Age related pharmacokinetic values (standardised clearance, *CL_{std}/F_{oral} ($l \times h^{-1} \times 70\ kg^{-1}$)

Age	Weight (kg)	CL_{std}/F_{oral} ($l \times h^{-1} \times 70\ kg^{-1}$)
40 weeks post-conception	3.3	5.9
3 months post-natal	6	8.8

6 months post-natal	7.5	11.1
1 year post-natal	10	13.6
2 years post-natal	12	15.6
5 years post-natal	20	16.3
8 years post-natal	25	16.3

* CLstd is the population estimate for CL

Special populations

Renal insufficiency

In cases of severe renal impairment (creatinine clearance 10 – 30 ml/min), the elimination of paracetamol is slightly delayed, the elimination half-life ranging from 2 to 5.3 hours. For the glucuronide and sulphate conjugates, the elimination rate is 3 times slower in subjects with severe renal impairment than in healthy subjects. Therefore, when giving paracetamol to patients with severe renal impairment (creatinine clearance ≤ 30 ml/min), the minimum interval between each administration should be increased to 6 hours (see section 4.2).

Elderly subjects

The pharmacokinetics and the metabolism of paracetamol are not modified in elderly subjects. No dose adjustment is required in this population.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans beyond the information included in other sections of the SmPC.
Studies on local tolerance of paracetamol in rats and rabbits showed good tolerability.

Absence of delayed contact hypersensitivity has been tested in guinea pigs.
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

Mannitol
EDTA
Sodium Metabisulphite
Di-Sodium Hydrogen Phosphate Dihydrate
Hydrochloric Acid
Water For Injection

6.2 Incompatibilities

Not Applicable

6.3 Shelf-Life
24 months

6.4 Special Precautions for storage
Store protected from light, temperature not exceeding 30°C. Do not refrigerate or freeze.

6.5 Nature and Content of container
100ml bottle along with package insert.

6.6 Special precautions for disposal and other handling
Not Applicable

7. Marketing Authorization Holder
GALPHA LABORATORIES LIMITED

8. Marketing Authorization Number
CTD9478

9. Date of first authorization/renewal of the authorization
16/06/2023

10. Date of revision of the text
09/05/2025