PATIENT INFORMATION LEAFLET

MIKONID 750 mg/200 mg/100 mg vaginal ovule
For intravaginal use.

- ***Active substance(s):*** Each ovule contains 750 mg metronidazole, 200 mg miconazole nitrate and 100 mg lidocaine (base).
- ***Excipient(s):*** Polyethylene glycol 400 and hard fat.

Read all of this PATIENT INFORMATION LEAFLET carefully before you start taking this medicine, because it contains important information for you.

- *Keep this 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 only. Do not pass it on to others.*
- *If you go to a doctor or hospital during the use of this medicine, inform your doctor about this.*
- *Follow the instructions in this leaflet exactly. Do not use* ***higher or lower*** *doses than the dose which was recommended for you.*

What is in this Leaflet:

1. What MIKONID is and what it is used for?

- MIKONID is a medicinal product in an ovule form, which is applied into the vagina. This drug belongs to the pharmaceutical classes of antibacterial (acting against bacteria) and antifungal (acting against fungal infections) drugs.
- Each whitish ovule contains 750 mg metronidazole, 200 mg miconazole nitrate and 100 mg lidocaine as active substances. MIKONID is available in a package containing 7 pieces of ovule and 7 pieces of finger cot used to apply the drug into the vagina.
- MIKONID is used for the treatment of vaginitis caused by bacteria, which is manifested with the symptoms of itching and burning, abnormal discharge, swelling and inflammation in the vagina.

2. What you need to know before you use MIKONID?
Do not use MIKONID
If;

- you are allergic to any of the active substances contained in MIKONID, its derivatives or any of the above mentioned excipients or similar antifungal drugs (fungicides) (Redness, swelling or breathing problems, swelling of the lips, face, throat, or tongue may be allergic symptoms.)
- you are in the first trimester of the pregnancy period
- you have a sexually transmitted disease called trichomonal vaginitis caused by a single cell parasitic organism during the first 3 months of pregnancy
- you have porphyria (an hereditary, metabolic disorder of the circulatory system)
- you have epilepsy
- you have serious hepatic dysfunction, you should not use MIKONID.

- you are using contraceptive methods such as diaphragm and condom, do not use simultaneously with MIKONİD.

During the treatment with MIKONID and within 3 days after the treatment, alcohol consumption should be avoided.

During the treatment with MIKONID and within the last 2 weeks, drugs that contain disulfiram, used for the treatment alcoholism, should not be used.

Warnings and precautions

Metronidazole

- If you use the medicine at higher doses and for longer periods (more than 10 days) than your doctor has recommended, then you may experience weakness, pain, numbness, tingling in arms and legs (symptoms of peripheral neuropathy), and epilepsy-like seizures (convulsion). In this case, stop using the medicine and contact your doctor or a hospital.
- If you have an active or chronic severe nervous system disease, inform your doctor before using this medicine.
- Serious skin reaction conditions such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) or acute generalized exanthematous pustulosis (AGEP) have been reported with metronidazole. The most common risk of serious skin reactions is within 48 hours of starting treatment, typically within 1 week. If symptoms or signs of these diseases appear, treatment with MIKONID should be discontinued immediately and you should contact your doctor or a medical service center immediately.
  - SJS / TEN initially appears on the body in the form of a target type red point or often centrally bubble circular patches. In addition, mouth, throat, nose, genital area and eye (red and bulging eyes) ulcers may occur. Serious skin rashes usually occur before fever and / or flu-like symptoms. Rashes can cause skin peeling and the spread of life-threatening side effects.
  - AGEP appears at the beginning of the treatment with swelling under the skin and water-filled blisters accompanied by red, scaly diffuse redness and fever. It is most commonly seen on skin folds, body and upper extremities (hands and arms).
- If you are a dialysis patient, consult your doctor before using this medicine.
- If you have liver failure and hepatic encephalopathy (neurological and psychological disease seen in patients with impaired liver function), metronidazole can worsen your symptoms. Therefore, if you have such a disease, MIKONID should be used carefully and under the supervision of your doctor. In such a case, the dose of MIKONID will be adjusted by your doctor.
- Because of metronidazole, the color of your urine may darken.
- As a result of taking alcohol together with disulfiram, which is used in the treatment of alcohol dependence, a poisoning-like reaction may be observed, therefore alcohol should not be taken for at least 48 hours during and after treatment.
- In patients with Cockayne syndrome, a rare hereditary disease that occurs with developmental retardation during childhood, the use of MIKONID should be discontinued immediately and a doctor should be consulted if any of the possible signs of liver damage such as abdominal pain, nausea, changes in stool color or jaundice occur.

