PATIENT INFORMATION LEAFLET

İBUPROFEN-PF 800 mg/8 ml solution for I.V. Infusion
Administered intravenously.
Sterile

- ***Active substance:*** Each 8 ml concentrated solution contains 800 mg ibuprofen (100 mg ibuprofen per ml).
- ***Excipients:*** Arginin, water for injection.

Before using this medicine, read all of this PATIENT INFORMATION LEAFLET carefully. Because, this leaflet includes important information for you.

- *Keep this PATIENT INFORMATION LEAFLET. You may need to read it again.*
- *If you have any further questions, ask your doctor or pharmacist.*
- *This medicine has been prescribed for you. Do not pass it on to others.*
- *During the use of this medicine, tell that you are using this medicine when you go to a doctor or hospital.*
- *Follow these instructions exactly as written. Do not use **higher or lower** dose other than your recommended dose.*

The following subjects are covered herein:

Headings are included.

1. What is İBUPROFEN-PF and what is it used for?

- İBUPROFEN-PF is a colorless and clear solution administered intravenously. Each 8 mL solution contains 800 mg drug substance called Ibuprofen. Ibuprofen, which is the drug substance of İBUPROFEN-PF, belongs to a group of painkillers called nonsteroidal anti-inflammatory drugs (NSAIDs). The concentrated solution introduced in the vial must be diluted before use.
- İBUPROFEN-PF is presented in a colorless Type I glass vial that is closed with a stopper and flip off cover as 1 or 10 pieces.
- İBUPROFEN-PF is indicated in following cases:
  - In the treatment of mild and moderate pain,
  - Opioid analgesics with moderate and severe pain,
  - Treatment of fever.

2. Before you are given İBUPROFEN-PF

Risks related to cardiovascular system

- NSAIDs can cause fatal thrombotic events, heart attacks and an increased risk of stroke. This risk may increase depending on the duration of use. Patients with cardiovascular disease or those with cardiovascular disease risk factors may have a higher risk.
- İBUPROFEN-PF should not be used to treat pain before coronary artery bypass surgery**.**

Risks related to digestive system

NSAIDs cause serious fatal side effects such as bleeding, wound formation, and perforation of the stomach or intestine. These side effects can occur at any time, with or without prior warning. Elderly patients are at higher risk for these serious effects.

DO NOT USE İBUPROFEN-PF under the following circumstances

If,

- You are hypersensitive (allergic) to ibuprofen or one of the excipients in this medicine,
- You have asthma or hives or have already had allergic reactions to ibuprofen, acetyl salicylic acid and other NSAIDs,
- You are in the period before or after coronary artery bypass surgery (correction of cardiovascular occlusion),
- You have acetyl salicylic acid triad (nasal polyps, asthma and susceptibility to acetyl salicylic acid),
- You are in the last 3 months of pregnancy,
- You have severe heart failure (shortness of breath even at rest),
- You have severe renal failure,
- You have severe liver failure

USE İBUPROFEN-PF WITH CARE in the following cases

If,

- You have asthma or have had asthma before; may cause shortness of breath.
- You have previously had gastrointestinal ulcers or other gastrointestinal diseases; inflammation may be seen in these tables.
- You have kidney disease; renal function may need to be monitored. The risk of impaired renal function is increased in patients with long-term use of ibuprofen and similar NSAIDs in patients with heart failure and hepatic impairment, in diuretics and in the elderly, in those taking antipyretic drugs.
- You have liver disease,
- You have heart disease or if you have high blood pressure (blood pressure); water retention in various parts of the body and as a result swelling (oedema) may occur.

- Ibuprofen and similar drugs have been associated with a small increase in the risk of heart attack (myocardial infarction) and stroke, especially when used at high doses and for extended periods of time. If you have heart or vascular diseases, have had a previous stroke, or if you think you are at risk (for example, if you have high blood pressure, high cholesterol or diabetes, or if you smoke), you should discuss your treatment with your doctor or pharmacist.
- Ibuprofen and similar NSAIDs are used for a long time (continuous), ulcers, bleeding and perforation of the gastrointestinal tract may occur, even if no such disease has been previously used. Risk of such undesirable effects increases in patients with previous illnesses, elderly people, high drug doses and treatment duration.
- Any bruising occurs on your body for no reason, consult a doctor.
- You feel cold, chills and fever suddenly, weakness, headache and vomiting, or a feeling of stiffness in your neck, seek medical attention immediately; some form of inflammation of the brain (aseptic meningitis).
- Redness, rashes appear on your skin,
- You have complaints about vision.

As with other NSAIDs, İBUPROFEN-PF may mask symptoms of infection. Using the lowest dose that is effective in relieving the symptoms of your disease for the shortest time will minimize the possibility of undesirable effects of the drug.

