SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Brand Name : PARALIFE
Generic Name: Paracetamol Infusion 1.0% w/v
Strength : 1.0% w/v
Pharmaceutical form: Infusion

2. QUALITATIVE AND QUANTATIVE COMPOSITIONS

Each 100 ml contains:
Paracetamol BP ..... 1000 mg
Water for Injection BP …….. q.s.
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Infusion (Clear colourless to pale yellow liquid filled in LDPE bottle)

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

PARALIFE solution for infusion is indicated for the short-term treatment of moderate pain, especially following surgery, and for the short-term treatment of fever, when administration by 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 Dosage and method of administration

Intravenous use

PARALIFE solution for infusion should not be mixed with other medicinal products. Paracetamol 1 g per administration, i.e. one 100 ml bottle, up to four times a day. The minimum interval between each administration must be 4 hours in patients without hepatic impairment. The maximum daily dose from all sources of Paracetamol must not exceed 4 g. The Paracetamol solution is administered as a 15-minute intravenous infusion.

It contains no antimicrobial agent and is for single use in one patient only.

Dosage for renal and hepatic failure. In patients with renal and/or hepatic impairment the minimum interval between doses must not be less than 6 hours.

4.3 Contraindications

PARALIFE 10mg/ml, solution for infusion is contraindicated:

- In patients with hypersensitivity to paracetamol or to propacetamol hydrochloride (prodrug of paracetamol) or to any of the excipients.
- In cases of severe hepatocellular insufficiency.
- In patients with hepatic failure.

4.4 Special warnings and precautions for use

It is recommended that a suitable analgesic oral treatment be used as soon as this route of administration is possible. In order to avoid the risk of overdose, check that no other medicines administered do not contain Paracetamol. Doses higher than those recommended entail the risk of very serious liver damage.

Clinical signs and symptoms of liver damage are not usually seen until two days, and up to a maximum of 4-6 days, after administration. Treatment with antidote should be given as soon as possible.

Precautions for use

Paracetamol should be used with caution in cases of:

- Hepatocellular insufficiency,
- Severe renal insufficiency (creatinine clearance <30 mL/min) (see section on dosage and method of administration and Pharmacokinetic properties),
- Chronic alcoholism,
- Chronic malnutrition (low reserves of hepatic glutathione),
- Dehydration.

The total dose of Paracetamol should not exceed 4 g per day. it is important to consider the contribution of all Paracetamol containing medications, including non-prescription, oral or PR forms of the drug to this total daily Paracetamol dose prior to administering Paracetamol IV. If the daily dose of Paracetamol from all sources exceeds the maximum, severe hepatic injury may occur.

4.5 Interaction with other medicinal products

- 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 taken with the concomitant intake of **enzyme-inducing substances**.
- Concomitant use of paracetamol (4000 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.
- 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 risks factors.

4.6 Fertility, Pregnancy and lactation

Pregnancy category A

Paracetamol has been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Clinical experience of the intravenous administration of Paracetamol is limited. However, epidemiological data from the use of oral therapeutic doses of Paracetamol indicate no undesirable effects in pregnancy or on the health of the foetus / newborn infant.

Prospective data on pregnancies exposed to overdoses did not show any increase in the risk of malformation.

No reproductive studies with the intravenous form of Paracetamol have been performed in animals.

However, studies with the oral route did not show any malformation or foetotoxic effects.

Nevertheless, Paracetamol IV should only be used during pregnancy after a careful benefit-risk assessment. In this case, the recommended dosage 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 IV may be used in breastfeeding women; caution should be used when administering Paracetamol IV to women who are breast feeding.

4.7 Effects on ability to drive and use machines

Not relevant

4.8 Undesirable effects

As with all Paracetamol products, adverse drug reactions are rare (>1/10000, <1/1000) or very rare (1<1/10000).

The overall incidence of adverse events in Paracetamol IV treated patients compared to placebo within the clinical trial set is given below:

Adverse events in adults greater than 1%

Neurological: dizziness, headache, dystonia

Gastrointestinal: vomiting, dry mouth, diarrhoea, constipation, nausea, dyspepsia, enlarged abdomen, gastrointestinal disorder NOS

Haematological: anaemia, post -operative haemorrhage

Hepatobiliary: increase in gamma GT, increase in SGPT

Psychiatric: insomnia

Skin and appendage: injection site pain, injection site reaction, post-operative site reaction, pruritis.

