PATIENT INFORMATION LEAFLET

POLAMİNOFEN 10mg/ml solution for I.V. infusion
Administrated Intravenously

Sterile

- ***Active ingredient:*** Each 1 ml of solution contains 10 mg paracetamol.
- ***Excipients:*** Mannitol, cysteine hydrochloride monohydrate, disodium phosphate dihydrate, sodium hydroxide, water for injection.

Please read this PATIENT INFORMATION LEAFLET carefully before starting to use the drug; because important information is included here.

• Keep this PATIENT INFORMATION LEAFLET. You may need to re-read it later.

• In case you have additional questions, please consult your doctor or pharmacist.

• This drug is prescribed personally for you, do not give to others.

• During the use of this drug, please tell your doctor that you are using this drug when you visit your doctor or a hospital.

• Please follow these instructions strictly. Do not use dosages ***higher or lower*** *than the dosage recommended to you.*

What is in this leaflet:

1. What is POLAMİNOFEN and what it is used for

- Each 1 ml of POLAMİNOFEN contains 10 mg paracetamol.
- POLAMİNOFEN is a colorless or slightly yellow, clear solution presented in 100 mL bags.
- POLAMİNOFEN belongs to a class of medicines called analgesics (pain relief) and antipyretics (reducing fever).

- POLAMİNOFEN is used in adults, adolescents and children weighing more than 33kg (approx. 11 years of age).
- POLAMİNOFEN is indicated for the short-term treatment of moderate pain (especially following surgery), and for the short-term treatment of fever, when intravenous administration is clinically justified by an urgent need to treat pain or fever and/or when other routes of administration are not possible.

2. What you need to know before you use POLAMİNOFEN
Do NOT use POLAMİNOFEN:
If

- You are hypersensitive (allergic) to proparacetamol hydrochloride (prodrug of paracetamol) or any of the other
  ingredients of POLAMİNOFEN (see list of excipients)
- You suffer from severe liver disease
- It should be used with caution under doctor control in patients with anemia, lung disease, liver and kidney dysfunction.
- Sudden (acute) high doses cause severe liver toxicity.
- May cause liver damage in adults at long-term (chronic) daily doses.
- It should be used with caution in alcoholic liver patients.

Take SPECIAL CARE with POLAMİNOFEN:
If:

- you are taking other medicines containing paracetamol,
- you suffer from liver insufficiency,
- you suffer from severe kidney insufficiency,
- you suffer from anemia,
- you suffer from an enzyme deficiency called Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency (which can result in reduced levels of hemoglobin in your blood, destruction of red blood cells, and development of hemolytic anemia [a type of anemia]),
- you have frequent or excess alcohol consumption (3 or more glasses of alcoholic drinks/day),
- you suffer from lack of appetite and in case of nutritional imbalance/malnutrition,
- you suffer from dehydration

Acute doses of POLAMİNOFEN result in severe hepatotoxicity. Daily doses in adults can result in hepatic damage.

The daily dose of paracetamol should not exceed 2000 mg due to the risk of liver poisoning (hepatotoxicity) in alcohol users.

Rash, urticaria or a skin infection may occur in patients using paracetamol for the first time or with a history of paracetamol. In this case, the drug should be discontinued and an alternative

treatment should be switched after consulting with a doctor. Patients who experience skin reactions with paracetamol should not use this drug or any other drug containing paracetamol. This condition can cause severe cases which can be fatal (see section 4. Possible Side Effects) Tell your doctor even if these warnings have applied to you at any time in the past.

Taking POLAMİNOFEN with food and drinks
POLAMİNOFEN does not interact with food and drinks.

Pregnancy
Ask your doctor or pharmacist before taking this medicine.

POLAMİNOFEN should not be used during pregnancy unless absolutely necessary. Your doctor will discuss the potential risks of using POLAMİNOFEN during pregnancy.

If you notice that you are pregnant during your treatment, consult your doctor or pharmacist.

Breastfeeding
Ask your doctor or pharmacist before taking this medicine.
If you are breastfeeding, you can use POLAMİNOFEN only if your doctor decides that it is necessary.

Driving and using machines
Do not drive or operate any machines if you feel discomfort after taking POLAMİNOFEN. It is not known whether POLAMİNOFEN affects the ability to drive and use machines.

Important information on some of the ingredients contained in POLAMİNOFEN
This medicinal product contains <1 mmol sodium (23 mg) per dose, i.e., essentially "sodium-free."

