Primolut® Nor 5 mg

tablets

Active substance: Norethisterone acetate

Package leaflet: Information for the user

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

Read all of this leaflet carefully before you start taking this medicine.
- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

1. WHAT PRIMOLUT NOR 5 mg IS AND WHAT IT IS USED FOR

Primolut-Nor 5 mg is a so-called progestogen, a synthetic hormone product, that has properties in common with the natural, female hormone, progesterone. Primolut Nor 5 mg also has an androgenic residual effect (androgen is a generic term for male sex hormones).
Indication:
dysfunctional bleeding.

2. BEFORE YOU TAKE PRIMOLUT NOR 5 mg

Do not take Primolut Nor 5 mg in the following cases. If you notice one of these risk factors while you are taking Primolut Nor 5 mg, you will have to stop taking the medicine immediately.
Do not take Primolut Nor 5 mg,
- if you are hypersensitive to the active substance, Norethisterone acetate, or to one of the other components of Primolut Nor 5 mg.
- in the case of and intact or disrupted pregnancy,
- while breast feeding.
- in the event of unexplained bleeding from the vagina,
- if you have an active venous thromboembolic diseases (repositioning of blood vessels by a blood clot e.g. deep vein thrombosis or pulmonary embolism),
- if you have had or now have cardiovascular diseases (such as, cardiac infarction, stroke, ischaemic heart disease),
- with Diabetes mellitus (sugar diabetes) with vascular changes,
- if you have had or now have severe liver malfunctions (including elimination disorders, such as Dubin-Johnson syndrome and Rotor syndrome), as long as your liver values have not returned to normal,
- if you have jaundice (cholestatic icterus),
- if you have had or now have liver tumours (benign or malignant),
- if you have had jaundice, continuous itching and/or bullous eruptions (Herpes gestationis) during an earlier pregnancy.
- if you have had known or suspected sex-hormone dependent, malignant tumours, such as breast cancer.

Take special care with Primolut Nor 5 mg:
Please, inform your doctor, if you get one of the diseases / risk factors listed below or if an existing condition worsens, while you are taking Primolut Nor 5 mg. The doctor will conduct an individual risk/benefit analysis, before you start taking or continue to take Primolut Nor 5 mg.

▶ Primolut Nor 5 mg and thrombosis
Based on the results of scientific studies, it has been concluded that the use of oral ovulation inhibitors containing oestrogen and progestogen is associated with an increased incidence of thromboembolic diseases (repositioning of blood vessels by a blood clot). Consequently, the possibility of an increased risk of thromboembolism should be taken into consideration, in particular if you have a history of thromboembolic disease.
The generally recognised risk factors for venous thromboembolism (VTE) are
- a positive personal or family medical history (VTE in siblings or parents relatively early in life),
- age,
- obesity (adiposity),
- longer periods of immobilisation, major surgery or serious injuries.

The increased risk of thromboembolism in childbed also has to be considered.
Blood clots may also rarely occur in blood vessels of the heart or of the brain (causing cardiac infarction or stroke).
A thrombosis can sometimes result in lasting disabilities and even be fatal.
Stop treatment immediately, if you notice symptoms of arterial or venous thrombotic events, or if you suspect you do.

▶ Gynaecological and general examinations
Before you start taking the product, you are advised to have a thorough general medical and gynaecological examination (including the breast and a cytological cervical smear) and, above all, have pregnancy ruled out. You are advised to have checkups every six months during prolonged use.

▶ Liver
After recovering from a viral hepatitis (when the liver parameters have returned to normal), you should wait for about six months before using a product, such as Primolut Nor 5 mg.

▶ Androgenic residual effect
The Norethisterone acetate contained in Primolut Nor 5 mg showed an androgenic residual effect in animal studies, which, however, only very rarely occur clinically, when the product has been used as instructed. There are, however, women with an individual sensitivity to androgenic impulses, without presenting any sure signs for this.
As a result, it cannot be ruled out that there may be isolated cases of slight virilisation. This also applies to the risk of a virilisation of female foetuses, when women become pregnant during treatment.

▶ Issues surrounding potential teratogenic (causing malformations) effects.
There was an occasional case of virilisation of the external genitals of female neonates reported back when Norethisterone was administered in high doses for lengthy periods to maintain pregnancy. There have not yet been any reports of this effect being associated with Norethisterone enanthate; though, it cannot be completely ruled out. Teratogenic effects caused by Norethisterone are improbable.

▶ Blood pressure
When treatment with Primolut Nor 5 mg causes a serious increase in blood pressure, you may have to discontinue using the product after having carefully taken into consideration all individual risks relevant to the application.