If these warnings are valid for you, even at any time in the past, please consult your doctor.

Using İBUPROFEN-PF with food and beverages
In terms of application method, it is safe to use simultaneously with food and drinks.

Pregnancy
Please consult your physician or pharmacist before taking the drug.

Tell your doctor if you are pregnant or think you may be pregnant. You should not use İBUPROFEN-PF if you are in the last 3 months of your pregnancy

If you realize that you are pregnant during your treatment, immediately consult your physician or pharmacist.

Lactation
Please consult your physician or pharmacist before taking the drug.

It is not known whether ibuprofen, the active substance of İBUPROFEN-PF, passes into breast milk. If you are breastfeeding, consult your physician.

Ability to drive and use machines

There are no data on effects of İBUPROFEN-PF on use of the vehicle and machine or on the person during the work that requires full attention. Therefore, care must be taken when performing such works.

Vital information regarding some of the excipients contained in İBUPROFEN-PF

If you have no hypersensitivity to excipients contained in İbuprofen-PF, it is not expected to have a negative impact due to these substances.

Use in combination with other drugs

You may need to change the dose and/or take other measures if you take one of the following drugs:

- Aminoglycoside class antibiotics (eg. gentamicin, kanamycin, streptomycin)
- High blood pressure drug products
- ADE inhibitors, beta blockers and diuretics used in blood pressure and heart disease
- Cholestramine, a cholesterol lowering drug
- Sulphonylurea, a drug used in diabetes
- CYP2C9 inhibitors (group of drugs that inhibit proteins involved in the inactivation of drugs in the liver; eg voriconazole, fluconazole)
- Drug products that prevent blood clotting (e.g warfarin)
- Drug products that inhibit the activity of clotting blood flakes (antithrombocyte agents: eg acetyl salicylic acid, dipyridamole, clopidogrel) and selective seratonin reuptake inhibitors used for depression (e.g. fluoxetine, fluvoxamine, paroxetine, sertraline); When used with NSAIDs, they may increase the risk of bleeding in the gastrointestinal tract. Concomitant use of tyclopidine and ibuprofen should be avoided.
- Acetyl salicylic acid

Co-administration of acetylsalicylic acid and ibuprofen is not recommended because of the potential for increased side effects.

- Corticosteroids
- Ginkgo biloba herbal extract
- Diuretic agents (e.g. furosemide)
- Cardiac glycosides used in heart failure (e.g. digoxin, digitoxin)
- Caution should be exercised in concomitant use with captopril (a drug used in high blood pressure disease).
- Antibiotics of the quinolone class (e.g. ciprofloxacin)
- Other painkillers (other NSAIDs including COX-2 inhibitors, e.g. acetyl salicylic acid, naproxen) and methotrexate (a drug used in rheumatoid joint diseases and certain types of cancer)
- Lithium salts (used in mental illnesses)
- Mifepristone (abortifacient)
- Cyclosporine (a drug that suppresses the immune system)

- Tacrolimus (a drug that suppresses the immune system)
- Zidovudine (a drug used in human immunodeficiency)
- Alcohol

If you are currently taking or recently took any prescribed or over-the-counter drugs, please inform your physician or pharmacist.

3. How you will be given İBUPROFEN-PF ?

- **Instructions regarding correct use and dosage/administration frequency:**

Carefully follow all instructions given by your physician, nurse or pharmacist.
For pain relief, a dose of 400-800 mg is administered intravenously every 6 hours.
For antipyretic effect, a dose of 400 mg every 4-6 hours or 100-200 mg every 4 hours is administered.
Undesirable effects can be minimized by using the lowest effective dose necessary to control symptoms as soon as possible.
If you have a kidney problem, your doctor may administer a lower dose.
Your doctor will decide how often the treatments will be performed.

- **Administration route and method:**

İBUPROFEN-PF is administered only as intravenous infusion. This application should last a minimum of 30 minutes. The drug product should be diluted before use.
Before administration, visually check whether there is any foreign matter and coloration in the solution. If foreign matter or discoloration is present, solution should not be used.

- **Different age groups**

Use in children:
The use of İBUPROFEN-PF in children under 17 years of age has not been investigated. Therefore, the use of the drug in children is not recommended.
Use in the elderly:
Elderly patients are at higher risk of adverse effects that may occur in the digestive tract. Therefore, dose selection should be made very well in elderly patients and treatment should be started at the lowest possible dose level.