Other medicines and POLAMİNOFEN
Tell your doctor if:

- you are taking a medicine that contains probenecid, used in the treatment of gout - dosage adjustment may be necessary;
- you are taking pain medicines comprising salicylic acid derivatives (salicylamide, diflunisal),
- you are taking substances that induce enzymes involved in drug metabolism in the liver (these substances include, but are not limited to barbiturates [a group of medicines that act on the central nervous system, e.g. sedatives, sleeping pills, and medicines used to treat seizures]), isoniazid (a drug used in the treatment of tuberculosis), anticoagulants (medicines that prevent blood clotting), zidovudine (a medicine used to treat AIDS), amoxicillin+clavulanic acid (an antibiotic), and ethanol (sued as solvent in some medicines),

- you are taking medicines used to treat convulsions (e.g. barbiturates, carbamazepine, fenitoin),
- you regularly consume alcohol,
- you are taking medicines to prevent blood clotting (coumarin or indanthion derivatives),

Dose adjustment may be required.

POLAMİNOFEN contains mannitol. Since administration route, no warnings apply.

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

3. How to use POLAMİNOFEN
Do not take higher doses than indicated on the label. Do not exceed the prescribed dose.

The 100 ml bag is restricted to adults, adolescents, and children weighing more than 33 kg.

Your doctor will decide and give the dose you will receive depending on your condition. For further information, you can refer to the instructions intended for healthcare professionals and provided at the end of this leaflet.

Instructions for proper use and frequency of dose/administration:
It is recommended that a suitable analgesic oral treatment (oral pain medication) be used as soon as the patient can receive drugs via this route of administration.

Single dose or repeat doses can be administered for acute (sudden) pain or fever.
The paracetamol solution is administered as a 15-minute intravenous (into the vessel) infusion.

It is recommended as 10-15 mg/kg/dose (500 mg once a day for over children 30 kg) for

every 6 hours, 60 mg/kg (maximum 2 g daily maximum dose for children over 30 kg).

Minimum dose range should be 4 hours and not be given more than 4 times in a day.

The daily dose of paracetamol should not exceed 2000 mg due to the risk of liver poisoning (hepatotoxicity) in alcohol users.

Dose is adjusted based on patient weight. Recommended dose adjustments are listed in the table below. Your doctor will adjust the suitable dose for you.

Patient weight	Dose per administration	Volume per administration	Maximum dose (based on upper weight limit)	Maximum Daily Dose**
≤10 kg *	7.5 mg/kg	0.75 ml/kg	7.5 ml	30 mg/kg
>10 kg and ≤33kg	15 mg/kg	1.5 ml/kg	49.5 ml	60 mg/kg maximum 2 g
> 33 kg and ≤50kg	15 mg/kg	1.5 ml/kg	75 ml	60 mg/kg maximum 3 g
>50kg with additional risk factors for hepatotoxicity	1 g	100 ml	100 ml	3 g
>50kg and no additional risk factors for hepatotoxicity	1 g	100 ml	100 ml	4 g

*Data on the use in newborn infants is very limited and the definitive dose has not been established. Use in preterm infants less than 32-weeks old is not recommended.
In patients with creatinine clearance ≤30 mL/min, the daily dose should be reduced and the interval between each administration should be increased.

**The minimum interval between each dose should be 4 hours. In patients with renal impairment, this interval should not be less than 6 hours. The maximum number of doses administered within 24 hours shall not exceed 4.

In patients with severe renal impairment, the interval between each administration should not be less than 6 hours.

Entire bag of 100 ml (1000 mg) should not be used in patients under 50 kg, as the it can cause dosing error (overdose).

When giving doses less than 100 ml, the medicine should be withdrawn from the bag and administered separately.

Paracetamol solution is administered intravenously over a period of 15-minutes.

Pediatric doses up to 60 ml are administered over a period of 15-minutes, using a syringe.

The entire product should not be connected to the infusion kit as this would result in overdose in patients weighing ≤ 10 kg. The volume to be administered should be withdrawn to the syringe and diluted in a 0.9% sodium chloride solution or 5% glucose solution up to one ninth

(1 volume POLAMİNOFEN into 9 volumes diluent) and administered via infusion over minimum 15 minutes.

In order to prevent dosing errors in the newborn and infants (≤ 10 kg) and to avoid confusing milligrams (mg) and milliliters (mL) for each other, it is recommended to determine the volume to be administered in milliliters (mL). The volume (10 mg/mL) of POLAMİNOFEN administered in patients in this group of weight should never exceed 7.5 mL. Very small quantities will be required in the newborn and infants (≤ 10 kg).

Route and method of administration:
For intravenous administration.

The paracetamol solution is administered as a 15-minute intravenous infusion.

Different age groups
Use in children and adolescents (≤18 years):
The 100 ml bag is restricted to children weighing more than 33 kg.

