SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
IBU-BABY 60 mg suppository

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each suppository contains

Active substance:
Ibuprofen 60 mg

Excipients:
For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM
Suppository
Almost white, homogenous looking suppositories

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
It is indicated in the symptomatic treatment of fever and mild to moderate pain (such as teething pain, toothache, earache, headache of known origin, mild muscle pain, sore throat, pain associated with sprains and strains

When IBU-BABY is given rectally, absorption is less than oral use. Therefore, it is only recommended if oral use is not possible or if vomiting occurs.

4.2. Posology and method of administration
Posology/frequency and duration of administration:
IBU-BABY should be used in children older than 6 months and at least 6.0 kg body weight.
Undesirable effects can be minimized by using the lowest effective dose required to control disease symptoms as soon as possible (see Section 4.4).

Method of administration:
Used rectally.
The maximum daily ibuprofen dose should be 3-4 doses and should be no more than 20-30 mg per kg of body weight. No application should be done more frequently than 6 hours.

In children with body weights from 6.00 to 8.00 kg: One suppository is used at the beginning of treatment. If necessary, one more suppository can be given after 6-8 hours. Up to 3 suppositories can be given within 24 hours.

In children with body weights from 8.00 to 12.5 kg: One suppository is used at the beginning of treatment. If necessary, one more suppository can be given after 6 hours. Up to 4 suppositories can be given within 24 hours.

IBU-BABY is used for a maximum of 3 days.

Patients should be informed that they should consult a doctor if symptoms do not disappear or become severe during this time.

It is for short time use.

Additional information on special populations:

Renal/Hepatic failure:
Caution should be used when used in patients with renal, hepatic or cardiac failure because the use of NSAIDs such as ibuprofen may result in impaired renal function. In these patients, the dose should be kept as low as possible and renal function should be monitored. It causes sedation in patients with severe hepatic insufficiency. IBU-BABY should not be used in patients with hepatic insufficiency.

Pediatric population:
The method of administration in the pediatric population is given above.
It is not recommended to use for children younger than 6 months and less than 6.0 kg body weight

Geriatric population:
In the elderly, the incidence of undesirable effects such as gastrointestinal bleeding (GB) and perforation, which may be fatal on the digestive system, is increasing. Therefore, the smallest effective dose and the shortest duration of treatment should be preferred if elderly patients need to use NSAIDs.

Combination therapy with protective drugs (e.g. misoprostol or proton pump inhibitors) should be considered for these patients and patients needing concomitant low doses of acetylsalicylic acid (ASS) or other drugs that increase gastrointestinal risk (see 4.5).

4.3. Contraindications
IBU-BABY is contraindicated in the following situations:

-Patients with hypersensitivity to ibuprofen or non-steroidal anti-inflammatory/analgesic medicines (NSAIDs) or any of the ingredients in this medicine

- Patients with bronchospasm, asthma, rhinitis or urticaria in the past in association with the use of acetylsalicylic acid or another NSAID,

- Patients with past history of gastrointestinal bleeding or perforation associated with NSAID therapy,

- Patients with recurrent peptic ulcer disease or hemorrhages, active ulcerative colitis, Crohn's disease (defined as two or more proven, marked ulceration or bleeding episodes) in the past or present

- Increased bleeding tendency,

- Severe hepatic failure -,

- Severe renal failure,

- Severe cardiac failure (NYHA Class IV),

- Women in the third trimester of pregnancy,

- In the period before or after coronary artery by-pass surgery,

- In children younger than 6 months and less than 6.0 kg body weight

4.4. Special warnings and precautions for use

Kardiyovasküler (KV) risk
- NSAIDs may cause increased risk of cardiovascular thrombotic events, myocardial infarction and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

- IBU-BABY is contraindicated for treatment of pain prior to coronary artery by-pass surgery.

Gastrointestinal (GI) risks
NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration and perforation of the stomach or intestines, which can be fatal. These adverse events can occur at any time with or without prior warning symptoms. Elderly patients are at a greater risk for serious gastrointestinal events.

