Racamol
(Paracetamol) Infusion

ریسامول
(پیراسیٹامول) انفیوژن

1g/100ml

1 گرام/100 ملی لیٹر

COMPOSITION
Each ml contains:
Paracetamol……..10mg
(As per Innovator's Specifications)

DESCRIPTION
Racamol (Paracetamol) Infusion is used as an analgesic (relieves pain) and an antipyretic (lowers fever). It is used for short-term treatment of moderate pain, especially following surgery and short-term treatment of fever. Its molecular formula is $C_8H_9NO_2$.

CLINICAL PHARMACOLOGY
Pharmacodynamics
The precise mechanism of the analgesic and antipyretic properties of paracetamol has yet to be established; it may involve central and peripheral actions.
Analgesic: Paracetamol may acts predominantly by inhibiting prostaglandin synthesis in the central nervous system (specifically COX-2) and, to a lesser extent, through a peripheral action by blocking pain impulse generation.
Antipyretic: Paracetamol act centrally on the hypothalamic heat-regulating center to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss.

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

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

Metabolism: Paracetamol is metabolized 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 metabolized 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.

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 18L/h.

Special Population
Elderly patients
The pharmacokinetics and the metabolism of paracetamol are not modified in elderly subjects. No dose adjustment is required in this population.
Neonates, 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 hours) than in adults. Neonates, infants and children up to 10 years excrete significantly less glucuronide and more sulphate conjugates than adults.

Renal insufficiency
In cases of severe renal impairment (creatinine clearance 10-30ml/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.

THERAPEUTIC INDICATIONS
Racamol (Paracetamol) 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.

DOSAGE AND ADMINISTRATION
Racamol (Paracetamol) Infusion is administered as a 15-minute intravenous infusion. The 100ml vial is restricted to adults, adolescents, and children weighing more than 33kg.

Dosing is based on patient weight as shown in the table:

Patient weight	Dose per administration	Volume per administration	Maximum volume of paracetamol, solution for infusion (10mg/ml) per administration (ml)**	Maximum Daily Dose***
≤10 kg *	7.5mg/kg	0.75ml/kg	7.5ml	30mg/kg
>10kg to ≤33kg	15mg/kg	1.5ml/kg	49.5ml	60mg/kg not exceeding 2g
>33kg to ≤50kg	15mg/kg	1.5ml/kg	75ml	60mg/kg not exceeding 3g
>50kg with additional risk factors for hepatotoxicity	1g	100ml	100ml	3g
>50kg and no additional risk factors for hepatotoxicity	1g	100ml	100ml	4g

*Pre-term newborn infants: No safety and efficacy data are available for pre-term newborn infants.

****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 insufficiency must be at least 6 hours. No more than 4 doses to be given in 24 hours.

Special Population
Severe renal insufficiency
It is recommended, when giving paracetamol to patients with severe renal impairment (creatinine clearance ≤30ml/min), to increase the minimum interval between each administration to 6 hours.

ADVERSE REACTIONS
Rare: Malaise, hypotension and increased levels of hepatic transaminases.
Very Rare: Hypersensitivity reactions, skin reactions, thrombocytopenia, leucopenia and neutropenia.

CONTRAINDICATIONS
It is contraindicated in patients with:
- Hypersensitivity to paracetamol or to propacetamol hydrochloride (prodrug of paracetamol) or to any of the excipients.
- Severe hepatocellular insufficiency.

WARNINGS AND PRECAUTIONS
Paracetamol should be used with caution in cases of:

- Hepatocelluar insufficiency
- Severe renal insufficiency (creatinine clearance <30ml/min)
- Chronic alcoholism
- Chronic malnutrition (low reserves of hepatic glutathione)
- Dehydration

Pregnancy
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 newborn. Nevertheless, Paracetamol solution for infusion 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 Infusion may be used in breast-feeding women.

DRUG INTERACTIONS
- Probenecid causes an almost 2-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 t½ of Paracetamol.
- Caution should be taken with the concomitant intake of enzyme-inducing substances.
- Concomitant use of Paracetamol (4g 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.

OVERDOSAGE
There is a risk of poisoning, 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
Symptoms that generally appear within the first 24 hours and comprises of nausea, vomiting, anorexia, pallor and abdominal pain. Overdose of 7.5g or more of paracetamol in a single administration in adults or 140mg/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 and 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 IV 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 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.

STORAGE
- Store below 30°C.
- Protect from heat & light.

PRESENTATION
Racamol (Paracetamol) Infusion 1g/100ml is available as pack of 1 vial of 100ml.

To be sold on the prescription of a registered medical practitioner only.

Keep all medicines out of the reach of children.

Manufactured by :
Indus Pharma (Pvt.) Ltd.
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