Miconazole

- Severe allergic reactions (hypersensitivity reactions), including life-threatening reactions (anaphylaxis and angioedema), have been reported during treatment with vaginal capsules containing miconazole and other drugs containing miconazole. If an allergy or irritation-

like reaction occurs, discontinue treatment immediately and contact your doctor or nearest healthcare provider immediately.
- If it is deemed necessary by your doctor, your partner may also be treated.
- Miconazole does not stain skin or clothing.
- Concomitant use of vaginally administered drugs and latex condoms or diaphragms (preservatives) can reduce the effectiveness of the relevant contraceptive methods. Therefore, MIKONID and latex condoms or diaphragms should not be used concomitantly.

Lidocaine
- Lidocaine can lead to heart rhythm disturbances, difficulty breathing, coma and even death, especially when applied to large skin surfaces and when covered with dressings. These effects are unlikely to occur when used as stated in the "Instructions for proper use and dose / frequency of administration" section, as MIKONID is administered as an ovule. Follow strictly to the dosage and duration of treatment recommended by your doctor.
- You may be more sensitive to lidocaine if you have become suddenly ill (acutely), debilitated, or of advanced age.

General warnings
- MIKONID should not be used in young people who are not sexually mature and virgin.
- MIKONID may damage latex. Therefore, concomitant use of ovules with condoms and contraceptive diaphragms should be avoided. Otherwise, contraceptive use may fail to prevent pregnancy.
- During MIKONID treatment, do not use other vaginal products (e.g. tampon, douche and spermicides).
- If severe irritation occurs in the administration site due to the use of MIKONID, stop using the drug immediately and contact your doctor or a hospital.

If these warnings apply to you, even if at any time in the past, please consult your doctor.

MIKONID with food and drink
Do not drink alcohol while using MIKONID and for at least 48 hours after your treatment ends. Drinking alcohol while using MIKONID can cause nausea, vomiting, stomach pain, flushing, rapid or irregular heartbeat and headache.

Pregnancy
Consult your doctor or pharmacist before taking this medicine.

There is insufficient information about the use of MIKONID in pregnant women in the first 3 months of pregnancy. Therefore, MIKONID should not be used in the first 3 months of pregnancy. In the period after the first 3 months of pregnancy, the risk-benefit ratio should be evaluated by the doctor and should not be used during pregnancy unless necessary.

Your doctor can only decide if you can use MIKONID in the case of being pregnant.

Since the effects of the drug substances contained in MIKONID on the development of fetus and newborns are not fully known, people who have to use the drug should be protected from pregnancy with a suitable method of contraception.

Consult your doctor or pharmacist immediately if you recognize that you are pregnant during your treatment.

Breastfeeding
Consult your doctor or pharmacist before taking this medicine.

Metronidazole, an active substance of MIKONID, passes into breast milk. Therefore, breastfeeding should be discontinued during the treatment; breastfeeding should be restarted after 24 to 48 hours of the discontinuation of the treatment.

It is not known whether miconazole nitrate pass into breast milk.

Lidocaine passes into breast milk. Therefore, caution should be exercised in nursing mothers.

