PARASARAN INFUSION 1000mg/100ml

(PARACETAMOL BP)

LABEL CLAIM:

Each 100ml vial contains:
Paracetamol BP …1000mg.
[Mfg. Specs. Surge.]

COMPOSITION:

- Paracetamol
- Mannitol
- Disodium Hydrogen Phosphate Anhydrous
- Sodium Metabisulphite
- Sodium Hydroxide
- W.F.I. Q.S to Make Volume

EXCIPIENTS WITH KNOWN EFFECTS:

Mannitol: Digestive disorders

DESCRIPTION:

Parasaran Infusion is a sterile, clear, colorless, non-pyrogenic, isotonic formulation of Paracetamol intended for intravenous infusion.

INDICATIONS:

Paracetamol 10mg/ml 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.

DOSAGE AND ADMINISTRATION:

Intravenous use. The 50ml vial is restricted to term new-born infants, infants, toddlers and children weighing less than 33mg. The 100ml vial is restricted to adults, adolescents, and children weighing more than 33kg.

Patient weight	**Dose per administration**	**Volume per administration**	**Maximum volume of Paracetamol, solution for infusion (10mg/ml) per administration based on upper weight limits of group (ml)*** **	**Maximum Daily Dose****

<10kg*	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
> 33 kg 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 new-born infants:** No safety and efficacy data are available for pre-term new-born infants.

****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.

*****Patients weighing less will require smaller volumes:** 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.

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.

Instructions for Intravenous Administration: The Paracetamol solution is administered as a 15-minute intravenous infusion.

Patients weighing > 10kg: The glass vial/bag of Paracetamol, solution for infusion, 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/bag and diluted in a 0.9%

sodium chloride solution or 5% glucose solution up to one tenth (one volume Paracetamol, solution for infusion, into nine volumes diluent) and administered over 15 minute. A 5 or 10ml 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 7.5ml per dose. The user should be referred to the product information for dosing guidelines. **Text for the 50ml and 100ml vials:** To remove solution, use a 0.8mm needle (21 gauge needle) and vertically perforate the stopper at the spot specifically indicated. After dilution the solution should be used immediately. However , if the solution is not used immediately, do not store for more than one hour (infusion time included).

CONTRAINDICATIONS:

Parasaran (Paracetamol) Infusion is contraindicated in patients with known hypersensitivity to Paracetamol or to any of the excipients in the intravenous formulation. In patients with severe hepatic impairment or severe active liver disease.

WARNINGS & PRECAUTIONS:

For single use only.

Any unused solution should be discarded. Administration of paracetamol in doses higher than recommended may result in hepatic injury, including the risk of severe hepatotoxicity and death. Do not exceed the maximum recommended daily dose of Paracetamol. Use with caution when administering Paracetamol in patients with the following conditions: hepatic impairment or active hepatic disease, alcoholism, chronic malnutrition, severe hypovolemia (e.g., due to dehydration or blood loss), or severe renal impairment (creatinine clearance < 30ml/min). There have been reports of hypersensitivity and anaphylaxis associated with the use of Paracetamol. Clinical signs included swelling of the face, mouth, and throat, respiratory distress, urticaria, rash, and pruritus. Discontinue Parasaran immediately if symptoms associated with allergy or hypersensitivity occur. Do not use Parasaran in patients with Paracetamol allergy.

DRUG INTERACTIONS:

Substances that induce or regulate hepatic cytochrome enzyme CYP2E1 may alter the metabolism of paracetamol and increase its hepatotoxic potential. The clinical consequences of these effects have not been established. Effects of ethanol are complex, because excessive alcohol usage can induce hepatic cytochromes, but ethanol also acts as a competitive inhibitor of the metabolism of Paracetamol. Chronic oral Paracetamol use at a dose of 4000mg/day has been shown to cause an increase in international normalized ratio (INR) in some patients who have been stabilized on sodium warfarin as an anticoagulant. As no studies have been performed evaluating the short-term use of Parasaran in patients on oral anticoagulants, more frequent assessment of INR may be appropriate in such circumstances.

FERTILITY, PREGNANCY AND LACTATION

Pregnancy:

PARASARAN 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: No undesirable effects on nursing infants have been reported. Consequently, **PARASARAN** may be used in breast-feeding women.

Paediatric Use: The effectiveness of Parasaran for the treatment of acute pain and fever has not been studied in paediatric patients < 2 years of age.

USE IN SPECIFIC POPULATIONS:

Patients with Hepatic Impairment: Paracetamol is contraindicated in patients with severe hepatic impairment or severe active liver disease and should be used with caution in patients with hepatic impairment or active liver disease. A reduced total daily dose of paracetamol may be warranted.

Patients with Renal Impairment: In cases of severe renal impairment (creatinine clearance < 30ml/min), longer dosing intervals and a reduced total daily dose of Paracetamol may be warranted.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Paracetamol has no or negligible influence on the ability to drive and use machines.

UNDESIRABLE EFFECTS

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:

Organ System	**Rare ≥1/10,000 to <1/1,000**	**Very rare <1/10,000**
Blood and Lymphatic system disorders		Thrombocytopenia, Leucopenia, Neutropenia
Vascular Disorders	Hypotension	
Hepatobiliary Disorders	Increased levels of hepatic transaminases	

General Disorders and administration site conditions	Malaise	Hypersensitivity reaction

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

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.

Very rare cases of serious skin reactions have been reported (drug-induced Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalised exanthematous pustulosis (AGEP)).

OVERDOSAGE:

In acute Paracetamol overdose, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycaemic coma, and thrombocytopenia may also occur. Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis, and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion. If a Paracetamol overdose is suspected, obtain a serum Paracetamol assay as soon as possible, but no sooner than 4 hours following oral ingestion. Obtain liver function studies initially and repeat at 24-hour intervals. Administer the antidote N-acetylcysteine (NAC) as early as possible. Withhold NAC therapy if the paracetamol is below the lower line.

PHARMACOLOGY:

Mechanism of Action:

The precise mechanism of the analgesic and antipyretic properties of Paracetamol is not established but is thought to primarily involve central actions.

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 of Paracetamol 10mg/ml Solution for Infusion is about 15mg/ml and 30mg/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 1.5mg/ml) were observed in the cerebrospinal fluid at and after the 20th minute following infusion.

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 18L/h.

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 h) than in adults. In neonates, the plasma half-life is longer than in infants i.e. around 3.5 hours. Neonates, infants and children up to 10 years excrete significantly less glucuronide and more sulphate conjugates than adults.

INSTRUCTIONS:

- Store below 30°C.
- Protect from heat & light.
- Do not refrigerate or freeze.
- Keep out of the reach of children.

PRESENTATION:

Parasaran 1000mg/100ml I.V. solution for infusion is available in pack of 1's.

MEDECINE UNDER PRESCRIPTION: List I.

MARKETING AUTHORIZATION HOLDER:

SARAN PHARMA
ABIDJAN COCODY 2 PLATEAUX DERRIERE L'EN, RUE J5, LOT 269, SECTION KX PARCELLE 104, 08 BP 3121 ABIDJAN 08 RCI

MANUFACTURED BY:

Surge Laboratories (Pvt.) Ltd.
10th Km, Faisalabad Road, Bikhi
District, Sheikhupura-Pakistan.

DATE OF LAST REVISION:

November 2024