Data on the use in newborn infants is very limited and the definitive dose has not been established. Use in preterm infants less than 32-weeks old is not recommended.

In order to prevent dosing errors in the newborn and infants (≤ 10 kg) and to avoid confusing milligrams (mg) and milliliters (mL) for each other, it is recommended to determine the volume to be administered in milliliters (mL). The volume (10 mg/mL) of POLAMİNOFEN administered in patients in this group of weight should never exceed 7.5 mL. Very small quantities will be required in the newborn and infants (≤ 10 kg).

Use in the elderly (≥65 years)
No dose adjustment is necessary in elderly patients.

Special conditions of use:
Renal insufficiency
In patients with severe renal impairment (creatinine clearance ≤30 mL/min), a minimum interval of 6 hours is recommended between each administration of POLAMİNOFEN

Hepatic insufficiency
Dose should not exceed 3 g/day in patients with chronic or active hepatic disease, and particularly patients with hepatocellular insufficiency, chronic alcoholism, chronic low reserves of hepatic glutathione (malnutrition), and dehydration.

Due to the risk of hepatotoxicity, the daily dose of paracetamol administered to individuals who consume alcohol should not exceed 2 grams.

If you feel that the effect of POLAMİNOFEN is too strong or too weak, consult your doctor or pharmacist.

If you take more POLAMİNOFEN than you should:
There is a possibility of toxicity when paracetamol is administered to adults at a single dose of 7.5 g or more, or to children at a dose of 140 mg/kg.
If you take more POLAMİNOFEN than you should, you may experience nausea, vomiting, loss of appetite, abdominal pain, and pallor. In this case, refer to your doctor or go to the nearest hospital immediately.

If you took more POLAMİNOFEN than you should, tell your doctor or pharmacist.

If you forget to take POLAMİNOFEN:
Do not take a double dose to make up for a forgotten dose.

Possible reactions that may occur when treatment with POLAMİNOFEN is discontinued:
Possible reactions that may occur when treatment is discontinued are not known.

4. Possible side effects
Like all medicines POLAMİNOFEN may cause side effects in patients who are sensitive to its ingredients.

Stop using POLAMİNOFEN and contact your doctor or emergency department of the nearest hospital IMMEDIATELY, if any of the following applies to you:
• Swollen face and throat due to allergy (angioneurotic edema)
• Unexplainable redness, swelling, blistering or loss of skin
• Hypersensitivity reaction (hypersensitivity)
• Very severe reaction of the body to allergic substances; sudden hypersensitivity (anaphylaxis)
• Shock associated with the sudden onset of hypersensitivity reaction (anaphylactoid shock)
• Certain hepatic dysfunctions (liver insufficiency, liver inflammation, changes in enzyme levels)
All of these are very serious side effects.

If you experience any of these side effects, you are seriously allergic to POLAMİNOFEN. You may need urgent medical attention or hospitalization.

All of these side effects are very rare.

Frequency is classified as follows:
- Very common: Affects more than 1 user in 10
- Common: Affects 1 to 10 users in 100
- Uncommon: Affects 1 to 10 users in 1.000

- Rare: Affects 1 to 10 users in 10.000
- Very rare: Affects less than 1 user in 10.000
- Not known: Cannot be estimated from the available data

Rare:

- Hypotension
- Elevated levels of hepatic transaminases
- Increased heart rate
- Weakness
- Malaise (fatigue)

Very rare:

- Thrombocytopenia (decrease in the number of blood platelets (cells involved in the formation of clots)), leucopenia (decrease in white blood cells), neutropenia (decrease in the number granulocytes)
- Hypersensitivity reaction

Post-marketing side effects:

Rare:

- Redness of skin
- Rash, itching
- Facial redness
- Urticaria (hives)
- Allergic edema
- Angioedema (swelling of the face, tongue, and throat due to allergy)
- Acute generalized exanthematous pustulosis (acute diffuse small intestinal papules accompanied by high fever)
- Erythema multiforme (a condition which manifests with blistering of the mouth and across the body), Steven-Johnson syndrome (a common and severe skin condition which manifests with flu-like symptoms and fever, formation of blisters in the mouth, eyes, and/or genital organs)
- Toxic epidermal necrolysis (a serious condition of the skin characterized by pustules, exfoliation and loss of tissue)

Not known:

- Thrombocytopenia (decreased level of thrombocytes -one of the blood cells-)
- Increased heart rate
- Nausea, vomit
- Administration site reactions

If you get any side effects, including any site effects not listed in this leaflet, talk to your doctor or pharmacist.

5. How to store POLAMİNOFEN

Keep POLAMİNOFEN out of the sight and reach of children and in its original container.

