Package leaflet: information for the user
Primolut Nor 10 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 is and what it is used for

Primolut Nor is a so called progestin preparation, i.e. a synthetic hormone preparation that has similar properties to progesterone, which is a natural female hormone.
Primolut Nor is used to treat various kinds of bleeding disorders and absence of menstruation (amenorrhea) caused by various reasons, to alleviate symptoms of premenstrual syndrome, to treat mastopathy, to postpone menstruation, and to treat endometriosis.

2. What you need to know before you take Primolut Nor

Do not take Primolut Nor
- if you are allergic to norethisterone acetate or any of the other ingredients of this medicine (listed in section 6);
- if you are pregnant or think you might be pregnant;
- if you are breast-feeding;
- if you have had severe problems with the way your liver works and your liver function is still abnormal. Symptoms of liver disease may include, for example, yellowing of the skin and/or itching all over your body.
- if you have or have ever had a (benign or malignant) liver tumour;
- if you have or have ever had a blood clot in one of your veins or arteries (thrombosis), in a deep vein (deep vein thrombosis), in a blood vessel in your lungs (pulmonary embolism), a heart attack or cerebrovascular accident (stroke caused by a blood clot or rupture of a blood vessel in your brain);
- if you have a condition that may be a sign of a future heart attack (e.g. angina pectoris, which can cause severe pain in your chest which can spread to your left arm) or stroke (e.g. a mini-stroke without residual consequences, known as a transient ischaemic attack);
- if you have a certain type of migraine with so-called focal neurological symptoms, such as problems with your vision, difficulty speaking, weakness or numbness in any part of your body;
- if you have severe or multiple risk factors for developing blood clots (venous and arterial thrombosis) (see "Warnings and precautions");
- if you have diabetes with blood vessel damage;

- if you have confirmed or suspected sex hormone-dependent tumours (e.g. breast or genital organ tumour).

Do not use Primolut Nor if you have hepatitis C and are taking medicines containing ombitasvir/paritaprevir/ritonavir and dasabuvir (see also section "Other medicines and Primolut Nor")

If any of the aforementioned conditions occurs for the first time while you are using Primolut Nor, stop taking the treatment immediately and consult a doctor.

Warnings and precautions
Talk to your doctor or pharmacist before taking Primolut Nor.

Before starting or resuming treatment with Primolut Nor, your doctor will carry out a thorough general and gynaecological examination, including a breast examination, examination of your abdomen, a Papanicolaou smear (Pap test) and a check on your blood pressure. It is also necessary to check that you are not pregnant. As a precautionary measure, your doctor will decide which checks will need to be performed and how often.

The progestogen contained in this medicine is partially converted to oestrogen. The general warnings associated with the use of oestrogen-/progestogen-containing **combined oral contraceptives** must therefore also be taken into consideration for Primolut Nor.

In some situations, particular care must be taken when using Primolut Nor, and your doctor may have to see you regularly. You must talk to your doctor before starting to use Primolut Nor if any of the following conditions applies to you or if any of these conditions develops or gets worse while you are using Primolut Nor:
- if you smoke;
- if you have diabetes (metabolic disorder with high levels of sugar in the blood);
- if you are overweight;
- if you have high lipid levels in your blood (hypertriglyceridaemia) or a positive family history of this condition. Hypertriglyceridaemia has been linked to an increased risk of developing pancreatitis (inflammation of the pancreas);
- if you have high blood pressure;
- if you have heart problems (heart valve problems, heart rhythm problem);
- if you have a history of thrombosis/thromboembolism (blood clot);
- if there are cases of thrombosis in your family (thromboembolism in a brother/sister or parent at a relatively young age), heart attack or stroke at a young age;
- if you have inflammation of a vein (superficial phlebitis);
- if you have varicose veins;
- if there are cases of breast cancer in your family;
- if you have a history of chloasma (yellow-brown patches on the skin, particularly the face); if this happens, avoid excessive exposure to the sun or ultraviolet rays;
- if you have a history of depression; if depression comes back in a severe form, stop taking Primolut Nor;
- if you suffer from migraine;
- if you suffer from epilepsy (see "Other medicines and Primolut Nor");
- if you have high levels of cholesterol or triglycerides (fatty substances in the blood);
- if you have liver or gallbladder disease (jaundice and/or cholestatic pruritus; gallstone formation);
- if you have Crohn's disease or ulcerative colitis (inflammatory bowel diseases);
- if you suffer from systemic lupus erythematosus (SLE, an immune system disorder);
- if you suffer from haemolytic uraemic syndrome (HUS, a disease that causes kidney damage);
- if you have sickle cell anaemia;
- if you have a condition that occurred for the first time during pregnancy or previous use of sex steroids (e.g. loss of hearing caused by otosclerosis, a blood disorder known as porphyria, a rash called herpes gestationis, a disorder of the nerves called Sydenham’s chorea);

