PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Primolut®-Nor

Tablets

Each tablet contains:
Norethisterone acetate 5 mg

Inactive and allergenic ingredients: see section 6 "Further Information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1) WHAT IS THE MEDICINE INTENDED FOR?

Primolut-Nor is intended for use in several circumstances: Progestogenic treatment of dysfunctional menstrual cycles, primary and secondary amenorrhea, pre-menstrual syndrome, menstrual cycle regulation and inflammation of the endometrium (endometriosis).

Therapeutic group: Primolut-Nor belongs to a group of medicines called progestogens, which are female hormones.

2) BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to norethisterone acetate or to any of the additional ingredients contained in the medicine. For the list of inactive ingredients, see section 6 "Further Information".
- You are pregnant or think you may be pregnant.
- You are breastfeeding.
- You have ever suffered from a blood circulation problem, including a blood clot (thrombosis) in the legs (deep vein thrombosis), in the lungs (pulmonary embolism), in the heart (heart attack), in the brain (stroke), or any other part of your body.
- You have any symptoms of a blood clot, such as chest pain, shortness of breath and/or sudden, unexplained cough.
- You have any condition which raises your risk for a blood clot (thrombosis).
- You have ever suffered from a migraine with visual disturbances.
- You are suffering (or recovering) from a liver disease and the blood test results show that your liver is not yet working normally.
- You are suffering, or have suffered in the past, from liver tumors.
- You suffer from diabetes with blood vessel damage.
- You have any type of cancer which may worsen with exposure to female sex hormones (including breast cancer).
- You have genital bleeding problems, for which the cause is not yet known.
- You suffer from a condition called endometrial hyperplasia that is not being treated.
- Do not use Primolut-Nor if you have hepatitis C and are taking medical preparations that contain ombitasvir/paritaprevir/ritonavir and dasabuvir (also see "If you are taking, or have recently taken, other medicines").
- You have suffered from any of the following conditions when you were pregnant:
  - Yellowing of the skin (idiopathic gestational jaundice).
  - Itching over the whole body (gestational pruritis).

If one or more of these conditions apply to you, tell the doctor and do not use the medicine.

Before using the medicine, your doctor will talk to you about your and your family's medical history. The doctor will measure your blood pressure and confirm that you are not pregnant. Additional tests may be necessary, such as a breast examination, depending on your medical needs and/or concerns.

Special warnings regarding use of the medicine

Before treatment with Primolut-Nor, tell the doctor if:

- You are smoking.
- You have diabetes (a metabolic disease which includes high blood sugar levels). Primolut-Nor can cause changes in blood sugar levels. If you are diabetic, your doctor will check your blood sugar levels regularly before starting and during treatment.
- You are overweight (body mass index [BMI] ≥30 kg/m^2).
- You suffer from high blood pressure.
- You suffer from a heart valve disturbance or specific heart rate disturbance (heart problems).
- You suffered in the past from thrombosis/embolism or if someone in your close family suffered from thrombosis, heart attack or stroke at a young age.
- You suffer from migraine, asthma or kidney problems.
- You suffer from epilepsy (see in section 2 "If you are taking, or have recently taken, other medicines").
- You suffer from inflammation of the veins (superficial phlebitis).
- You have varicose veins.
- Anyone in your immediate family has had breast cancer.
- You have previously had chloasma, a condition where brown blotches may appear on the facial skin. You may be advised to avoid exposure to the sun and to ultraviolet light while you are using Primolut-Nor.
- You have previously suffered from depression.
- You or someone in your close family has ever had high blood levels of cholesterol or triglycerides (fats). High blood fat levels are associated with an increased risk of developing pancreatitis (inflammation of pancreas).
- You have a disease of the liver or gall bladder.
- You have rare medical conditions such as systemic lupus erythematosus (SLE), sickle cell anemia, Crohn's disease or ulcerative colitis.
- You have hemolytic uremic syndrome (HUS).
- You have conditions that occurred for the first time or worsened during pregnancy or previous use of sex hormones (hearing loss, porphyria or Sydenham's chorea).
- You have hereditary angioedema. Consult a doctor immediately if you experience symptoms of angioedema such as swelling of the face, tongue or throat, and/or difficulty swallowing, or rash, together with difficulty breathing. Preparations containing estrogens may induce or worsen symptoms of angioedema.
- You have an intolerance to certain types of sugar (galactose intolerance, a medical condition called Lapp lactase deficiency, glucose-galactose malabsorption).
- You are using other medicines as listed in section 2 "If you are taking, or have recently taken, other medicines".

Before using Primolut-Nor, tell the doctor if any of these conditions apply to you. In addition, tell the doctor if one or more of these conditions develop or worsen while using the medicine, because you may need to stop taking it.

Primolut-Nor and blood clots

The active ingredient in Primolut-Nor (progestogen) is partly converted into estrogen; therefore, consider the general warnings given for combined oral contraceptive pills ("the Pill").

Do not take Primolut-Nor if you have a blood clot or have any medical condition which raises your risk of developing blood clots.