Transition of rectally administered ibuprofen to blood may be less predictable than oral administration.

There is a risk of rectal perforation during administration.

Particular attention should be paid to the following patient groups:
- Systemic lupus erythematous and mixed connective tissue disease (aseptic meningitis symptoms such as neck stiffness, headache, nausea, vomiting, fever and loss of sense of direction)
- Gastrointestinal disorders and chronic inflammatory bowel disease (ulcerative colitis, Crohn's disease), rectal or anus diseases

- High blood pressure and/or cardiac failure

- History of gastrointestinal bleeding or perforation related to previous ibuprofen therapy

- Hepatic dysfunction

Bronchospasm may occur in patients with bronchial asthma, chronic rhinitis, sinusitis, nasal polyp or allergic disease, or who have had one of these diseases in the past.

Sufficient amount of fluid intake is essential in case of dehydration. For example, special attention should be paid to children with severe dehydration due to diarrhea, otherwise dehydration may lead to acute renal failure.

Medical surveillance is essential in patients who are treated immediately after a serious surgical operation.

Urinary excretion and renal function should be particularly monitored in the treatment of patients with heart / kidney / liver failure, diuretic treatment, or dehydration after a serious surgical operation.

Undesirable effects can be minimized by using the lowest effective dose required to control disease symptoms for the shortest period of time.

Special caution should be taken (consultation with a doctor or pharmacist) in patients with history of high blood pressure and / or heart failure before starting treatment. Because fluid retention, high blood pressure and edema have been reported in the presence of NSAID-therapy.

Use with other NSAIDs should be avoided.

In the elderly, the incidence of undesirable effects such as gastrointestinal bleeding (GB) and perforation, which may be fatal on the digestive system, is increasing. Therefore, the smallest effective dose and the shortest duration of treatment should be preferred if elderly patients need to use NSAIDs

Especially in the elderly, there is an increased risk of serious side effects such as gastrointestinal bleeding and perforation, which can be fatal. The lowest effective dose should be administered to these patients.

As with other NSAIDs, İBUPİRREX may mask the signs of infection.

Cardiovascular and cerebrovascular effects:
Clinical trials indicate that the use of ibuprofen, especially at high doses (2400 mg / day), may be associated with a small increase in the risk of arterial thrombotic events (e.g., myocardial infarction or stroke). Taken together, epidemiological studies do not suggest that low-dose ibuprofen (e.g., ≤ 1200 mg / day) may be associated with an increased risk of myocardial infarction.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), current ischemic heart disease, peripheral artery disease and / or cerebrovascular disease should be treated with ibuprofen only after careful evaluation and avoiding high doses (2400 mg / day).

Careful assessment should be done before the initiation of long-term therapy in patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidemia, diabetes, smoking), especially when high doses of ibuprofen (2400 mg / day) are required.

Cardiovascular thrombotic events
Clinical trials of several COX-2 selective and non-selective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, including myocardial infarction (MI) and stroke, which can be fatal. COX-2-selective or non-selective NSAIDs may be at similar risk. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at higher risk. To minimize the risk of cardiovascular adverse events in patients treated with NSAIDs, the lowest effective dose and the shortest course of treatment should be preferred. Even if no cardiovascular symptoms have been seen in the past, physicians and patients should remain alert for the development of such adverse events. Patients should be informed about the signs and / or symptoms of severe cardiovascular events and the steps to take if they occur.

There is no consistent evidence that concurrent use of aspirin with NSAIDs reduces the risk of serious cardiovascular thrombotic events associated with the use of NSAIDs. The concurrent use of aspirin and an NSAID increases the risk of severe gastrointestinal effects.

It has been determined that the incidence of myocardial infarction and stroke is increased in two large, controlled clinical trials using COX-2 selective NSAIDs for the treatment of pain in the first 10-14 days following coronary artery by-pass surgery.

Hypertension
NSAIDs, including IBU-BABY, can lead to onset of new hypertension or worsening pre-existing hypertension. In either case, these may contribute to the increased incidence of cardiovascular events. Patients receiving thiazide or loop diuretics may have impaired response to these therapies when taking NSAIDs.

