PACKAGE LEAFLET: INFORMATION FOR THE USER
Primolut-Nor 5 mg tablets
Norethisterone acetate

Read all of this 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. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Primolut-Nor 5 mg is and what it is used for

It belongs to the group of medicines known as progestins.
It is indicated in secondary amenorrhoea (absence of menstruation) and endometriosis (growth of the endometrium - the tissue lining the uterus - outside the uterus).

2. What you need to know before you take Primolut-Nor 5 mg

Do not take Primolut-Nor 5 mg
You must not take Primolut-Nor if any of the conditions mentioned below apply. If any of these appears for the first time while you are using Primolut-Nor, stop the treatment immediately and consult your doctor.
- If you are pregnant or suspect you may be pregnant.
- If you are breast-feeding.
- If you have (or have in the past had) a heart attack or stroke (caused by a blood clot or a ruptured blood vessel in the brain).
- If you have (or have in the past had) a condition that might be indicative of: (i) a future heart attack (for example, angina pectoris, which causes severe chest pain and may radiate to the left arm) or (ii) a stroke (for example, a mild stroke that leaves no permanent effects, known as a «transient ischaemic attack»).
- If you have a major risk factor or various risk factors for the formation of blood clots.
- If you have (or have in the past had) a certain type of migraine (with so-called focal neurological symptoms, such as visual symptoms, speech difficulties or weakness or numbness in some part of the body).
- If you have diabetes associated with circulatory problems.
- If you have or have had a severe liver disease and the the liver function test values have not yet returned to normal.
- If you have a yellowish pigmentation of the eyes and skin (jaundice) due to a hereditary disease (Dubin-Johnson and Rotor syndrome) or if you have experienced jaundice and/or intense itching in previous pregnancies.
- A history of blisters on the skin during previous pregnancies (pemphigoid or herpes gestationis).
- If you have hepatitis C and are taking medicines that contain ombitasvir/paritaprevir/ritonavir and dasabuvir (see also Other medicines and Primolut-Nor 5 mg).

- If you have or have had (benign or malignant) liver tumours.
- If you have or suspect you have any sex hormone-dependent malignancy.
- If you are allergic to the active substance or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Consult your doctor or pharmacist before starting to take Primolut-Nor.
The sex steroid (progesterone) contained in this medicine is partially converted into oestrogen. Therefore, any general warnings related to the use of combined oral contraceptives must also be taken into account in addition to those for Primolut-Nor.
Under certain circumstances, special caution is necessary when taking Primolut-Nor and your doctor may have to examine you periodically.

If you have any of the following conditions, you must contact your doctor as soon as possible, as the use of Primolut-Nor must be stopped:
- If a migraine-like headache occurs for the first time or the frequency of exceptionally severe headaches is increased.
- If you have sudden perceptual changes.
- If you have the first signs of thrombophlebitis or thromboembolic symptoms (such as unusual pain or inflammation of the leg or legs, pain on breathing or cough with no clear cause).
- If you have a feeling of pain or tightness in the chest
- If you are scheduled to have major surgery (treatment must be stopped six weeks prior to surgery).
- If you need to be immobilised for a prolonged period (for example, after accidents or surgery).
- If jaundice occurs (yellowish discolouration of the whites of the eyes and skin) or inflammation of the liver without jaundice.
- If you have generalised itching.
- If your blood pressure is raised significantly and persistently.

You must be monitored carefully by your doctor in the following situations:
- If you have diabetes (metabolic disease with high levels of sugar in the blood).
- If you have chloasma (brown-coloured spots on the skin). This can occur occasionally, particularly if you have a history of chloasma gravidarum (during pregnancy). If you have a tendency to chloasma, you must avoid exposure to sunlight or to ultraviolet rays while taking Primolut-Nor.
- If you have high levels of lipids in the blood (hypertriglyceridaemia) or a family history of this disorder. Hypertriglyceridaemia has been associated with an increase in the risk of developing pancreatitis (inflammation of the pancreas).
- If you have in the past had a type of depression called endogenous depression. Your doctor must assess whether to discontinue the treatment if severe depression occurs.