- **Special usage cases:**

Renal/Liver failure:
Caution should be exercised in patients with renal, liver or heart failure, as the use of NSAIDs such as İBUPROFEN-PF may result in impaired renal function. In these patients, the dose should be kept as low as possible and renal function should be monitored.
Especially when high doses of İBUPROFEN-PF are required, careful consideration should also be made before long-term treatment is initiated in patients with risk factors for the heart and veins (e.g. high blood pressure, excessive fat in the blood, diabetes , smoking).
If you have severe kidney, liver and heart failure, you should not use İBUPROFEN-PF.

Talk to your doctor or pharmacist if you have the impression that the effect of İBUPROFEN-PF is too strong or too weak.

If you have taken more İBUPROFEN-PF than you should have:
If you have used İBUPROFEN-PF more than you should have or more than prescribed consult a physician or a pharmacist.

If you have used İBUPROFEN-PF more than you should or if your children have accidentally used this medicine, always consult a doctor or nearest hospital for advice and advice on the risk.

Symptoms; nausea, abdominal pain, vomiting (may be bloody streaks), headache, tinnitus, blurred consciousness, and shaky eye movements. In high doses, drowsiness, chest pain, palpitations, loss of consciousness, convulsions (especially in children), weakness and dizziness, blood in the urine, feeling of chills, breathing problems have been reported.

If you have received more İBUPROFEN-PF than you should; some effects may occur including abdominal pain, nausea, vomiting, drowsiness and dizziness.

If you have taken İBUPROFEN-PF at higher doses than recommended, you should be followed carefully by your doctor.

If you forget to use İBUPROFEN-PF
Do not take double doses to compensate for forgotten doses.

Possible effects once İBUPROFEN-PF treatment is concluded
Your doctor will tell you how long your treatment with İBUPROFEN-PF will continue. Do not discontinue treatment unaware of your doctor because stopping İBUPROFEN-PF may cause your disease to worsen.

4. What are the possible side effects?

Like all medicines, people who are sensitive to substances contained in IBUPROFEN-PF may have side effects. The most common of these are usually mild and probably disappear after a short time.

Stop using İBUPROFEN-PF and notify your doctor IMMEDIATELY or contact the emergency department of your nearest hospital:

- Allergic reaction
- Common, severe allergic reaction (anaphylaxis)
- Respiratory reactions such as asthma, aggravation of asthma, shortness of breath or distressed breathing (dyspnea),
- Itch (Pruritus)
- Minor bleeding in the skin and mucous membranes (purpura)

- Hypersensitivity to the face and throat causing swelling (oedema) (angioedema)
- Inflammatory skin disease with fluid-filled blisters (including Stevens-Johnson syndrome)
- Disease in the mouth and in other areas of the body with red rash of different sizes (erythema multiforme)
- A serious disease with skin-filled blisters, skin peeling and tissue loss (toxic epidermal necrolysis)
- Hives (urticaria)
- Photosensitivity and fluid-filled blistering (vesiculobullose) rash
- Aseptic meningitis (meningitis)

These are all very serious side effects.
If you have one of these, you have a serious allergy to IBUPROFEN-PF.
You may need urgent medical attention or hospitalization.
All of these very serious side effects are very rare.

Side effects are listed as follows according to their incidence.

Very common:	It can be seen in at least one of 10 patients.
Common:	Less than one in 10 patients, but more than one in 100 patients.
Uncommon:	Less than one in 100 patients, but more than one in 1,000 patients.
Rare:	Less than one in 1,000 patients, but more than one in 10,000 patients.
Very rare:	Less than one in 10,000 patients can be seen.
Unknown:	Cannot predict with available data.

Very common:
- Nausea
- Vomiting
- Flatulence in the stomach and intestines due to gas. (Flatulence)
- Headache

Common:
- Anemia
- Increased number of cells mediating blood clotting (thrombocythemia)
- Decrease in potassium, protein and albumin in blood (hypokalemia, hypoproteinemia, hypoalbuminemia)
- Increase in blood urea, sodium, LDH (an enzyme in blood)
- Decrease in the number of neutrophils in the blood (a type of white blood cell) (neutropenia)
- Stomach, intestinal bleeding (gastrointestinal hemorrhage)
- Tar-colored, foul-smelling stool due to bleeding (melena)
- Vomiting (hematemesis) such as blood or coffee grounds
- High blood pressure (hypertension)

- Decrease in blood pressure (hypotension)
- Allergic rhinitis
- Insomnia, anxiety and anxiety caused by fear (anxiety)
- Oedema
- Fluid retention
- Urinary retention (urinary retention)
- Dizziness
- Indigestion (dyspepsia)
- Abdominal pain / discomfort
- Tiredness
- Constipation
- Cough
- Lung inflammation caused by bacteria (bacterial pneumonia)
- Debris

Uncommon:

