ALGORENS

Instructions for the medicinal product

Trade name: Algorens.
International Nonproprietary Name: Paracetamol.
Dosage form: Solution for infusion.
Composition: Each 100 ml contains:
Paracetamol BP 1000 mg;
Excipients q.s.
Pharmacotherapeutic group: Other analgesics and antipyretics.
ATC Code: N02BE01.
Pharmacological action:
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 10 mg/ml solution for Infusion 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 10 mg/ml solution for Infusion reduces fever within 30 minutes after the start of administration with a duration of the antipyretic effect of at least 6 hours.
Pharmacokinetics:
Adults:
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 10 mg/ml Solution for Infusion 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 10 mg/ml Solution for Infusion 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.
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.
Indications for use:
Algorens infusion 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.
Contraindications:
Hypersensitivity to paracetamol, paracetamol hydrochloride (prodrug of paracetamol) or to any other component of the drug;
In cases of severe hepatocellular insufficiency;
Children under the age of 1 year.
Should be used with caution in cases of : hepatocellular insufficiency, severe renal insufficiency (creatinine clearance Less-than or equal to 30 ml/min), chronic alcoholism, chronic malnutrition (low reserves of hepatic glutathione), dehydration.
Pregnancy and Nursing Mother:
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. Nevertheless, Algorens 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.
After oral administration, paracetamol is excreted into breast milk in small quantities. No undesirable effects on nursing infants have been reported. Consequently, Algorens Solution for Infusion may be used in breast-feeding women.
Dosage and directions for use:
Take care when prescribing and administering paracetamol, solution for infusion, to avoid dosing errors due to confusion between milligram (mg) and millilitre (mL), which could result in accidental overdose and death. Take care to ensure the proper dose is communicated and dispensed. When writing prescriptions, include both the total dose in mg and the total dose in volume. Take care to ensure the dose is measured and administered accurately.
The paracetamol solution is administered as a 15-minute intravenous infusion.
Patients weighing ≤ 10 kg:
• The bottle of Algorens, 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 bottle 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 10 ml 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.
To remove solution, use a 0.8 mm needle (21 gauge needle) and vertically perforate the stopper at the spot specifically indicated.
The 100 ml bottle is restricted to adults, adolescents, and children weighing more than 33 kg.

Posology: Dosing based on patient weight (please see the dosing table here below:

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

* *Pre-term newborn infants:* No safety and efficacy data are available for pre-term newborn 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 less-than or equal to 30mL/min), to increase the minimum interval between each administration to 6 hours.
Side-effects:
The frequency of adverse events listed below is defined using the following convention: very common (≥ 1/10); common (≥ 1/100 to /10); uncommon (≥ 1/1,000 to 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000), not known (cannot be estimated from the available data).
General: Rare: Malaise. Very rare: Hypersensitivity reaction.
Cardiovascular: Rare: Hypotension.
Liver: Rare: Increased levels of hepatic transaminases.
*Skin and subcutaneous tissue disorders: V*ery rare: cases of serious skin reactions have been reported.
*Platelet/blood: V*ery rare: 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.
Overdose:
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 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 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.
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.
Drug interaction:
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 (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.
Cautions:
Risk of medication errors:
Take care to avoid dosing errors due to confusion between milligram (mg) and milliliter (mL), which could result in accidental overdose and death.
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 containing paracetamol are administered at the same time.
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.
Effects on ability to drive and use machines:
Not relevant.
Presentation:
1X1, 100 ml FFS Plastic bottle in a monocarton, with instructions for use.
Storage:
Keep in dry place, protected from light at a temperature below 30°C. Keep out of reach of children.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Prescription only medicine (POM).

02Z

BELINDA

Manufactured for:
BELINDA LABORATORIES PVT. LIMITED
E-186, Room No.1, Basement, Greater Kailash-I, New Delhi - 110048, Delhi, India.
Manufactured by:
Abaris Healthcare Pvt. Ltd
Plot No.- 1407-11, Vill- Rajpur, Tal- Kadi,
City: Rajpur, Dist: Mehsana, Gujarat State, INDIA