You must also consult your doctor if the following disorders occur or worsen while using Primolut-Nor:
- If you have any disease that appeared for the first time during pregnancy or previous use of hormonal contraceptives: jaundice (yellowish discolouration of the whites of the eyes and skin), generalised itching, kidney stones, a blood disease called porphyria, systemic lupus erythematosus, a nervous disease in which involuntary movements occur (Sydenham's chorea), skin rash with blisters during pregnancy (herpes gestationis), hearing loss.
- If you have hereditary angio-oedema. You must contact your doctor immediately if you experience symptoms of angio-oedema, such as swelling of the face, tongue and/or throat, and/or difficulty swallowing or urticaria, together with difficulty in breathing.
- If you have a liver disease.
- If you have Crohn's disease or ulcerative colitis (inflammatory bowel disease).
- If any of the disorders/risk factors mentioned below are present or worsen, your doctor must weigh the benefit of using Primolut-Nor against the possible risks before deciding whether you should start or continue treatment.

Vascular (blood vessel) disorders
The use of medicines containing progestins (including norethisterone) and oestrogens is associated with an increased frequency of thromboembolic disorders or thromboembolism (formation of clots in the blood vessels). The increased risk of thromboembolic disorders occurring is greater if you have experienced them in the past.
Thromboembolism is also increased during the puerperium (the period extending from birth until the woman's genital organs and general health have returned to the state prior to pregnancy.(
The formation of blood clots in the veins can be fatal in 1- 2% of cases.
Venous thromboembolism (thromboembolic disorder affecting the veins), which manifests as deep venous thrombosis and/or pulmonary embolism (when the blood clot travels to the lungs and blocks the blood vessels), can occur with the use of any combined oral contraceptive.
In extremely rare cases, blood clots can form in other parts of the body, such as the liver, intestines, kidney, brain or eyes.

The risk of a blood clot in veins or arteries or a stroke increases with:
- Age.
- If you are overweight.
- If any of your immediate family (sibling, father or mother) has had a blood clot in the leg, lungs or any other organ or has had a heart attack or a stroke at an early age.
- If you are due to undergo surgery, have suffered a serious accident or need to be immobilised for a prolonged period. It is important that you tell your doctor in advance that you are taking Primolut-Nor as your treatment may need to be interrupted. Your doctor will tell you when to start Primolut-Nor again. This usually happens two weeks after recovering your mobility.
- If you smoke: you are strongly advised to stop smoking while you are using Primolut-Nor, especially if you are over 35 years old.
- If you have high levels of cholesterol or triglycerides in your blood.
- If you have high blood pressure.
- If you have migraine.
- If you have heart problems (valve disorders, changes of heart rhythm).

Consult your doctor if you have any of the following conditions while you are taking Primolut-Nor:
- If you have diabetes.
- If you have systemic lupus erythematosus (a disease of the immune system).
- If you have haemolytic uraemic syndrome (a disease of the blood that causes damage to the kidney).
- If you have Crohn's disease or ulcerative colitis (inflammatory bowel disease).
- If you have sickle cell disease (a hereditary disease of the red blood cells).
- If the frequency or intensity of migraines increases.
- If you have a hereditary predisposition to venous or arterial thrombosis.

Stop treatment with Primolut-Nor and contact your doctor immediately if you notice possible signs of a blood clot, such as:
- severe pain and/or inflammation in either of your legs.
- sudden and severe chest pain, which may radiate to your left arm.
- sudden difficulty in breathing.
- sudden cough without a clear reason.
- unusual, intense or prolonged headache.
- partial or complete loss of vision or double vision.
- difficulty speaking or inability to speak.
- dizziness or fainting.
- weakness, abnormal sensations or numbness in any part of the body.
- difficulty moving.
- severe abdominal pain.

Tumours
Breast cancer has been observed slightly more often in women using combined contraceptives but it is not known whether this is due to the treatment. For example, it may be that more tumours are detected in women using combined contraceptives because they are examined more often by the doctor. The risk of breast tumours decreases gradually after the discontinuation of combined hormonal contraceptive use. It is important that you examine your breasts regularly and contact your doctor if you notice a lump.
In rare cases benign liver tumours, and even more rarely malignant liver tumours, have been reported in users of hormonal substances such as that contained in Primolut-Nor. In individual cases, these tumours have caused life-threatening internal abdominal bleeding.
Contact your doctor if you have unusually severe abdominal pain.