- Thrombocytopenia (reduction in the number of cells mediating platelet-blood clotting)
- Excessive decrease in the number of white blood cells that can develop suddenly (agranuocytosis)
- Aplastic anemia (severe reduction in the number of blood cells)
- Hemolytic anemia (a kind of anemia)
- Inhibition of clustering of cells that mediate blood clotting (inhibition of platelet aggregation)
- Decrease in the number of white blood cells (leukocytes) (leukopenia)
- Gastrointestinal perforation
- Inflammation of the inner membrane of the stomach (gastritis) - stomach burn
- Liver inflammation (hepatitis)
- Renal failure (renal failure)
- Wound formation due to tissue thinning in the mouth (oral ulceration)
- Reduction of creatinine excretion from kidney (decreased creatinine clearance)
- Blur of vision
- Vision changes
- Decreased hearing
- Wound on duodenum (duodenal ulcer)
- Gastric ulcer (gastric ulcer)
- Jaundice
- Abnormal liver function test
- Toxic kidney disorders in various forms (including interstitial nephritis and nephrological syndrome)
- Itching
- Hives

- Skin edema formation (angioedema) with rash-like rash
- Light sensitive reaction on skin
- Skin rash (purpura)
- Asthma
- Temporary narrowing of the air passage to the lungs (bronchospasm)
- Difficulty breathing (dyspnea)
- Sleepiness (somnolence)
- Paresthesia

Rare:

- Aseptic meningitis (with symptoms such as neck stiffness, headache, nausea, vomiting, fever, loss of direction)
- Serious allergic reaction (anaphylactic reaction)
- Tinnitus
- Confusion
- See, hear, feel things that are not (hallucination)
- Depression
- Inflammation of the eye nerves (optic neuritis)
- Dizziness caused by inner ear discomfort (vertigo)
- Toxic optic neuropathy (Sudden loss of vision and pain in the eye)
- Liver damage
- Life-threatening allergic reaction to the skin or mouth surface causing painful, red or purple rash and puffiness (bullous skin inflammation, including Steven-Johnson syndrome)
- A serious disease with skin-filled blisters, skin peeling and tissue loss (toxic epidermal necrolysis)
- Disease with erythema multiforme (red erythema) in the form of collection of water in the mouth and other areas of the body or different sizes

Very rare:

- Liver failure
- Pancreatic inflammation (pancreatitis)

Unknown:

- Inflammation of the large intestine (colitis) and exacerbation of Crohn's disease

If you have one of these, you may need immediate medical attention or hospitalization.

The use of drugs such as IBUPROFEN-PF, especially at high doses (2400 mg / day), may cause a small increase in the risk of heart attack (myocardial infarction or stroke).

A severe skin reaction, known as DRESS syndrome, may occur. The symptoms of DRESS are; rash, fever, swelling of the lymph nodes and increased eosinophils (a type of white blood cell).

Inform your doctor or pharmacist if you encounter any side effects not mentioned in these patient information leaflet.

5. Storage of IBUPROFEN-PF

Keep IBUPROFEN-PF out of the reach of children and in its packaging.

The IBUPROFEN-PF infusion solution should preferably be used immediately. If the solution is not used immediately, its storage before use is the responsibility of the healthcare professional; The solution should be stored at room temperature below 25°C.

The total time between dilution, storage and end of use should not exceed 24 hours.
Store at room temperature below 25°C before opening the package.

Use in accordance with expiration dates.
Do not use IBUPROFEN-PF after the expiry date on the packaging.

Do not use İBUPROFEN-PF if you notice defects in the product and / or packaging.

Do not put in trash if the product is expired or out of use! Give it to collection system specified by Ministry of Environment and Urbanization.

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These patient information leaflet were approved on 18.08.2019.

THE FOLLOWING INFORMATION IS FOR HEALTH STAFF THAT APPLY THIS DRUG.

How should IBUPROFEN-PF be prepared and applied?

IBUPROFEN-PF is used by intravenous infusion.
IBUPROFEN-PF should be diluted prior to intravenous infusion.
The diluted solution should be at a final concentration of 4 mg / mL or less.
As dilution solution; 0.9% Sodium Chloride, 5% Dextrose or ringer lactate solutions may be used.

400 mg dose: 4 mL IBUPROFEN-PF should be diluted with at least 100 mL solution.

If the solution and packaging are suitable, parenteral drugs should be visually inspected prior to administration for particle contamination and coloring. If visually opaque particles, discoloration or other impurities are observed, the solution should not be used.

Infusion time should be a minimum of 30 minutes.

Since there is no data on the compatibility of IBUPROFEN-PF with other substances administered intravenously, IBUPROFEN-PF should not be mixed with other drugs / substances and should always be administered via a separate infusion tube.