NSAIDs, including IBU-BABY, should be used with caution in patients with hypertension. The blood pressure should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.

Congestive heart failure and edema
Fluid retention and edema have been reported in some patients using NSAIDs. IBU-BABY should be used with caution in patients with fluid retention or heart failure.

Headache may develop when painkillers are used at high doses for a long time and in an improper manner. This headache should not be treated with a higher dose of the drug.

In general, the use of painkillers as a habit, and especially combination with more than one pain reliever, can lead to renal impairment (analgesic nephropathy) as well as the risk of renal damage.

Kidney, liver and blood tests are essential for patients who have been treated for a long time.

IBU-BABY should not be used in combination with other NSAIDs and selective cyclooxygenase-2-inhibitors.

Ibuprofen administration may affect ovulation as other drugs known to inhibit cyclooxygenase / prostaglandin synthesis. For this reason, it is not recommended to use to women who want to become pregnant. It is useful to take into consideration the discontinuation of ibuprofen administration in women who have problems in getting pregnant or have undergone infertility checks.

Elderly patients: Undesirable effects are more common in elderly patients receiving NSAID therapy; especially gastrointestinal bleeding, perforation and even fatal outcomes are possible.

Gastrointestinal (GI) effects, ulceration, bleeding and perforation risk:
NSAIDs, including IBU-BABY, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the stomach, small intestine or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Symptoms manifest in only one out of five patients with severe upper gastrointestinal adverse reactions in the treatment of NSAIDs. Upper gastrointestinal ulcer, hemorrhage or perforation occurs in approximately 1% of patients who receive NSAID therapy for 3-6 months and in 2-4% of patients who receive treatment for one year. These trends continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.

NSAIDs should be prescribed very carefully in patients with a prior history of ulcer disease or gastrointestinal bleeding. Patients with a prior history of peptic ulcer disease and/or gastrointestinal bleeding who use NSAIDs have a greater than 10-fold increased risk for developing a gastrointestinal bleeding compared to patients treated with neither of these risk factors. Other factors that increase the risk of gastrointestinal bleeding in patients using NSAIDs

include concomitant use of oral corticosteroids or anticoagulants, longer duration of NSAID therapy, smoking, alcohol use, older age, poor general health status. Particular attention should be paid to this patient population during treatment because sudden fatal gastrointestinal events are most often seen in elderly or debilitated patients.

To minimize the potential risk for gastrointestinal adverse event in patients receiving NSAID therapy, the lowest effective dose should be used for the shortest possible duration. Patients and physicians should remain alert for signs and symptoms of gastrointestinal ulceration and bleeding during NSAID treatment and, promptly initiate additional evaluation and treatment if a gastrointestinal adverse reaction is suspected. Even NSAID therapy should be discontinued until the possibility of a serious gastrointestinal adverse effects have disappeared.

The risk of gastrointestinal bleeding, ulcer or perforation is higher with increased NSAID dose; bleeding or perforation complications (see section 4.3) can occur, especially in patients with ulcers in the past and elderly patients. In this group of patients, treatment should be started with the lowest possible dose. Combination therapy with protective drugs (e.g. misoprostol or proton pump inhibitors) should be considered for these patients and patients needing concomitant low doses of acetylsalicylic acid (ASS) or other drugs that increase gastrointestinal risk (see 4.5).

Patients who have experienced gastrointestinal toxicities in the past, and especially elderly patients should report any unusual symptoms (especially gastrointestinal bleeding) in the abdominal region, particularly at the beginning of treatment.

Likewise, particular attention should also be paid to patients receiving simultaneous oral corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors or thrombocyte aggregation inhibitors such as ASS, which will increase the risk of ulceration or bleeding (see 4.5).

If gastrointestinal hemorrhage or ulcer disease occur in patients receiving IBU-BABY treatment, treatment should be discontinued.

Patients with past history of gastrointestinal disturbances (colitis ulcer, Crohn's disease) should use NSAID medicines with caution; their general condition may worsen (see 4.8).

