Bosch

For Healthcare Professionals only

Bofalgan®

Solution for I.V. Infusion

1g/100mL Infusion

(Paracetamol)

بوفالگن

اگرام/۱۰۰ ملی لیٹر انفیوژن

(پیراسیٹامول)

WARNING: Risk of Medication Errors and Hepatotoxicity

Take care when prescribing, preparing, and administering paracetamol infusion to avoid dosing errors, which could result in accidental overdose and death. In particular, be careful to ensure that:

- Dose in milligrams (mg) and milliliters (mL) is not confused, which could result in accidental overdose and death.
- Infusion pumps are properly programmed, and
- The total daily dose of paracetamol from all sources does not exceed the maximum daily limits.

Paracetamol has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the liver injury cases are associated with the use of doses that exceed the maximum daily limits and often involve more than one paracetamol-containing product.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100mL vial contains:
Paracetamol BP…….1g
(Product specs: Bosch)

PHARMACEUTICAL FORM

Solution for I.V. infusion

CLINICAL PARTICULARS

Therapeutic Indications

Bofalgan 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 when other routes of administration are not possible.

POSOLOGY AND METHOD OF ADMINISTRATION

Intravenous (IV) use.
The product is restricted to adults, adolescents and children weighing more than 33 kg.

Posology:
Dosing based on patient weight:

Patient weight	Dose per adminis.	Volume per adminis.	Maximum volume of Paracetamol (10mg/mL) per administration based on upper weight limits of group (mL)*	Maximum Daily Dose **
> 33 kg to ≤ 50 kg	15 mg/kg	1.5 mL/kg	75 mL	60 mg/kg not exceeding 3 g
>50 kg with additional risk factors for hepatotoxicity	1 g	100 mL	100 mL	3 g
>50 kg and no additional risk factors for hepatotoxicity	1 g	100 mL	100 mL	4 g

*Patients weighing less will require smaller volumes.

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.
The minimum interval between each administration must be at least 4 hours. No more than 4 doses to be given in 24 hours.
The minimum interval between each administration in patients with severe renal insufficiency must be at least 6 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.
In adults with hepatocellular insufficiency, chronic alcoholism, chronic malnutrition (low reserves of hepatic glutathione), and dehydration, the maximum daily dose must not exceed 3 g.

Method of Administration
Paracetamol infusion is administered within a 15-minute intravenous (IV).

- To remove solution in the vials, use a 0.8 mm needle (21-gauge needle) and vertically perforate the stopper at the spot specifically indicated.
- As for all solutions for infusion, it should be remembered that close monitoring is needed notably at the end of the infusion, regardless of administration route. This monitoring at the end of the infusion applies particularly for central route infusions, in order to avoid air embolism.

Contraindications

- Hypersensitivity to the active substance
- In cases of severe hepatocellular insufficiency.

Special warnings and Precautions for use

Warnings

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, it should be checked that no other medicines administered 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 seen after two days of drug administration with a peak seen after 4-6 days. Treatment with antidote should be given as soon as possible.

This medicinal product contains less than 1mmol sodium (23mg) per 100mL of Paracetamol, i.e. essentially 'sodium free'.

Precautions for use:

Paracetamol should be used with caution in cases of:

- Hepatocellular insufficiency,
- Severe renal insufficiency (creatinine clearance ≤30mL/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. 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.

Fertility, Pregnancy and Lactation

Pregnancy:

It should only be used during pregnancy after a careful benefit-risk assessment. 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.

Effects on ability to drive and use machines

Not relevant

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:

System organ class	Adverse reaction	Frequency
Blood and lymphatic system disorders	Thrombocytopenia, Leucopenia, Neutropenia	Very rare
Cardiovascular	Hypotension	Rare
Liver	Increased levels of hepatic transaminases	Rare
General disorders and administration site conditions	Malaise	Rare
	Hypersensitivity reaction	Very rare

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. Erythema, flushing, pruritus and tachycardia have also been reported.

Overdose

There is a risk of liver injury (including fulminant hepatitis, hepatic failure, cholestatic hepatitis, cytolytic hepatitis), particularly in elderly, 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. Symptoms generally appear within the first 24 hours and comprise nausea, vomiting, anorexia, pallor and abdominal pain.

Clinical symptoms of liver damage are usually evident initially after two days and reach a maximum after 4 to 6 days.

Immediate hospitalization before beginning treatment, a blood sample for plasma paracetamol assay should be taken, as soon as possible after the overdose.

The treatment includes administration of the antidote, N-acetylcysteine (NAC) by the IV 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.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Pharmacotherapeutic group: Other Analgesics and Antipyretics, ATC Code: N02BE01

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 a duration of the antipyretic effect of at least 6 hours.

Mechanism of action

The precise mechanism of the analgesic and antipyretic properties of paracetamol has yet to be established; it may involve central and peripheral actions.

Pharmacokinetic Properties

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 is about 15µg/mL and 30µg/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 1.5µg/mL) were observed in the cerebrospinal fluid at and after the 20th minute following infusion.

Metabolism:

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 (60-80%) 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.

Special populations:
Renal insufficiency:
In cases of severe renal impairment (creatinine clearance 10-30mL/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 ≤30mL/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.

PHARMACEUTICAL PARTICULARS
Incompatibilities
Paracetamol infusion should not be mixed with other medicinal products.

Shelf life
2 years.

Special precautions for storage
Protect from heat & sunlight, Store below 25°C.
Do not refrigerate or freeze.
The expiration date refers to the product correctly stored at the required condition.
Do not use if solution contains undissolved particle.
Do not use in case of colour change.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
Keep out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.

Nature and contents of container
Bofalgan 1g/100mL infusion filled in clear glass vial of glass type II, the vial is closed with a rubber stopper and sealed with an aluminum seal.

MARKETING AUTHORISATION HOLDER
Head Office:
Bosch Pharmaceuticals (Pvt.) Ltd.,
8, Modern Society, Tipu Sultan Road,
Karachi-75350 (Pakistan)
Manufacturing Site:
Bosch Pharmaceuticals (Pvt.) Ltd.,
Plot No. 209, Sector 23 Korangi Industrial area Karachi.

MARKETING AUTHORISATION NUMBER(S)
070607

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7th November 2023

ہدایات:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
گرمی اور روشنی سے محفوظ ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں ۔
- ریفریجریٹر میں رکھنے یا منجمد ہونے سے بچائیں ۔
- محلول میں کوئی غیر حل پذیر ذرات نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔
- رنگ تبدیل ہونے پر استعمال نہ کریں۔
- بچوں کی پہنچ سے دور رکھیں۔

صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

Manufactured by:
Bosch Pharmaceuticals (Pvt) Ltd.
209, Sector 23, Korangi Industrial Area,
Karachi - Pakistan

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(Paracetamol)

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اگرام/۱۰۰ ملی لیٹر انفیوژن

(پیراسیٹامول)

FIRST & ONLY CERTIFIED HALAAL

PHARMACEUTICAL COMPANY