Driving and using machines
As long as you use the drug at the dosage and the duration recommended by your doctor MIKONID does not affect your ability to drive or use machines. However, if you experience side effects such as drowsiness, dizziness, confusion, seeing or hearing things that are not present (hallucination), seizure (convulsion), temporary vision problems (such as blurred or double vision), fatigue, weakness during the use of MIKONID, do not drive or use machine.

Important information about excipients in MIKONID
MIKONID does not contain an excipient that requires special warning.

Other medicines and MIKONID
It is especially important to tell your doctor or pharmacist if you are taking alcohol or any of the following medicines:

- Drugs used for prevention of blood clotting (e.g. drugs containing active substances including acenocoumarol, anisindione, dicumarol, phenindione, phenprocoumon and warfarin).
- Drugs, which contain cimetidine and cisapride that are used to treat gastric and duodenal ulcers.
- Drugs used for treatment of allergic diseases (e.g. astemizole and terfenadine)
- Drugs which suppress immune system and contains the active substance called cyclosporine
- Drugs used in the treatment of diabetes and contains the active substance called glimepiride.
- Drugs used for the treatment of urinary problems like incontinence, frequent urination and urinary leak (e.g. drugs contain oxybutynin and tolterodine)
- Drugs use for psychiatric disorders which contain the active substance called pimozide
- Drugs used to treat alcoholism that contain the active substance called disulfiram.
- Drugs used in cancer treatment (e.g. drugs contain fluorouracil and trimetrexate as active substances)
- Drugs used in epilepsy treatment (e.g. drugs contain carbamazepine, fosphenytoin, phenobarbital and phenytoin)
- Drugs used to treat mood disorders that contain the active substance called lithium.
- Anesthetic drugs and the analgesics that contain the active substances called oxycodone and fentanyl used particularly to relieve severe pain in cancer patients.
- Drugs used for asthma treatment that contain the active substance called theophylline.

- Drugs used for cardiac arrhythmia that contain the active substances called amiodarone and procainamide.
- Drugs used for hypertension and cardiac disorders that contain the active substance called propranolol
- Drugs used in the treatment of cardiac arrhythmia (anti-arrhythmic drugs)
- Tranquilizing drugs of a pharmaceutical class called barbiturates.
- Busulfan drug used in cancer treatment
- Cholesterol-lowering drugs, e.g. simvastatin and lovastatin
- Medicines such as dihydropridine and verapamil used to treat high blood pressure

If you currently have been receiving or have recently received any prescription or nonprescription medicine, please notify your doctor or pharmacist about these.

3. How to use MIKONID?

- **Instructions for use and dosage/frequency of administration:**

Unless recommended by your doctor otherwise, for initial treatment apply 1 ovule at bedtime for 7 days. For recurrent infections, your doctor may recommend to use 1 ovule for 14 days (preferably at nights).

Using the product during the period of menstruation may lessen the activity of MIKONID and may cause difficulty in using, therefore it is not recommended to use during these periods.

- **Route of administration and method:**

MIKONID is only for intravaginal application.

Wash your hands before and after using the medicine. Before applying the drug, lie on your back. Slightly bent your knees. By using finger cot included in the package, insert 1 ovule into the vagina as it goes. After inserting the ovule keep continue lying for half an hour if possible.

Comply with the duration of treatment prescribed by your doctor.

Do not swallow MIKONID or do not use it otherwise.

- **Different age groups:**

Use in children:
MIKONID should not be administered in children under the age of 12.

Use in elderly:
Adult dosage is administered to those over 65 years of age.

- **Special cases of use:**

Renal Failure:
If you are undergoing dialysis, you should consult your doctor before starting MIKONID treatment.

Hepatic Failure:
If you suffer from hepatic failure, MIKONID should be administered cautiously and under the supervision of your doctor. In this case, MIKONID dosage will be adjusted by your doctor.

If you have impression that the effect of MIKONID is very strong or weak, tell a doctor or pharmacist.