Effects on the kidneys
Caution should be exercised when initiating ibuprofen therapy in patients with significant dehydration.

As with other NSAIDs, long-term ibuprofen administration has resulted in renal papillary necrosis and other pathological renal changes. Renal toxicity has been observed in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion.

In these patients, administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and, secondarily a decrease in renal blood flow which may accelerate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.

Advanced renal failure
No information is available from controlled clinical studies regarding the use of IBU-BABY in patients with advanced renal failure. Therefore, the use of IBU-BABY is not recommended in

patients with advanced renal failure. If IBU-BABY therapy must be initiated, close monitoring of the patients renal function is advisable.

Anaphylactoid reactions
As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to IBU-BABY (see Contraindications, Special warnings and precautions for use -Pre-existing Asthma). If an anaphylactoid reaction occurs, immediate medical treatment should be given to the patient.

Skin reactions
Severe skin reactions have been very rarely reported while under NSAID therapy. Some of these are exfoliative dermatitis, Stevens-Johnson Syndrome and toxic epidermal necrolysis (Lyell-Syndrome) which can be fatal (see 4.8). The highest risk for such reactions is seen at the beginning of treatment. In a large majority of cases the reaction occurred within the first month of treatment. Ibuprofen should be discontinued if skin sensitivities, mucous lesions, or other signs of hypersensitivity are detected.

In exceptional cases, varicella infection can lead to serious skin infections and soft tissue complications. In these cases, it is necessary to consider the role of NSAIDs in aggravating skin infections and soft tissue complications. Therefore, it is recommended not to give ibuprofen in case of varicella infection.

Pregnancy
It should be used with caution in the first 6 months of pregnancy (see Section 4.6 Pregnancy and lactation). IBU-BABY should not be used as in other NSAIDs in the third trimester of pregnancy; because it can cause the premature closure of ductus arteriosus (the gap between the two large arteries [aorta and pulmonary artery] from the heart that is open before birth and needs to close following birth)

Precautions
General
IBU-BABY cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should gradually and slowly reduce their treatment if a decision is made to discontinue corticosteroids.

The pharmacological activity of ibuprofen in IBU-BABY in reducing [fever and] inflammation may diminish the utility of diagnostic signs used in detecting complications of presumed non-infectious, painful conditions.

Hepatic effects
Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs, including IBU-BABY. These laboratory abnormalities may progress, may remain unchanged, or maybe transient with continuing therapy. Notable elevations of ALT or AST (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice, fatal fulminant hepatitis, liver necrosis, and hepatic failure, some of them with fatal outcomes have been reported

A patient with symptoms and/or signs suggesting liver failure, or with abnormal liver test values, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with IBU-BABY. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), IBU-BABY should be discontinued

Hematologic effects
Anemia is sometimes seen in patients receiving NSAIDs, including IBU-BABY. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including IBU-BABY, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia.

NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is qualitatively less, of shorter duration, and reversible.

IBU-BABY generally does not affect platelet count, prothrombin time (PT) or partial thromboplastin time (PTT). Patients receiving IBU-BABY who are affected adversely by changes in platelet functions and who may experience events such as coagulation disorders should be carefully monitored and patients receiving anticoagulants should be monitored carefully.

Preexisting asthma
The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm, which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and NSAIDs has been reported in such aspirin-sensitive patients, IBU-BABY should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma (see Section 4.3 Contraindications).

Laboratory tests
Because serious GI tract ulcerations and bleeding can occur without warning symptoms, physicians should monitor for signs or symptoms of GI bleeding. Patients on long-term treatment with NSAIDs should have their CBC and biochemistry profile checked periodically. If clinical signs and symptoms consistent with liver or renal disease develop, systemic manifestations occur (e.g., eosinophilia, rash etc.), or abnormal liver tests persist or worsen, IBU-BABY should be discontinued

4.5. Interaction with other medicinal products and other forms of interaction
It is essential to consider the clinical and biological parameters in patients receiving ibuprofen simultaneously with the drugs listed below.