The risk of blood clots in the veins or arteries is slightly higher in women who use a combined oral contraceptive pill than in women who do not. Recovery from such blood clots is not always complete, and they may cause a stroke, heart attack or bleeding into the brain (subarachnoid hemorrhage). In very rare cases, these blood clots can be fatal.

You are at greater risk of having a blood clot:

- As you get older
- If you're immobile for a long time because of major surgery, injury or illness
- If you smoke
- If you or any of your close family has had blood clots
- If you are overweight (BMI ≥ 30 kg/m^2)
- If you have a blood fat metabolism disorder
- If you have a blood disorder
- If you have high blood pressure
- If you suffer from migraines
- If you have a heart valve disorder or a particular type of irregular heartbeat (atrial fibrillation)
- If you recently had a baby
- If you have diabetes
- If you have certain medical conditions such as systemic lupus erythematosus (SLE), sickle cell anemia, Crohn's disease or ulcerative colitis.

Tell the doctor if one or more of these conditions apply to you. Taking Primolut-Nor may further increase the risk of a blood clot and it may not be suitable for you.

To reduce the risk of blood clots, stop treatment with Primolut-Nor:

- Six weeks before a planned operation
- Before any surgery to the legs
- Before medical treatment for varicose veins
- If you are going to be immobile for a long time (e.g., if you need bed-rest after an accident or surgery, or if you have a broken leg with a cast).

Signs of a blood clot include:

- A migraine for the first time or a migraine that is worse than normal
- Unusually severe or frequent headaches
- Any sudden eyesight change (such as loss of vision or blurred vision)
- Any sudden change in hearing, speech, sense of smell, taste or touch
- Pain or swelling in the leg
- Stabbing pain when breathing
- Cough for no apparent reason
- Breathlessness
- Pain and tightness in the chest
- Sudden weakness or numbness in one side or part of your body
- Dizziness or fainting

Refer to a doctor as soon as possible if you notice possible signs of a blood clot. Do not take any more Primolut-Nor until instructed to do so by the doctor.

Primolut-Nor and cancer

If you are suffering, or have suffered in the past, from breast cancer, do not take combined oral contraceptives pills (the Pill). The Pill slightly increases the risk of breast cancer. The risk goes up the longer you are taking the Pill, but returns to normal within about 10 years of stopping it. Because breast cancer is rare in women under the age of 40, the extra cases of breast cancer in current and recent Pill users is small. For example:

- Of 10,000 women who have never taken the Pill, about 16 will have breast cancer by the time they reach the age of 35.
- Of 10,000 women who took the Pill for 5 years in their early twenties, about 17–18 will have breast cancer by the time they reach the age of 35.
- Of 10,000 women who have never taken the Pill, about 100 will have breast cancer by the time they are 45 years old.
- Of 10,000 women who took the Pill for 5 years in their early twenties, about 110 will have breast cancer by the time they reach the age of 45.

Your risk of developing breast cancer is higher if:

- You have a close relative (mother, sister or grandmother) who has had breast cancer
- You are overweight (BMI ≥ 30 kg/m^2)

Refer to a doctor as soon as possible if you notice any changes in your chest, such as dimpling of the skin, changes in the nipple or any lumps you can see or feel.

Very rarely, the Pill has been linked with some forms of liver cancer in women who took it for a long time. These tumors may lead to bleeding in the abdomen.

Taking the Pill has also been linked to liver diseases, such as jaundice and non-cancerous liver tumors, but this is rare.

Refer to a doctor as soon as possible if you have severe stomach pain that does not go away, or yellow skin or eyes (jaundice). You may need to stop taking Primolut-Nor.

Laboratory tests

Taking Primolut-Nor may affect the results of some blood and urine tests. If you have to undergo blood or urine tests, tell the doctor that you are taking Primolut-Nor.

Drug interactions:

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Some medicines may:

- Influence the blood levels of Primolut-Nor
- Reduce the effectiveness of the preparation
- Cause unexpected bleeding

These include:

- Medicines used for the treatment of:
  - Epilepsy (e.g., primidone, phenytoin, barbiturates, carbamazepine, oxcarbazepine, topiramate, felbamate).
  - Tuberculosis (e.g., rifampicin).
  - Treatment for the AIDS virus (HIV) and hepatitis C virus infections (so-called protease inhibitors and non-nucleoside reverse transcriptase inhibitors, e.g., ritonavir, nevirapine and efavirenz).
  - Fungal infections (e.g., griseofulvin, azole antifungals, for example, itraconazole, voriconazole, fluconazole).
  - Bacterial infections (macrolide antibiotics, e.g., clarithromycin, erythromycin).
  - Certain heart diseases, high blood pressure (calcium channel blockers, e.g., verapamil, diltiazem).
  - Arthritis, arthrosis (etoricoxib).
  - High blood pressure in the blood vessels in the lungs (bosentan).
  - The herbal preparation St. John's wort (Hypericum), which is primarily used for the treatment of depression.
  - Grapefruit juice.