Respiratory: alveolitis, coughing

Endocrine/Metabolic: hyperglycemia, hypokalemia

General: fatigue, fever, oedema-peripheral, chest pain

Post market adverse events for propacetamol/Paracetamol

As with all Paracetamol products, adverse drug reactions are rare (1/10000, 1/1000) or very rare (1/10000), they are described below:

As with all paracetamol products, adverse drug reactions are rare (≥ 1/10 000 to <1/1 000) or very rare (<1/10 000). They are described below:

System Organ Class		**Rare** (≥ 1/10 000 to <1/1 000)	**Very rare** (<1/10 000)	**Not known** (cannot be estimated from the available data)
Blood and lymphatic system disorders		—	Thrombocytopenia, Leucopenia, Neutropenia	—
Immune system disorders		—	Hypersensitivity reaction (1, 3)	—
Cardiac disorders		—	—	Tachycardia (2)
Vascular disorders		Hypotension	—	Flushing (2)
Hepatobiliary disorders		Increased levels of hepatic transaminases	—	—
Skin and subcutaneous tissue disorders		—	serious skin reactions (3)	Pruritus (2), Erythema (2)
General disorders and administration site conditions		Malaise	—	—

(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.
Frequent adverse reactions at injection site have been reported during clinical trials (pain and burning sensation).

Reporting of suspected adverse reactions

Healthcare professionals are requested 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.

Emergency measures

- 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 i.v. 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. The optimal time for administration of NAC and necessary duration of therapy have not been established for overdose of Paracetamol IV.

  Symptomatic treatment.
- Hepatic tests must be carried out at the beginning of treatment and repeated every 24 hours. In most cases hepatic transaminases return 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 Pharmacodynamics

Paracetamol is a non-opiate para-aminophenol derivative that exhibits analgesic and antipyretic activity. The precise mechanism of the analgesic and antipyretic properties of Paracetamol has yet to be established; it may involve central and peripheral actions.

Paracetamol IV 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 IV reduces fever within 30 minutes after the start of administration with duration of the antipyretic effect of at least 6 hours.

5.2 Pharmacokinetic properties

Adults

Absorption:

Paracetamol IV pharmacokinetics is linear upto 2 g after single administration and after repeated administration during 24 hours.

The peak plasma concentration is obtained as and from the end of infusion. The maximal plasma concentration (Cmax) of Paracetamol observed following intravenous infusion of 1 g of Paracetamol IV is about 30 µg/ml and about 15 minutes is required to obtain the maximal concentration (Tmax).

Distribution:

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

Metabolism:

Paracetamol IV 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.
At the therapeutic doses, CYP3A4, the major isoform of P450 in human liver, contributes to the production of the cytotoxic metabolite. For very high, supratherapeutic plasma concentration (1500mg/L) of Paracetamol, the 2E1 and 1A2 isoforms may also be involved.

Elimination:
The metabolites of Paracetamol IV 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.

5.3 Preclinical safety data
Not Applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients
Mannitol,
Disodium 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 below 30°C. Protect from light.
Keep medicine out of reach of children.

6.5 Nature and Contents of Container
Paracetamol Infusion 1.0% w/v is packed in 100 ml LDPE bottle.

6.6 Special Precautions for Disposal
There is no special instructions.

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESS

MAH

UNISEL LIMITED

P.O Box 39356-00623,
Nairobi, Kenya

Manufacturing Site

Akums Drugs & Pharmaceuticals Limited

Plot No. 2, 3, 4 & 5, Sector 6-B, IIE,
SIDCUL, Ranipur, Haridwar-249403,
Uttarakhand, India

8. MARKETING AUTHORIZATION NUMBERS

H2015/CTD1366/598

9. DATE OF FIRST REGISTRATION

17 December 2015

10. DATE OF THE REVISION OF THE TEXT

15.04.2026