Combination of the following agents should be avoided:
- Acetylsalicylic acid or other NSAIDs and glucocorticoids: These drugs may increase the risk of adverse drug effects in the gastrointestinal tract.
- Anticoagulants: There are limited warnings that anticoagulants increase the risk of bleeding and strengthen the effectiveness.

Special caution should be given in combination with the following agents:
- Antihypertensives (ACE inhibitors, angiotensin receptor blockers, beta-blockers, diuretics and drugs used in pulmonary hypertension (endothelin receptor antagonists, bosentan)): NSAIDs may reduce antihypertensive efficacy. When ACE inhibitors and angiotensin-II antagonists are administered concurrently with NSAIDs, including selective COX-2

inhibitors, there is an increased risk for acute renal failure, usually reversible in patients with renal insufficiency (e.g., dehydrated or elderly patients). Therefore, this combination should be applied carefully to patients with renal insufficiency, especially elderly patients. Patients should be adequately hydrated and renal function should be checked after combination therapy has begun and at regular intervals during treatment (see Section 4.4).

- Diuretics (thiazide, thiazide-like diuretics and convoluted diuretics) may also increase the risk of nephrotoxicity of NSAIDs. NSAIDs are able to eliminate the diuretic effect of furosemide and bumetanide, probably due to the inhibition of prostaglandin synthesis. It can also reduce the antihypertensive effect of thiazides.
- Lithium: NSAIDs lead to an increase in plasma lithium levels and a decrease in renal lithium clearance. The minimum lithium concentration increased by 15% and the renal clearance decreased by 20%. These effects are based on the inhibition of renal prostaglandin synthesis by NSAIDs. Therefore, when lithium is coadministered with NSAIDs, patients should be closely monitored for lithium toxicity.
- Methotrexate: NSAIDs have been reported to inhibit methotrexate accumulation competitively in rabbit kidney sections. This may indicate that these drugs may increase the toxicity of methotrexate. Caution should be exercised when administered in combination with methotrexate of NSAIDs.
- Tacrolimus: The risk of renal toxicity increases if taken with NSAIDs.
- Cyclosporine: Can pose a risk of renal toxicity.
- Glucocorticoids: May cause increased gastrointestinal ulcer or bleeding risk. (see 4.4).
- Anticoagulants: NSAIDs can potentiate the effect of anticoagulants such as warfarin (see 4.4). The effects of warfarin and NSAIDs on gastrointestinal bleeding are synergistic, such that the users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone.
- Platelet aggregation inhibitors and selective serotonin reuptake inhibitors (SSRIs): increase the risk of gastrointestinal bleeding. (see 4.4)
- Ticlopidine: NSAIDs should not be used in combination with ticlopidine due to the inhibition of platelet function.
- Aspirin (Acetylsalicylic acid): As with other products containing NSAIDs, they should not be given together because of the potential for increased adverse effects. Experimental data suggests that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when used simultaneously. Although there is uncertainty about the clinical extrapolation of these data, the possibility that long-term and continuous use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be ruled out. A clinically significant effect is not probably expected with occasional use of ibuprofen (see Section 5.1).
- Mifepristone: Due to the antiprostaglandin properties of NSAIDs, including acetylsalicylic acid, the effectiveness of the medicinal product may be theoretically reduced. Limited evidence suggests that NSAIDs administered on the same day as prostaglandin do not adversely affect the cervical maturation effects of mifepristone or prostaglandin and do not reduce the clinical efficacy of medical termination of pregnancy.
- Sulfonylurea: NSAIDs may potentiate the effects of sulfonylurea group drugs. Very rare hypoglycemia has been reported with the use of ibuprofen in patients receiving sulfonylurea therapy.
- Zidovudine: When NSAIDs are given with zidovudine, the risk of hematological toxicity may increase. Increased hematoma and hemarthrosis risk was reported in HIV (+) hemophilia patients receiving concurrent zidovudine and ibuprofen therapy.