- if you have hereditary angioedema. If you experience symptoms of angioedema such as swelling of the face, tongue and/or pharynx and/or difficulty swallowing or urticaria with breathing difficulties, talk to your doctor immediately. Medicines containing oestrogens can cause or aggravate symptoms of angioedema.

If any of the aforementioned conditions appears for the first time, occurs again or gets worse while you are using Primolut Nor, contact a doctor.

Primolut Nor and venous and arterial blood clots (thrombosis)
The progestogen contained in this medicine is partially converted to oestrogen, similar therefore to a progestogen/oestrogen combination. The general warnings associated with the use of **combined oral contraceptives** therefore apply to Primolut Nor.

The use of Primolut Nor, as for Combined Oral Contraceptives, is associated with an increased risk of venous thromboembolism (VTE) compared with non-use. This increased risk is nevertheless lower than the risk of VTE associated with pregnancy.
VTE may be life-threatening or may be fatal.

Venous thromboembolism (VTE) manifesting as deep vein thrombosis and/or pulmonary embolism may occur during use of all combined oral contraceptives.

Very rarely, thrombosis has been reported to occur in other vascular territories in users of combined oral contraceptives, e.g. hepatic, mesenteric, cerebral, renal or retinal veins and arteries. There is no consensus regarding the association of these events with the use of combined oral contraceptives.

The symptoms of venous or arterial thrombotic/thromboembolic events or of a cerebrovascular accident may include:

- unusual one-sided pain and/or swelling in a leg;
- severe and sudden chest pain, with or without radiation to the left arm;
- sudden breathing difficulties;
- sudden onset of cough;
- unusual, severe and prolonged headache;
- sudden partial or complete loss of vision;
- double vision;
- unclear speech or aphasia (loss of ability to speak or understand language);
- vertigo;
- collapse with or without focal seizures (the seizure starts in a specific part of the brain);
- sudden weakness or very marked numbness affecting one side or one part of the body;
- motor disturbances;
- "acute" abdomen (severe pathological condition affecting the abdomen).

The possibility of an increased synergistic risk of thrombosis must be taken into consideration in women with a combination of risk factors or who exhibit an individual risk factor of greater severity. This increased risk may be greater than a simple cumulative risk of the factors. In the event of a negative risk/benefit assessment, a combined oral contraceptive must not be prescribed (see section "Do not take Primolut Nor").

The risk of venous or arterial thrombotic/thromboembolic events or of cerebrovascular accidents increases with:
- age;
- obesity (body mass index greater than 30 kg/m²);
- a positive family history (arterial or venous thromboembolism in a sibling or parent at a relatively young age);

- prolonged immobilisation, major surgery, any surgery to the legs or major trauma;
- smoking (the risk increases further for heavy smokers and with increasing age, especially for women over 35 years of age);
- dyslipoproteinaemia (high levels of lipids in the blood);
- hypertension (high blood pressure);
- migraine;
- valvular heart disease (heart valve disease);
- atrial fibrillation (abnormal heart rhythm).