Primolut-Nor may influence other medicines, for example:

- Medicines containing ciclosporin.
- The anti-epileptic lamotrigine (may lead to an increased frequency of seizures).
- Theophylline (used to treat breathing difficulties).
- Tizanidine (used to treat muscle pain and/or muscle cramps).

Do not use Primolut-Nor if you have hepatitis C and are taking medicines containing ombitasvir/paritaprevir/ritonavir and dasabuvir. Concomitant use may cause an increase in liver function blood test results (increase in ALT liver enzyme levels). Treatment with Primolut-Nor can be resumed approximately two weeks after completion of treatment with these medicines (see in section 2 "Do not use the medicine if").

- Medicines whose activities may be affected by Primolut-Nor, such as ciclosporin, which is primarily used after an organ transplantation.

Further information that is important to know

Once you have finished treatment with Primolut-Nor, you will usually have a menstrual bleed 2-3 days after taking the last tablet. If you do not have a period, you must make sure that you are not pregnant before taking any more tablets.

Pregnancy and breastfeeding

Do not use the medicine if you are pregnant or breastfeeding. If you think you may be pregnant or are planning to have a baby, consult the doctor before taking the medicine.

When you complete treatment courses with Primolut-Nor, you will usually have a menstrual bleed (period) 2-3 days after taking the last tablet. If you do not have a period, make sure that you are not pregnant before taking more tablets.

Driving and operating machinery

It is unlikely that use of Primolut-Nor will affect your ability to drive or operate machinery.

Important information about some of the ingredients of the medicine

The preparation contains lactose. Each tablet contains 67.375 mg lactose monohydrate. If you have been told by a doctor that you have an intolerance to some sugars, contact your doctor before taking the preparation.

3) HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.

- The dosage and treatment regimen will be determined by the doctor only.

Consult the doctor or pharmacist if you are uncertain with regard to the number of tablets you should take, when to take them or for how long to take them.

Do not exceed the recommended dosage.

- Swallow the medicine whole with water.

There is no information regarding chewing, crushing and halving the tablet.

If you accidentally take a higher dosage

Taking too many tablets is not expected to cause severe problems. If you took too many tablets, contact your doctor, who will tell you what to do.

If you took an overdose or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine

If you forgot a dose, wait until it is time for the next dose prescribed for you. Do not take the forgotten dose. If you are concerned, contact the doctor or pharmacist.

Adhere to the treatment regimen as recommended by the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4) SIDE EFFECTS

As with any medicine, use of Primolut-Nor may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Stop using the medicine and refer to a doctor immediately if you experience any of the following conditions:

- Migraine for the first time
- Unusually severe headache, occurring more often than before
- Sudden changes in eyesight, hearing or speech
- Sudden changes to sense of smell, taste or touch
- Symptoms of blood clot formation or symptoms of inflammation of the veins combined with the formation of blood clots (thrombophlebitis):
  - Unusual pain in the leg(s)
  - Unusual swelling of the hands or legs
  - Sharp pains in the chest or sudden shortness of breath
  - Crushing pains or feelings of heaviness or tightness in the chest
  - Coughing for no apparent reason
  - Sudden weakness or numbness on one side of the body

In addition, immediately discontinue use of the medicine if:

- You become pregnant
- You develop jaundice or other liver problems
- You develop itching
- Your doctor finds that your blood pressure is too high

Very common side effects – effects that occur in more than one in ten users
- Vaginal bleeding, including spotting
- Periods that are much shorter than normal and where blood flow is reduced

Common side effects – effects that occur in up to 10 in 100 users
- Headache
- Nausea
- Absence of a period
- Swelling

Uncommon side effects – effects that occur in up to 1 in 100 users
- Migraine

Rare side effects – effects that occur in up to 1 in 1,000 users
- Hypersensitivity (allergic) reaction, including skin rash or hives

Very rare side effects – effects that occur in up to 1 in 10,000 users
- Visual disturbances
- Difficulty in breathing

Side effects of unknown frequency (effects whose frequency has not been estimated)
- Worsening of depression
- Dizziness
- Abdominal pain
- Jaundice
- Obstruction of the bile passage (cholestasis)

If a side effect occurs, if one of the side effects worsens, or if you are suffering from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5) HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- It is recommended to store at room temperature. Protect from light.
- Do not dispose of medicines in the wastewater or household waste. Ask the pharmacist how to dispose of medicines that are no longer in use. This can help protect the environment.

6) FURTHER INFORMATION

- In addition to the active ingredient, the medicine also contains:
  Lactose monohydrate, Maize starch, Polyvidone 25000, Talc, Magnesium stearate
- What the medicine looks and the contents of the package
  Primolut-Nor tablets are white, with the symbol "+" imprinted on one side and a hexagon with the letters "AP" imprinted on the other side.
  The tablets are provided in trays (blisters) in packages of 30 tablets.
- Registration Holder and Address: Bayer Israel Ltd., 36 Hacharash St., Hod Hasharon 45240.
- Manufacturer and address: Bayer Weimer GmbH and Co. KG, Weimer, Germany.
- Revised in February 2020.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 122 29 24814 00

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