For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

# Paracetamol Infusion IP 1% w/v

**GALENMOL®**

**FOR IV INFUSION ONLY**
1000 mg/100 ml

**COMPOSITION:**
Each 100 ml contains:

| | |
|---|---|
| Paracetamol IP | 1000 mg |
| Water for Injections IP | q.s. |

**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. 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 duration of the antipyretic effect of at least 6 hours.
**Pharmacokinetics**
***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 500mg and 1 g of Paracetamol is similar to that observed following infusion of 1g 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 500mg and 1 g of Paracetamol is about 15µg/ml and 30 µg/ml respectively.
***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.
***Metabolism:***
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.
**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
***Elderly subjects***
The pharmacokinetics and the metabolism of paracetamol are not modified in elderly subjects. No dose adjustment is required in this population.

**INDICATIONS**
Paracetamol 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 METHOD OF ADMINISTRATION**
For IV infusion use only.
**Note:** The 100ml bottle is restricted to adults, adolescents and children weighing more than 33 kg (approximately 11 years old).
**Posology :**
**Adolescents and adults weighing more than 50 kg :**
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.
The maximum daily dose must not exceed 4 g.
**Children weighing more than 33 kg (approximately 11 years old), adolescents and adults weighing less than 50 kg :**
Paracetamol 15 mg/kg per administration, i.e. 1.5 ml solution per kg up to four times a day.
The minimum interval between each administration must be 4 hours.
The maximum daily dose must not exceed 60 mg/kg (without exceeding 3g).
**Severe renal insufficiency**
It is recommended, when giving paracetamol to patients with severe renal impairment (creatinine clearance 30 ml/min), to increase the minimum interval between each administration to 6 hours.
In adults with hepatocellular insufficiency, chronic alcoholism, chronic malnutrition (low reserves of hepatic glutathione), dehydration: the maximum daily dose must not exceed 3 g.
The paracetamol solution is administered as a 15-minute intravenous infusion.
Paracetamol Solution for Infusion is supplied in single-use, ready-to-use infusion bags. Parenteral drug products should be inspected visually for particulate matter prior to administration. Check for minute leaks by firmly squeezing the bag. If leaks are detected, discard the solution, as sterility may be impaired.
**Do not use this I.V. infusion bag in series connections.** Additives should not be introduced into this solution. If Paracetamol injection is to be given concomitantly with another drug, each drug should be given separately in accordance with the recommended dosage and route of administration for each product. If the same I.V. line is used for sequential infusion of several drugs, the line should be flushed before and after infusion of Paracetamol injection with an infusion solution compatible with Paracetamol injection and with any other drug(s) administered via this common line.
**Instructions for use**
1) Suspend the fluid bag or bottle on the infusion stand. Unpack the Paracetamol and check for potential damage.
Check the firm position of the connections and tighten if necessary.
2) Close the roller clamp on the Paracetamol. If bags are being used, close the venting cap of the closure piercing device, but leave it open if bottles are used. Connect the closure piercing device to the infusion container.
Incline the drip chamber at an angle of 180° and slowly open the roller clamp.
Fill the drip chamber, then hang in the normal position, filling the remainder of the set. The Flow Stop in the protective cap allows the air to escape and the system can easily be completely primed. Close the roller clamp again.

**CONTRAINDICATIONS**
Paracetamol 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.

**WARNINGS AND PRECAUTIONS**
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 other medicines administered do not contain either paracetamol or propacetamol.
Doses higher than those recommended entail the risk of very serious liver damage. Clinical signs and symptoms of liver damage (including fulminant hepatitis, hepatic failure, cholestatic hepatitis, cytolytic hepatitis) are usually first seen after two days of drug administration with a peak seen, usually after 4-6 days. 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)
- Chronic alcoholism,
- Chronic malnutrition (low reserves of hepatic glutathione),
- Dehydration.

***Drug Interactions***
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 (4 g 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.

***Pregnancy and Lactations***
**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 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 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.

**UNDESIRABLE EFFECTS**
**Fixed drug eruption (FDE) has been reported with Paracetamol.**
As with all paracetamol products, adverse drug reactions are rare (>1/10000, <1/1000) or very rare (1<1/10000). They are described below :

| Organ System | Rare >1/10000, <1/1000 | Very rare <1/10000 |
|---|---|---|
| General | Malaise | Hypersensitivity reaction |
| Cardiovascular | Hypotension | |
| Liver | Increased levels of hepatic transaminases | |
| Platelet/blood | | Thrombocytopenia Leucopenia Neutropenia |

Very rare cases of hypersensitivity reactions ranging from simple skin rash or urticaria to anaphylactic shock have been reported and require discontinuation of treatment. Cases of erythema, flushing, pruritus and tachycardia have been reported.

**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.
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 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 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 light & moisture. Do not freeze.**
Keep medicine out of reach of children.

**PRESENTATION:** GALENMOL infusion 100 ml packed in a mono carton.

Manufactured by :
Pure & Cure Healthcare Pvt. Ltd.
(A subsidiary of **Akums Drugs & Pharmaceuticals Ltd.**)
Plot No. 26A, 27-30, Sector-8A,
I.I.E., SIDCUL, Ranipur,
Haridwar-249 403, Uttarakhand.

GALENGEN

Marketed by :
**Galengen Lifesciences Pvt. Ltd.**
First floor, South Wing, No: 51, 11th Cross
Street, 9th Main Road, Dhandeeswaram
Nagar, Velachery, Chennai-600042