- CYP2C9 inhibitors: Co-administration of ibuprofen with CYP2C9 inhibitors may increase exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazole and fluconazole (CYP2C9 inhibitors), an increased S (+) - ibuprofen exposure of about 80-100% was shown. Particularly in the case of high doses of ibuprofen combined with potent CYP2C9 inhibitors such as voriconazole or fluconazole, reduction of the dose of ibuprofen should be considered.
- Herbal extracts: Ginkgo biloba may potentiate the risk of bleeding due to NSAID use.
- Aminoglycosides: NSAIDs may reduce the excretion of aminoglycosides (especially in preterm infants)).
- Quinolone-derived antibiotics: Data from experimental animals indicate that NSAIDs may increase the risk of convulsions associated with quinolone antibiotics. The risk of developing convulsions in patients taking NSAIDs and quinolones together may increase.
- Cholestyramine: Simultaneous administration of ibuprofen and cholestyramine delays and reduces ibuprofen absorption (by 25%). These drugs should be taken at least 2 hours intervals.
- Captopril: Experimental studies show that ibuprofen acts counter to the effect of captopril on sodium excretion.
- Selective serotonin reuptake inhibitors, SSRI (e.g. paroxetine, fluoxetine, sertraline): Both SSRIs and NSAIDs cause an increased risk of bleeding, for example from the gastrointestinal tract. This risk is increased in case of combination treatment. The mechanism is likely to be associated with decreased serotonin reuptake in platelets.

Additional information for special populations:
No interaction studies have been conducted in special populations.

Pediatric population:
No interaction studies have been conducted in pediatric population.

4.6. Pregnancy and lactation
General recommendation
Pregnancy category: C (D in third trimester).

Women with childbearing capacity / Birth control (Contraception)
There is no information on the effect on birth control methods. It is recommended that women who are not planning to become pregnant, use or continue to use effective birth control methods throughout treatment, although knowing that the use of ibuprofen may affect fertility negatively

If ibuprofen is given to a woman who is thinking to become pregnant or is in the first and second trimester of pregnancy, the dose should be as low as possible and the duration of the treatment should be kept as short as possible. In the last three months of pregnancy, IBU-BABY should not be used because of the complications that may occur in mother and baby.

Occasional use of ibuprofen is not expected to affect the chance of getting pregnant, but if there are problems with pregnancy, an evaluation should be done before using this medicine.

Pregnancy
IBU-BABY has harmful pharmacological effects on pregnancy and / or fetus / newborn.

IBU-BABY should not be used during pregnancy unless it is necessary.

Inhibition of prostaglandin synthesis may adversely affect pregnancy and / or embryo / fetal development. The data obtained from epidemiological studies indicate an increase in the risk of miscarriage, gastroschisis and cardiac malformation after the use of prostaglandin synthesis inhibitor in the early period of pregnancy.

The risk is assumed to increase with the dose administered and duration of administration. Studies on animals have shown reproductive toxicity (see Section 5.3).

Reproductive studies conducted in rats and rabbits have not demonstrated evidence of developmental abnormalities. However, animal reproduction studies are not always predictive of human response. There are no adequate and well-controlled studies in pregnant women.
Non-steroidal anti-inflammatory drugs should be avoided in pregnancy (especially in late pregnancy) due to known effects in the fetal cardiovascular system (closure of ductus arteriosus).

In the first and second trimester of pregnancy, ibuprofen should not be given unless absolutely necessary. If ibuprofen is given to a woman who is trying to become pregnant or is in the first and second trimester of pregnancy, the dose should be as low as possible and the duration of the treatment should be kept as short as possible.

During the third trimester, all prostaglandin synthesis inhibitors may expose the fetus to the following:
- Cardiopulmonary toxicity (early closure of ductus arteriosus and pulmonary hypertension),
- Renal dysfunction that may progress to renal failure together with oligohydramnios

Increased incidence of dystonia, delayed delivery, and reduced survival rate are seen in rat studies with NSAIDs, as in other drugs known to inhibit prostaglandin synthesis. The effects of IBU-BABY on birth and birth pain are unknown.