Medical check-up
Before starting or resuming treatment with Primolut-Nor, your doctor must take a full medical history and perform a full physical and gynaecological examination for the purpose of ruling out any contraindications (see section» Do not take Primolut-Nor 5 mg («and observing the precautions (see section» Warnings and precautions .(«These examinations must be repeated periodically during the treatment, as determined by your doctor.

Laboratory tests
The use of progestin-type medicines may affect the results of certain laboratory tests. If you are told that you have to undergo any laboratory tests, inform your doctor that you are taking Primolut-Nor.

Other medicines and Primolut-Nor 5 mg
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
Some medicines
- may affect levels of Primolut-Nor in the blood.
- may reduce its efficacy.
- may cause unexpected bleeding.

These include:
- medicines used in the treatment of:
  - epilepsy (e.g. primidone, phenytoin, barbiturates, carbamazepine, oxcarbamazepine, topiramate, felbamate)
  - tuberculosis (e.g. rifampicin)
  - HIV and hepatitis C virus infections (so-called protease inhibitors and non-nucleoside reverse transcriptase inhibitors e.g. ritonavir, nevirapine, efavirenz(
  - fungal infections (griseofulvin, azole antifungals e.g. itraconazole, voriconazole, fluconazole)
  - bacterial infections (macrolide antibiotics e.g. clarithromycin, erythromycin)
  - some heart diseases, high blood pressure (calcium channel blockers e.g. verapamil, diltiazem)
  - arthritis, joint disease (etoricoxib)
  - high blood pressure in the blood vessels of the lungs (bosentan)
- medicinal plant-based products containing St John's wort (herbal medicine used mainly for the treatment of depressive states of mood)
- grapefruit juice

Primolut-Nor may influence the effect of other medicines, e.g:.
- medicines that contain ciclosporin
- the antiepileptic drug lamotrigine (which may result in an increase in the frequency of convulsions)
- theophylline (to treat respiratory problems)
- tizanidine (to treat muscle pain and/or muscle cramps)

Do not use Primolut-Nor if you have hepatitis C and are taking medicines that contain ombitasvir / paritaprevir / ritonavir and dasabuvir, since this may cause an increase in the results of liver function blood tests (increase

in the liver enzyme ALT). Primolut-Nor can be reinstated about 2 weeks after completing this treatment (see Do not take Primolut-Nor).

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
You must not take Primolut-Nor if you are pregnant or if you are breast-feeding your child.

Driving and using machines
It is not known, or there are no data on, what effect Primolut-Nor has when driving or operating machinery.

Primolut-Nor 5 mg contains lactose
This medicine contains lactose. If you have been told by your doctor that you have a sugar intolerance, talk to your doctor before taking this medicine.

3. How to take Primolut-Nor 5 mg

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.
Remember to take your medicine. Your doctor will determine how long you must take your treatment with Primolut-Nor. Do not stop the treatment early, as the desired effect may not be obtained.
The tablets must be swallowed whole with some liquid.
If you need additional contraceptive protection, you should use non-hormonal contraceptive methods (barrier methods, e.g. condoms.(

<u>For the treatment of secondary amenorrhoea (absence of menstruation):</u>
Your doctor will tell you what dose to take and must tell you to take medicines with oestrogens for 14 days before starting treatment with Primolut-Nor. Thereafter you take between 5 and 10 mg of norethisterone acetate daily (with a maximum of two tablets of Primolut-Nor 5 mg daily) for 10 days, thereby completing the treatment. Menstruation will occur a few days after taking the last tablet.
In patients with endogenous oestrogen production, 5 mg of norethisterone acetate are taken twice daily, from the 16th to the 25th day of the cycle, bearing in mind that the first day of menstruation is considered to be the first day of the cycle.