Tell your doctor if any of the aforementioned situations applies to you.

There is no consensus regarding the possible role of varicose veins and superficial thrombophlebitis in venous thromboembolism.

Other medical conditions that have been associated with adverse vascular events include:
- diabetes mellitus;
- systemic lupus erythematosus (immune system disorder);
- haemolytic uraemic syndrome (HUS), which causes kidney damage;
- chronic inflammatory bowel diseases (Crohn's disease or ulcerative colitis);
- sickle cell disease (sickle cell anaemia).

If an increase occurs in the frequency and severity of migraine (which may be an early sign of a cerebrovascular event), a doctor must be consulted immediately.

If your blood tests have shown that you have Activated Protein C resistance, hyperhomocysteinaemia (excessive concentration of homocysteine in the blood), antithrombin III deficiency, protein C deficiency, protein S deficiency or antiphospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant), you might have a hereditary or acquired predisposition for venous or arterial thrombosis.

Check with your doctor as soon as possible if:
- you notice any change in your state of health, particularly with regard to the situations described in the sections "Do not take Primolut Nor" and "Warnings and precautions";
- you feel a lump in your breast;
- you use other medicines (see "Other medicines and Primolut Nor");
- you experience unusual vaginal bleeding.

Stop the treatment immediately in the event of:
- first-time occurrence or worsening of migraine, or increase in the frequency of unusually severe headaches;
- sudden impairment of vision or hearing or other problems with perception;
- early symptoms of thrombophlebitis or thromboembolism, such as unusual leg pain or swelling, sharp pain when breathing or cough for no apparent reason;
- feeling of chest pain and tightness;
- surgery and state of immobilisation: six weeks before surgery and for the entire period of a state of immobilisation, e.g. following accidents;
- development of jaundice, hepatitis, generalised itching;
- marked increase in arterial blood pressure;
- pregnancy.

In the event of endocrine and liver function test abnormalities, stop taking the treatment and repeat the tests after approximately 2 months.

Primolut Nor and cancer
Breast cancer is observed slightly more often in women who use the combined pill, but it is not known whether this is due to the treatment. For example, it is possible that a higher number of tumours is diagnosed in women who use the pill because they have more frequent medical checks. The risk of developing breast cancer decreases gradually after combined hormonal contraception is stopped. It is important that you check your breasts regularly and contact a doctor if you feel any lumps.
In rare cases, benign liver tumours, and even more rarely, malignant liver tumours have been observed in women taking hormonal substances. These tumours may cause internal bleeding.

The most important risk factor for cervical cancer is human papillomavirus (HPV) infection. Some studies suggest an increase in the risk of cervical cancer in long-term users of contraceptives, but there is still controversy regarding the extent to which sexual behaviour or other factors such as human papillomavirus increase this risk.

Malignancies may be life-threatening or may be fatal.

Contact a doctor immediately if you experience severe abdominal pain.

Other medicines and Primolut Nor
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
Some medicines

- may have an influence on the levels of Primolut Nor in the blood
- may make it less effective
- may 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)
  - HIV and hepatitis C virus infections (called protease inhibitors and non-nucleoside reverse transcriptase inhibitors, e.g. ritonavir, nevirapine, efavirenez)
  - fungal infections (griseofulvin, azole antifungal agents, e.g. itraconazole, voriconazole, fluconazole)
  - bacterial infections (macrolide antibiotics, e.g. clarithromycin, erythromycin)
  - some heart disorders, high blood pressure (calcium channel blockers, e.g. verapamil, diltiazem)
  - arthritis, osteoarthritis (etoricoxib)
  - high pressure in the blood vessels of the lungs (bosentan)
- St John's wort (*Hypericum perforatum*, used mainly for the treatment of **depression**).
- grapefruit juice

Primolut Nor can **influence the effect** of other medicines, e.g.:

- medicines containing ciclosporin
- the antiepileptic drug lamotrigine (this may lead to an increase in the frequency of seizures)
- theophylline (used for the treatment of respiratory problems)
- tizanidine (used for the treatment of muscle pain and/or cramps)

Do not use Primolut Nor if you have hepatitis C and are taking medicines containing ombitasvir/paritaprevir/ritonavir and dasabuvir, because this can cause an increase in the results of blood tests relating to liver function (increase in the liver enzyme ALT). You can start taking Primolut Nor again approximately 2 weeks after the end of this treatment. See section "Do not take Primolut Nor".