The following can be seen in the mother and the newborn at the end of the pregnancy:
- Prolongation of bleeding time
- Inhibition of uterine contractions causing delayed birth and long birth duration
- Birth and onset of the birth may be delayed. The duration of birth can be prolonged with more bleeding tendency both in the mother and the child.

Consequently, IBU-BABY is contraindicated in the last trimester of pregnancy.

Lactation
It is not known whether the medicine passes into breast milk. Because many medicines are secreted into breast milk and IBU-BABY has a potentially serious side effect if newborns are breastfed, your doctor may decide to stop breastfeeding or use of medication by taking into account the importance of drug use.

Reproduction ability / Fertility
The use of ibuprofen may affect fertility negatively, so it is not recommended for women who are thinking to become pregnant. It is useful to take into consideration the discontinuation of ibuprofen administration in women who have problems in getting pregnant or have undergone infertility checks.

4.7. Effects on ability to drive and use of machines
IBU-BABY may cause undesirable effects such as dizziness, lethargy, fatigue and visual impairment. If these adverse effects are observed, patients should be warned not to drive and use machines.

4.8. Undesirable effects
The specified undesirable effects are classified according to the following rule:
Very common (≥ 1/10); common (≥ 1/100 to ≤ 1/10); uncommon (≥ 1/1000 to ≤ 1/100); rare (≥ 1/10000 to ≤ 1/1000); very rare (≤ 1/10.000); unknown (Frequency cannot be estimated from the available data).

Blood and lymphatic system disorders
Very rare: Hemolytic disorders (anemia, leukopenia, thrombocytopenia, pancytopenia, agranulocytosis). First symptoms are: fever, sore throat, superficial wound in mouth, flu-like complaints, severe fatigue, nasal bleeding and bleeding on the skin

Immune system disorders
Very rare: Serious hypersensitivity reactions may include: swelling of the face, tongue and throat, shortness of breath, accelerated heartbeat, decreased blood pressure (anaphylaxis, angioedema) or severe shock. Exacerbation of asthma and bronchospasm

In patients treated with ibuprofen in patients with current autoimmune disease (Systemic Lupus Erythematous and mixed connective tissue disease), symptoms of aseptic meningitis such as neck stiffness, headache, nausea, vomiting, fever and loss of sense of direction have been observed in some cases.

Hypersensitivity reactions
Uncommon: Urticaria, itching

Respiratory thoracic and mediastinal disorders
Uncommon: Asthma, bronchospasm, dyspnea

Nervous system disorders
Uncommon: Headache, dizziness, drowsiness, sleeplessness, tinnitus, fatigue, weakness.
Rare: Optic neuritis

Cardiac disorders
Very rare: Edema, hypertension and heart failure in association with NSAID-therapy.

Gastrointestinal disorders
Common: Stomach discomfort, abdominal pain, nausea, dyspepsia
Uncommon: Diarrhea, bloating, constipation, vomiting, gastrointestinal diseases (stomach ulcer, duodenal ulcer) with bleeding or perforations, black stool, bloody vomiting, severe pain in the upper abdomen, inflammation of the mouth mucosa and ulcer formation, exacerbation of existing bowel diseases (ulcerative colitis, Crohn's disease)

Hepatobiliary disorders
Very rare: Liver diseases (especially in long-term treatments), cholestatic jaundice, hepatitis, elevation of serum enzymes

Skin and subcutaneous tissue disorders
Very rare: Serious skin reactions such as erythema multiforme, toxic epidermal necrolysis and Stevens - Johnson syndrome
Not known: Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)
In some cases, severe infections of the skin and soft tissue infections in the varicella infection may occur.

Kidney and urinary tract disorders
Very rare: Decrease in urination, edema and acute renal failure, papilla necrosis and increased serum urea density especially in long-term treatments.

General disorders and administration site conditions
Uncommon: Rectum irritation
Clinical trials have shown that the use of ibuprofen, especially at high doses (2400 mg / day), may be associated with a small increase in the risk of arterial thrombotic events (e.g., myocardial infarction or stroke) (see Section 4.4).