<u>For the treatment of endometriosis (growth of the endometrium - the tissue lining the uterus - outside the uterus)</u>.
Treatment must be started between the 1st and 5th day of the cycle with 5 mg of norethisterone acetate twice daily. If spotting appears, the dose can be increased to 10 mg of norethisterone acetate twice daily (two tablets of Primolut-Nor 5 mg twice daily), reverting to the initial dose if the bleeding (or spotting) stops. The treatment must be continued for between at least 4 and 6 months. With an uninterrupted daily intake, you will probably have no ovulation or menstruation.
There are other doses on the market for the different dosage regimens.

If you take more Primolut-Nor 5 mg than you should
If you take more Primolut-Nor than you should, consult your doctor or pharmacist immediately.

If you forget to take Primolut-Nor 5 mg
Your doctor will tell you when to take Primolut-Nor. If you think you have forgotten a dose, contact your doctor as soon as possible.
Do not take a double dose to make up for forgotten doses.

If you stop taking Primolut-Nor 5 mg
While stopping treatment with Primolut-Nor does not cause any specific symptoms, it is possible that the previous disorders will return.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Side effects are more common during the first months of treatment and disappear when the treatment is continued.
The side effects listed below, ordered by organ system and frequency, have been reported in connection with the use of Primolut-Nor, although it has not been possible to establish a causal relationship between the side effects and treatment.

Very common :can affect more than 1 in 10 people
- uterine/vaginal bleeding, including spotting, hypomenorrhoea (scanty menstruation). These side effects have been reported only when the medicine is administered for treatment of endometriosis (growth of the endometrium - the tissue lining the uterus - outside the uterus).

Common :can affect up to 1 in 10 people
- headache
- nausea
- amenorrhoea (absence of menstruation)
  This side effect has been reported only when the medicine is administered for the treatment of endometriosis (growth of the endometrium - the tissue lining the uterus - outside the uterus).
- oedema (fluid retention)

Uncommon :can affect up to 1 in 100 people
- migraine

Rare :can affect up to 1 in 1,000 people
- hypersensitivity reactions (allergy)
- urticaria, rash

Very rare :can affect up to 1 in 10,000 people
- visual disturbances
- dyspnoea (difficulty breathing)

Frequency not known) cannot be estimated from the available data(
- thromboembolism (formation of clots in the blood vessels)
- liver tumours that have caused internal bleeding in the abdomen
- chloasma (brown-coloured spots on the skin)
- migraine headache or increased frequency of exceptionally severe headache, sudden perceptual changes, first signs of thrombophlebitis or thromboembolic symptoms (such as unusual pain or inflammation of the leg(s), pain on breathing or cough with no clear cause), feeling of pain or tightness in the chest, appearance of jaundice (yellowish discolouration of the whites of the eyes and skin), inflammation of the liver without jaundice, generalised itching, significant increase in blood pressure.

Reporting of adverse reactions
If you get any side effects, talk to your doctor or pharmacist. This includes possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Primolut-Nor 5 mg

Keep this medicine out of the sight and reach of children.
Store below 30°C.
Store in the original package to protect from light.
Do not use this medicine after the expiry date which is stated on the package after» EXP .«The expiry date refers to the last day of that month.
Do not throw away any medicines via wastewater or household waste. You can ask your pharmacist how to throw away medicines and containers you no longer need. These measures will help protect the environment.

6. Contents of the pack and other information

What Primolut-Nor 5 mg contains

- The active substance is norethisterone acetate. Each tablet contains 5 mg of norethisterone acetate.
- The other ingredients (excipients) are: lactose monohydrate, maize starch, povidone 25000, talc and magnesium stearate.

What Primolut-Nor 5 mg looks like and contents of the pack
Primolut-Nor 5 mg is available in boxes of 30 tablets, with 2 blisters strips of 15 tablets each.

Manufacturer:
Bayer Weimar GmbH & Co. KG,
D-99427 Weimar, Germany.

Marketing Authorization Holder:
Bayer AG
Kaiser-Wilhelm-Allee 1,
51373 Leverkusen, Germany.

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This is a medicament

- A medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

Keep medicament out of reach of children.

Council of Arab Health Ministers
Union of Arab Pharmacists