Store at room temperatures below 25°C.
Store in the refrigerator. Do not freeze.

For single use. Use the product immediately after opening the container. Unused solutions should be discarded.

Do not use this medicine after the expiry date.
Do not use POLAMİNOFEN after the expiry date which is stated on the label or outer carton. The "expiry date" denotes the last day of the month.

Do not use POLAMİNOFEN if you notice any defects in the product or package.

Keep in the bag in aluminum outer pack. Due to sterilization, moisture can occur between the bag and the outer packaging. This does not affect the quality of the solution.

Before administration, the product should be visually inspected for any particulate matter and discoloration. Do not use POLAMİNOFEN if you observe any particulate matter or notice any discoloration.

Do not dispose expired or unused medicines via the household waste! Send them to a waste collection system designated by the Ministry of Environment and Urbanization.

Marketing Authorization Holder and Manufacturer:

POLİFARMA İLAÇ SAN. VE TİC. A.Ş.
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THE FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS ONLY

Method of administration:

The paracetamol solution is administered as a 15-minute intravenous infusion.

In order to prevent dosing errors in the newborn and infants (≤ 10 kg) and to avoid confusing milligrams (mg) and milliliters (mL) for each other, it is recommended to determine the volume to be administered in milliliters (mL). The volume (10 mg/mL) of POLAMİNOFEN administered in patients in this group of weight should never exceed 7.5 mL. Very small quantities will be required in the newborn and infants (≤ 10 kg).

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.

For pediatric dosing, POLAMİNOFEN can be also administered after dilution. However, only a 0.9% sodium chloride solution or 5% glucose solution up to 1:10 (1 volume paracetamol into nine volumes diluent) can be used. After preparation, the solution should be used within one hour (including the infusion period).

Pediatric doses up to 60 mL are administered over a period of 15-minutes, using a syringe.

In patients <10 kg, infusion should be performed without suspending the bag.

Before administration, the product should be visually inspected for any particulate matter and discoloration. For single use only. Unused solutions should be discarded.

From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Any unused medicinal product or waste material should be disposed of in accordance with the Regulations on the “Control of Medical Waste” and “Packages and Packaging Material Waste Control.”

Instructions for Use

Check the solution before use.

The solution is administered by intravenous infusion through sterile and non-pyrogenic sets.

Use only products that are clear, free from particles and with intact package integrity.

Administer shortly after insertion of the infusion set.

Do not connect other solutions for infusion in series in order to avoid air embolism due to possible residual air contained in the bag.

Use an aseptic method to set up the infusion and administer the solution. The delivery kit should be primed with the solution in order to prevent air entering the system.
Additive medications can be added before and during the infusion, in aseptic conditions using a needle at the injection tip. Verify isotonicity of the final product prior to parenteral administration.

Thorough mixing of any additive is mandatory before administered to the patient. Solutions containing additive medicines should be used immediately and not stored for later use.

Adding other medication or using an incorrect administration technique might cause the appearance of fever reactions due to the possible introduction of pyrogens. In case of adverse reaction, infusion must be stopped immediately.

Do not store partially used solutions.
Do not reconnect partially used bags to any systems for administration to patients.

Opening:
1. Check the outer package for firmness and tightness, and discard if damaged.
2. Tear to open the protective outer pack.
3. Check the inner bag inside the protective pack for firmness by squeezing. Check the solution inside the bag for clarity and absence of foreign matter.

Preparation for administration:
1. Suspend the bag.
2. Remove the protective cap on the delivery tip.
3. Tightly press the spike of the administration kit onto the delivery tip.
4. Strictly observe the kit’s usage instructions when administering the solution to the patient.

Addition of additive medication:

Caution: As with all parenteral solutions, additives to be added to the solution must be compatible with the product. In case of any additives, compatibility must be checked during the final mix before the solution is administered to the patient.

Adding medication prior to administration

1. Disinfect the drug delivery tip.
2. Spike the medication to be added into the bag via the syringe with 19-22 gauge needle.
3. Mix solution and medication thoroughly. To mix with concentrated medicines such as potassium chloride, gently tap on the delivery tip of the bag while in upright position

Caution: Bags spiked with medication should be discarded.

Adding medication during administration

1. Close clamp on the set.
2. Disinfect the drug delivery tip.
3. Administer the drug to be added via the drug delivery tip fitted a syringe with 19-22 gauge needle.
4. Remove container from IV pole and turn to an upright position.
5. Mix the solution and medication by tapping gently on the delivery tip of the bag and syringe inlet while in this position.
6. Return the bag to its former position, open the clamp and continue administration.