Laboratory tests
Primolut Nor can influence the results of some laboratory tests. Tell your doctor if you need to have blood or urine tests.

Pregnancy and breast-feeding
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.

Do not take Primolut Nor if you are pregnant or breast-feeding or think you may be pregnant.

Driving and using machines
Primolut Nor does not alter the ability to drive or use machines.

Primolut Nor contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Primolut Nor

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Dose, method and time of administration
The tablets must be swallowed with a little liquid.
The efficacy of Primolut Nor may be reduced if the tablets are not all taken in accordance with the instructions.
Which contraceptive measures should be used: non-hormonal methods (but not the rhythm method or the basal temperature method). If, during treatment, withdrawal bleeding does not occur at regular intervals of approximately 28 days, the possibility of pregnancy should be considered, even if contraceptive measures have been taken. In this case, stop taking the treatment immediately until this has been ruled out.

The recommended treatment regimens are:

- **Functional metrorrhagia**

Taking half a Primolut Nor tablet (= 5 mg) three times daily for 10 days leads to cessation of uterine bleeding not associated with organic lesions within 1-3 days in most cases. Nevertheless, in order to ensure that the treatment is completely successful, it is necessary to take Primolut Nor regularly for the full 10-day period.
Approximately 2-4 days after completion of the treatment, a withdrawal bleed occurs resembling a normal period in terms of intensity and duration.

Slight bleeding during tablet-taking
Occasionally, slight bleeding may occur after the initial cessation of bleeding. Even in these cases, you must not pause or stop taking the tablets.

No cessation of bleeding, heavy breakthrough bleeding
If the bleeding does not stop despite the tablets being taken as directed, an organic cause or an extra-genital factor must be considered, for which other therapeutic measures are generally required. The same applies where, after initial cessation of bleeding, fairly heavy bleeding reappears during tablet-taking.

Prevention of recurrence
To prevent recurrences (i.e. the problem coming back after it has been cured with the treatment) in patients with anovulatory cycles, Primolut Nor may be taken prophylactically (1/2 tablet - 5 mg - 1-2 times daily from Days 16 to 25 of the cycle [Day 1 of the cycle = 1st day of the last period]).
Withdrawal bleeding will occur a few days after the last tablet is taken.

- **Primary and secondary amenorrhoea**

Hormone treatment of secondary amenorrhoea must be started only after pregnancy has been ruled out.

Sometimes, primary or secondary amenorrhoea is caused by a prolactinoma (a benign pituitary tumour that leads to an increase in the production of the hormone prolactin), the presence of which must be ruled out by a doctor before treatment with Primolut Nor is started, because it might get bigger.
Before the start of treatment with Primolut Nor, your doctor should prescribe you an oestrogen (e.g. for 14 days). You should then take half a Primolut Nor 10 mg tablet (= 5 mg) 1-2 times daily for 10 days. Withdrawal bleeding will occur a few days after the last tablet is taken.
If a sufficient level of endogenous oestrogen production has been reached, you doctor will assess whether the treatment with oestrogens should be stopped and cyclical bleeding induced by you taking half a Primolut Nor 10 mg tablet twice daily from Days 16 to 25 of the cycle.

- **Premenstrual syndrome, mastopathy**

Half a Primolut Nor 10 mg tablet taken 1-3 times daily during the luteal phase of the cycle (i.e. the second part of the cycle from ovulation to the start of your next period) may alleviate or improve premenstrual symptoms such as headache, depressed mood, fluid retention and breast tenderness.