4.9. Overdose
There is a risk of toxicity if the 200 mg / kg body weight dose is exceeded.

Overdose symptoms include nausea, vomiting, abdominal pain, headache, dizziness, drowsiness, nystagmus, visual disturbances, tinnitus and rarely hypotension, metabolic acidosis, kidney failure and loss of consciousness. Metabolic acidosis may occur in severe poisoning.

No specific antidote is available. If necessary, patients should be treated symptomatically. Where appropriate, it is useful to take intensive medical precautions.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Non-steroidal anti-inflammatory drugs
ATC Code: M01AE01

Mode of action:
Ibuprofen is a non-steroidal antipyretic / analgesic drug (NSAID) and has proven effective in inhibiting prostaglandin synthesis in inflammatory models performed in conventional animal experiments. In human, ibuprofen treats inflammation-related pains, reduces swelling and fever. In addition, ibuprofen inhibits reversible platelet aggregation.

The clinical effect of ibuprofen has been shown in the treatment of mild to moderate pain, such as teething pain, toothache, earache, headache, soft tissue injuries and pain after surgical intervention, post-vaccination fever, pain and fever associated with cold and flu.

Experimental data suggests that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when used simultaneously. In some pharmacodynamic studies, the efficacy of acetylsalicylic acid in the formation of thromboxane or platelet aggregation was reduced when a single dose of 400 mg ibuprofen was taken within 8 hours prior to the rapid-release acetylsalicylic acid dose (81 mg) or within 30 minutes after the dose. Although there is uncertainty about the clinical extrapolation of these data, the possibility that long-term and continuous use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic

acid cannot be ruled out. A clinically significant effect is not probably expected with occasional use of ibuprofen. (see Section 4.5).

5.2. Pharmacokinetic properties

General characteristics

Absorption:
Ibuprofen is rapidly absorbed following rectal administration. Moderate peak-plasma concentrations are obtained almost completely after 45 minutes of the administration of 60 mg suppository.

Distribution:
Ibuprofen shows a high degree of binding to plasma proteins and distributed into synovial fluid.

Biotransformation:
Ibuprofen metabolizes two inactive metabolites in the liver. These are either excreted with the unchanged ibuprofen or via the kidney as conjugates.

Elimination:
Renal elimination of ibuprofen is rapid and complete.
Elimination half-life is about 2 hours.

Special populations
There are no pharmacokinetic studies in children.
There are no significant changes in pharmacokinetics in elderly people.

5.3. Preclinical safety data
The subchronic and chronic toxicity of ibuprofen has been shown to be in the form of lesions and ulcers, especially in the gastrointestinal tract in animal studies. . It has not been found that ibuprofen has clinically significant mutagenic effects in in vitro and in vivo studies. There is no evidence that ibuprofen is carcinogenic in studies performed with rats and mice. Ibuprofen caused ovulation inhibition in the rabbit. Experimental studies have shown that ibuprofen passes the placenta. When the prostaglandin synthesis inhibitor is administered in animals, an increase in the number of embryo-fetal deaths at a low number is observed before and after implantation. It has also been shown that the administration of prostaglandin-synthesis-inhibitor to animals leads to an increase in possible disorders, including cardiovascular disorders during the development of organs.

6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients
Witepsol H5
Polysorbate 80

6.2. Incompatibilities
Not available.

6.3. Shelf life
24 months

6.4. Special precautions for storage
Store at room temperature below 25ºC.

6.5. Nature and contents of container
White PVC/PE strips

Each cardboard box contains 6 or10 suppositories.

6.6. Special precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with “Directive on Control of Medical Waste” and “Directive on the Control of Packaging and Packaging Waste”.

7. MARKETING AUTHORIZATION HOLDER
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8. MARKETING AUTHORIZATION NUMBER(S)
2017/699

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION
Date of the first authorization: 19.09.2017
Date of the renewal of the authorization:

10. DATE OF REVISION OF THE TEXT
18.09.2018