If you use more MIKONID than you should:
If you take more MIKONID than you should, tell your doctor or pharmacist.

Metronidazole
Systemic effects (affecting the whole body) caused by metronidazole can be seen when large amounts of ovules are administered; however, metronidazole administered vaginally is not expected to cause life-threatening symptoms.

In overdose, symptomatic (symptomatic) and supportive therapy is administered. Metronidazole has no special antidote (antidote). In case of suspected high overdose, symptomatic (symptomatic) and supportive therapy should be administered. Suicide attempts and accidental overdoses and oral metronidazole intake up to 12 grams have been reported. Those who have taken 12 grams of metronidazole can be cured.

When the dose recommended by your doctor is exceeded, nausea, vomiting, abdominal pain, diarrhea, itching, metallic taste in the mouth, unbalanced walking like a drunk (ataxia), mild orientation disorder (the person's inability to evaluate his / her own condition in terms of location, time, place), dizziness, burning, tingling, prickling sensations and numbness in arms and legs (paresthesia), seizures similar to epileptic seizures (convulsions), decreased number of white blood cells (leukopenia), darkening in urine color may occur.

Miconazole nitrate
If accidentally swallowed, vomiting and diarrhea may occur. Depending on the miconazole nitrate, a burning sensation in the mouth and throat, loss of appetite, nausea and headache may be seen.
In this case, symptomatic (symptomatic) and supportive therapy should be administered.

Lidocaine
Lidocaine can cause heart rhythm disturbances, difficulty breathing, convulsions (seizures), depression, coma and even death, especially when applied to large skin surfaces at very high doses.

If MIKONID is accidentally swallowed in large quantities, contact your doctor or a hospital immediately.

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

If you forget to use MIKONID, use your drug as soon as you remember. If the next dose is near to use, skip the missed dose.

If you stop using MIKONID:
Early discontinuation of the treatment may lead to recurrence of vaginitis, and reappearance of vaginitis symptoms. MIKONID treatment is not expected to cause any adverse effect if it the termination follows the duration of treatment recommended by your doctor.

4. Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them

If you notice any of the followings stop taking MIKONID and immediately inform your doctor or go to the nearest emergency department:

- Severe skin rashes and other skin related conditions (pustular eruptions, acute generalized exanthematous pustulosis, itching, flushing)
- Swelling of hands, feet, wrists, face, lips, tongue and throat, difficulty breathing (angioedema)
- Hives (urticaria)
- Encephalopathy, which is a brain disease that resolves with discontinuation of drug use (eg confusion, fever, headache, imagination, paralysis, sensitivity to light, discomfort in vision and movement, stiff neck), and subacute cerebellar syndrome (eg unbalanced gait, disrupted speech, gait disturbance, involuntary eye movements and tremors)
- Serious skin reactions accompanied by swelling, water-filled blisters, skin rash, peeling and similar symptoms, such as erythema multiforme, Stevens-Johnson syndrome or toxic epidermal necrolysis, fixed drug eruptions
- Life-threatening hypersensitivity reactions (anaphylactic and anaphylactoid reactions) and allergic reactions, the symptoms of which may be rash, swelling, very low blood pressure (anaphylactic shock in severe cases)
- Fever

These are all very serious side effects.

If you have any of them, this means you have serious allergy to MIKONID. You may need emergency medical care or hospitalization.

