

SUMMARY OF PRODUCT CHARACTERISTIC

1. NAME OF THE MEDICINAL PRODUCT

PARACETAMOL
SANMOL[®]
Infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 mL contains:

Paracetamol 1000 mg

Inactive ingredient(s):

No.	Ingredients	Function	Quantity Per 100 mL
1.	Sodium Metabisulfite	Antioxidant	15 mg
2.	Mannitol	Tonicity agent	4000 mg
3.	L-Histidine Pyrogen Free	Antioxidant	172.7 mg
4.	Sodium Hydroxide	Alkalizing agent	qs
5.	Hydrochloric Acid	Acidifying agent	qs
6.	Water For Injection	Solvent	ad 100 mL

3. PHARMACEUTICAL FORM

Solution for Intravenous Infusion

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

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.

4.2 Posology and method of administration

Intravenous route: The 50 mL bottle is restricted to children weighing from 10 kg (approximately one year old) to 33 kg. The 100 mL 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 3 g).
- Children weighing more than 10 kg (approximately 1 year old) and weighing less than 33 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 2 g).

- 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.

Method of administration :

The paracetamol solution is administered as a 15-minute intravenous infusion. It can also be diluted in a 0.9% sodium chloride solution or a 5% glucose solution up to one tenth. In this case, use the diluted solution within the hour following its proportion (infused time included). As for all solutions for infusion presented in glass bottle. It is reminded that a close monitoring is needed notably at the end of the infusion, regardless the administration route. This monitoring at the end of the perfusion applies particularly for central route infusion, in order to avoid embolism.

4.3 Contraindications

- Hypersensitivity to paracetamol or to propacetamol hydrochloride (prodrug of paracetamol) or to any of the excipient
- Severe hepatocellular insufficiency
- Patients with hepatic failure or active liver disease.

4.4 Special warnings and precaution for use

Warnings :

It is recommended to use a suitable analgesic oral treatment as soon as this administration route is possible. In order to avoid the risk of overdose, check that other medicines administered do not contain Paracetamol.

Doses higher than the recommended entails risk for very serious liver damage.

Clinical symptoms and signs on liver damage are usually seen first after two days with a maximum 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

4.5 Interaction with other medicinal products and other forms interactions

Probenecid causes an almost 2-fold reduction in clearance of paracetamol by inhibiting its conjugation with glucuronic acid. A reduction of the paracetamol dose should be considered for concomitant treatment with probenecid.

Caution should be paid to the concomitant intake of enzyme-inducing agents. These substances include but are not limited to: barbiturates, isoniazid, anticoagulants, zidovudine, amoxicillin + clavulanic acid, carbamazepine and ethanol. Induction of

metabolism of paracetamol from enzyme inducers may result in an increased level of hepatotoxic metabolites.

Concomitant use of paracetamol (4 g per day for at least 4 days) with oral coumarin anticoagulants including warfarin 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 one week after paracetamol treatment has been discontinued.

Phenytoin administered concomitantly may result in decreased paracetamol effectiveness and an increased risk of hepatotoxicity. Patients receiving phenytoin therapy should avoid large and/or chronic doses of paracetamol. Patients should be monitored for evidence of hepatotoxicity.

Busulfan – busulfan is eliminated from the body via conjugation with glutathione. Concomitant use with paracetamol may result in reduced busulfan clearance.

Salicylamide - salicylamide may prolong the elimination half life (t_{1/2}) of paracetamol.

4.6 Pregnancy and Lactation

Pregnancy: Paracetamol should only be used during pregnancy after a carefully 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 un-desirable 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 machine

Not Applicable

4.8 Undesirable effects

- Dizziness, headache, dystonia, nausea, vomiting, constipation
- Simple skin rash or urticaria to anaphylactic shock have been occurred and require discontinuation of treatment
- Malaise
- Hypersensitivity reaction
- Hypotension
- Increased level of hepatic transaminases
- Thrombocytopenia, leucopenia, neutropenia.

4.9 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 generally appear within the first 24 hours and comprise: nausea, vomiting, anorexia, pallor, abdominal pain.

Overdose, 7.5 g or more of Paracetamol in a single administration in adults and 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 and ALT), Lactate dehydrogenase and bilirubin are observed together with decreased prothrombine 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 hospitalization.
- Before beginning treatment, take a tube of blood for plasma Paracetamol assay, as soon as possible after overdose.
- The treatment includes administration of the antidote, N-acetylcystein (NAC), by the i.v. or oral route, if possible before the 10th hour. NAC can, however, give some degree protection even after 10th hour, 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 restitution of liver function. In very severe cases, however, liver transplantation may be necessary.

5. CLINICAL PARTICULARS

Analgesic and antipyretic for Systemic Use.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sodium Metabisulfite
- Mannitol
- L-Histidine Pyrogen Free
- Sodium Hydroxide
- Hydrochloric Acid
- Water For Injection

6.2 Incompatibilities

Paracetamol infusion should not be mixed with other medicinal product.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30⁰C, away from light. Do not refrigerate or freeze. Before administration, the product should be visually inspected for any particulate matter and discoloration. For single use only. The product should be used immediately after

opening and any unused solution should be discarded. If diluted in 0.9% sodium chloride or 5% glucose, the solution should be used immediately. However, if the solution is not used immediately, store below one hour (infusion time included).

6.5 Nature and contents of container

Box of 1 bottle @ 100 mL

6.6 Special precautions for disposal and other handling

N/A

7. MARKETING AUTHORIZATION HOLDER

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8. DATE OF REVISION OF THE TEXT

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