PRESCRIBING INFORMATION

BRAMOL INFUSION (IV)
(Paracetamol)

COMPOSITION:
Each 100 ml contains:
Paracetamol 1000mg
Mfg. Specs. Brookes.

DESCRIPTION:
Bramol (Paracetamol) solution for infusion is a clear and slightly yellowish solution. It contains 10mg/ml of Paracetamol BP. Paracetamol is also known as acetaminophen. Paracetamol is used to relief fever and mild to moderate pain in all age groups.

PHARMACOLOGY:
Pharmacodynamic Properties:
The precise mechanism of the analgesic and antipyretic properties of paracetamol has yet to be established; it may involve central and peripheral actions. Bramol (Paracetamol) 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. Bramol (Paracetamol) 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.

PHARMACOKINETIC PROPERTIES
Adults
Absorption:
Bramol (Paracetamol) pharmacokinetics is linear up to 2 g 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 1000mg of Paracetamol 10 mg/ml Solution for Infusion is about 30 µg/ml.
Distribution:
The volume of distribution of paracetamol is approximately 1 L/kg. Bramol (Paracetamol) is not extensively bound to plasma proteins. Following infusion of 1000 mg 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:
Bramol (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. 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 (60-50%) 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.

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. Patients with severe renal impairment (creatinine clearance ≤30 mL/min), the minimum interval between each administration should be increased to 6 hours.
Elderly:
The pharmacokinetics and the metabolism of paracetamol are not modified in elderly subjects. No dose adjustment is required in this population.

INDICATIONS:
Bramol (Paracetamol) 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 METHOD OF ADMINISTRATION:
Intravenous use:
The 50 ml vial is restricted to term newborn infants, infants, toddlers and children weighing less than 33kg.The 100 ml vial is restricted to adults, adolescents, and children weighing more than 33 kg.

Patient weight	Dose per Administration	Volume per Administration	Max. volume of solution for Infusion (Upper weight Limit***)	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 and at least 6 hours with severe renal insufficiency. No more than 4 doses to be given in 24 hours.
Method of Administration:
Take care when prescribing and administering paracetamol, solution for infusion, ensuring the proper dose is communicated and dispensed. 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 glass vial 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 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

CONTRAINDICATIONS:
In patients with hypersensitivity to paracetamol or to any of the excipients.
In cases of severe hepatocellular insufficiency.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:
Warnings

RISK OF MEDICATION ERRORS
Take care to avoid dosing errors due to confusion between milligram (mg) and millilitre (mL), which could result in accidental overdose and death.

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.
Precautions:
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.
Interaction with other medicinal products and other forms of interaction:
Probenecid causes an almost 2- fold reduction in clearance of paracetamol by inhibiting its conjugation with glucuronic acid. Salicylamide may prolong the elimination $t_{\frac{1}{2}}$ 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.
Pregnancy:
Clinical experience of the intravenous administration of paracetamol is limited.
Paracetamol 10 mg/ml Solution for Infusion should only be used during pregnancy after a careful benefit-risk assessment.
Lactation:
After oral administration, paracetamol is excreted into breast milk in small quantities. No undesirable effects on nursing infants have been reported.

SIDE EFFECTS:
The frequency of adverse events listed below is defined using the following convention:
very common (≥ 1/10); common (≥ 1/100 to 1/10); 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).

Organ System	Rare	Very rare
General	Malaise	Hypersensitivity reaction
Cardiovascular	Hypotension	
Liver	Increased levels of hepatic transaminases	
Skin and subcutaneous tissue disorders		Very rare cases of serious skin reactions have been reported.
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.

OVERDOSE:
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.
The treatment includes administration of the antidote, N-acetylcysteine (NAC) by the I.V. or oral route, if possible before the 10th hour.

STORAGE:
Store at temperature below 30°C away from light.
Do not refrigerate or freeze.

PRESENTATION:
Bramol Infusion is available in 100ml glass vial in a carton.

brookes
Manufactured by:
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