Side effects were listed by frequency as following:
Very common: may affect more than 1 in 10 people
Common: may affect up to 1 in 10 people
Uncommon: may affect up to 1 in 100 people
Rare: may affect up to 1 in 1,000 people
Very rare: may affect up to 1 in 10,000 people
Not known: frequency cannot be estimated from the available data

If you notice any of the followings immediately inform your doctor or go to the nearest emergency department:

Very common
• Vaginal discharge

Common
• Irritation of the skin (irritation), redness, itching, dryness or rash at the application site
• Headache, dizziness
• Inflammation of the vagina (vaginitis), irritation of the inside and outside of the vagina, discomfort in the female reproductive organs (pelvic)

Uncommon
• Depression

• Feeling thirsty

Rare
• Burning, itching, irritation, skin rashes in the vagina
• Abdominal pain

Very rare
• Blood cell deficiency (Agranulocytosis, neutropenia, thrombocytopenia, pancytopenia)
• Mood changes
• Mental disorders (psychotic disorders) that include symptoms such as loss of consciousness and seeing and hearing things that are not present.
• Somnolence
• Seizure (convulsions)
• Temporary visual disturbances (such as blurred vision, double vision, myopia)
• Increased liver enzymes (AST, ALT, alkaline phosphotase), liver and pancreatic diseases (cholestatic or mixed hepatitis and hepatocellular liver damage, jaundice and pancreatitis that resolves with discontinuation of drug use)
• Muscle and joint pain (myalgia and arthralgia)
• Urine color darkening
• Hallucinations (seeing, hearing or feeling something that is not present), speech and gait disorders

Not known
• Reduction in the number of white blood cells (leucopenia), assessed by whole blood count and an indication of an inflammation in the body
• Combination of the symptoms such as weakness due to insufficient oxygenation of the tissues, tachycardia, trouble breathing and cyanosis (symptoms of methemoglobinemia)
• Decreased appetite and weight loss (anorexia)
• Depressed mood
• Heart rhythm disorder (arrhythmia), significant shortness of breath and severe chest pain, edema, flushing
• Decreased blood pressure, slow heart rate (bradycardia), hypotension
• Slow heartbeat, superficial breathing and severe weakness (cardiovascular collapse) caused by circulatory failure
• Heart-related problems such as increased defibrillation threshold, heart block, and suppression of the sinus node
• Tingling, numbness in the fingers or toes, and paleness and coldness of the hands and feet (arterial spasm)
• Epilepsy-like seizures (convulsion), coma
• Loss of consciousness
• Uncoordinated, unbalanced gait (ataxia)
• Loss of ability to recognize time, people and or places and inability to understand what is happening (confusion)
• Loss of ability to recognize places, time and people (disorientation)
• Disrupted speech, psychiatric disorder (psychosis)
• Experiences of perception of things that are not present (hallucination)
• Pronounced drowsiness and immobility (lethargy)
• Burning, tingling, pricking sensation and numbness usually in legs (paresthesia)
• Weakness, pain, numbness, tingling sensation in the hands and feet (symptoms of peripheral sensory neuropathy)

• Excessive sensitivity of the skin to touch or pain (hyperesthesia) or reduced sense (hypoesthesia)
• Tinnitus
• Insomnia
• Irritability, nervousness
• Uneasiness (anxiety)
• Chill, tremor, hot-flushes
• Fatigue or weakness, paleness, drowsiness
• Alteration in taste, mouth sores, coated tongue, metallic taste
• Dry mouth
• Nausea, vomiting, stomach pain
• Abdominal pain or cramps
• Constipation or diarrhea
• Restlessness (agitation)
• Feeling extremely cheerful (euphoria)
• Local irritation and sensitization, contact dermatitis, a skin disease caused by contact
• Cerebral cortex inflammation (aseptic meningitis)
• Inflammation of the eye nerves (optic neuropathy, neuritis)
• Hearing impairment, hearing loss, tinnitus

Since the active ingredients pass less into the blood because these are administered vaginally, these side effects are much less likely to occur as a result of ovule use.

If you notice any side effects not listed in this leaflet, please inform your doctor or pharmacist.

5. How to store MIKONID?
Keep this medicine out of the sight and reach of children, in the original package.
Store at room temperature below 25°C. Do not refrigerate.

Use in accordance with expiry date
Do not use MIKONID after the expiry date which is stated on the package.

Do not use MIKONID if you notice any damage to the product and/or package.

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