- **Timing of menstruation**

Where periods are too frequent, menstruation may be postponed by administration of Primolut Nor. However, this method must be limited to patients who are not at risk of pregnancy during the treatment cycle.
Dose: half a Primolut Nor 10 mg tablet (= 5 mg) 2-3 times daily for no more than 10-14 days, starting approximately 3 days before the estimated date of menstruation. Menstruation will occur 2-3 days after discontinuation of treatment.

- **Endometriosis**

Treatment must start between Days 1 and 5 of the cycle with half a Primolut Nor 10 mg tablet (= 5 mg) twice daily, with the dose being increased if necessary to one tablet per day in the presence of spotting. If this disappears, the initial dosage may be resumed. Treatment must be continued for at least 4-6 months. If the medicine is taken each day without interruption, ovulation and menstruation will not usually occur.

If you take more Primolut Nor than you should
No cases of overdose have been reported.
If you accidentally take too much Primolut Nor, contact a doctor immediately or go to the nearest hospital.

If you forget to take Primolut Nor
Take only the last missed tablet as soon as you remember and then continue taking the tablets at the usual time the next day.

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 administration of Primolut Nor and tend to subside as treatment continues.

- **Very common side effects** (may affect more than 1 in 10 users)
  Bleeding from the uterus/vagina, including light bleeding between periods (spotting)*, hypomenorrhoea (reduction in the menstrual blood flow)*.

- **Common side effects** (may affect up to 1 in 10 users)
  Headache, nausea, amenorrhoea* (absence of a menstrual cycle), generalised swelling (oedema).

- **Uncommon side effects** (may affect up to 1 in 100 users)
  Migraine.

- **Rare side effects** (may affect up to 1 in 1,000 users)
  Hypersensitivity reactions, urticaria, rash.

- **Very rare side effects** (may affect up to 1 in 10,000 users)
  Visual disturbances, dyspnoea (breathing difficulties)
  * in the indication Endometriosis.

Other adverse reactions reported are:
- variations in libido,
- vertigo,
- nerve irritation phenomena,
- hirsutism (excessive hair growth),
- variations in liver function tests and haemagglutination assays.

Following the instructions contained in the package leaflet reduces the risk of side effects.

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

To report any side effect(s):
Egypt:
Egyptian Pharmaceutical Vigilance Centre
Hotline: 15301
Email: pv.followup@edaegypt.gov.eg
Website: www.edaegypt.gov.eg

United Arab Emirates (UAE):
Pharmacovigilance & Medical Device section
Tel: 80011111 / +971 42301000
Email: pv@mohap.gov.ae
Website: www.mohap.gov.ae
P.O.Box 1853 Dubai

Kuwait:
Drug &Food Control, Ministry of Health, Kuwait
Tel.: +965-24811532 Fax: +965-24811507
Email : Adr_reporting@moh.gov.kw
Website: http://eservices.moh.gov.kw/SPCMS/DrugCmp.aspx

Other Countries:
Please contact the relevant competent authority

5. How to store Primolut Nor

Keep this medicine out of the sight and reach of children.
Do not store above 25°C. Protect from light.

Do not use this medicine after the expiry date which is stated on the pack after EXP. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Primolut Nor contains
The active substance is norethisterone acetate. 1 tablet contains 10 mg norethisterone acetate.
The other ingredients are: lactose monohydrate, maize starch, povidone 25, talc, magnesium stearate.

What Primolut Nor looks like and contents of the pack
White, cross-scored tablets on one side with an emblem 'AR' in a hexagon on the other side.
Each pack contains 30 tablets (2 PVC/Aluminum blisters x 15 tablets).

Manufacturer
Bayer Weimar GmbH & Co. KG,
Dobereinerstrasse 20,
99427 Weimar, Germany.

Marketing Authorisation Holder
Bayer AG
Kaiser-Wilhelm-Allee
51368 Leverkusen, Germany.

This package leaflet was last revised in 05/2020

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