▶ Other
Yellowish-brown pigment spots (chloasma) can occasionally occur, particularly in women, who have had this type of pigment spots during an earlier pregnancy (Chloasma gravidarum). Women with a proclivity for chloasma should avoid exposure to the sun or ultraviolet radiation whilst taking Primolut Nor 5 mg.
Patients with depression in their medical history need to be closely monitored. Stop taking the medicine in the event of severe depression recurring.
Please, note:
Treatment with Primolut Nor 5 mg does not have a contraceptive effect. Use a non-hormonal method, if you desire contraception (that is with the exception of the calendar-based method, also known as the Knaus-Ogino Method, and the temperature-based method). If you do not have a withdrawal bleed in regular intervals of about every 28 days, whilst using this treatment regimen (see above), you may be, despite contraceptive measures, pregnant. Do not continue the treatment, until you have undergone an differential diagnostic examination.
Inform your doctor, if you have diabetes (mellitus), since this disease requires careful monitoring.
It has been verified in recent investigations, that Norethisterone acetate is partially metabolised into Ethinyl estradiol. Since the oestrogenic effects of Norethisterone have always been supposed and now observed in clinical practice, these findings concerning its metabolic properties do not change anything in the existing recommendations for use.
The conditions described below tell you when to take particular care whilst using Primolut Nor 5 mg. Please, ask your doctor for advice. This also applies, if one of these criteria did pertain to you at one time in the past.
Only use Primolut Nor 5 mg after a careful risk-benefit assessment, in the event of
- thrombophlebitis (inflammation of the venous walls, associated with the formation of a blood clot in this region),
- having had a blood clot form (thromboembolic diseases, such as deep vein thromboses, stroke, cardiac infarction) including conditions, that increase the susceptibility thereto,
- endogenous depression,
- porphyria, in all the forms of reduced liver function,
- disturbances in lipid metabolism.

It cannot be ruled out that the increased risk of thromboembolic complications in diabetics is intensified by treatment with higher doses.
Reasons for discontinuing the use of Primolut Nor 5 mg:
- headaches, that are initially migraine-like or that occur with unusual intensity,
- sudden sensory malfunction (sight, hearing disturbances, among others).
- first signs of venous inflammation with the formation of a blood clot (thrombophlebitis) (such as unusual pain or swelling in the legs),
- sharp pain whilst breathing or inexplicable coughing,
- pain and tightness in the chest,
- pending surgery (six weeks in advance),
- immobilisation (e.g. after injuries)

In all of these cases, there can be an increased risk of blood clotting (thrombosis).
Discontinue the use of Primolut Nor 5 mg in the event of
- jaundice, inflammation of the liver or itching over the entire body,
- increase in epileptic seizures,
- intense rise in blood pressure
- pregnancy.

If you are being treated for absent menstrual bleeding and do not have a withdrawal bleed in regular intervals of about every 28 days, do not continue use until you have the results of a differential diagnostic examination (see, 'Please, note' above).
Taking Primolut Nor 5 mg with other medicines:
Please inform your doctor or pharmacist if you are taking/using or have recently taken/used any other medicines, even those not prescribed.
The required amounts of medicines used to treat diabetes (mellitus) can change.
Some medicines can reduce the efficacy of Primolut Nor 5 mg. These medicines include those that speed up the metabolism of Primolut Nor 5 mg, such as medicines for treating epilepsy (e.g. phenytoin, barbiturates, primidone, carbamazepine, oxcarbazepine) and tuberculosis (e.g. rifampicin, rifabutin) or antibiotics against infections (e.g. griseofulvin) and herbal medicinal products, that contain St. John's wort (Hypericum perforatum) (used primarily to treat depression).
Primolut Nor 5 mg can also impair the metabolism of other medicinal products. Accordingly, the concentration of active substances in the body can be affected (e.g. that of cyclosporin).
Note: Refer also to the package leaflet of the concomitant medication, in order to determine any possible interactions.
▶ Laboratory tests
The use of Primolut Nor 5 mg can affect the results of certain laboratory tests.
Pregnancy and breast-feeding
Do not use Primolut Nor 5 mg during pregnancy or whilst breast feeding.
Ask your doctor or pharmacist for advice before taking any medicine.
The ability to drive and use machines.
No special precautionary measures are necessary.
Important information about some of the ingredients of Primolut Nor 5 mg:
This medicinal product contains lactose. For this reason, please take Primolut Nor 5 mg only after consultation with your doctor, if you know that you suffer from an intolerance of certain sugars.

3. HOW TO TAKE PRIMOLUT NOR 5 mg

Always take Primolut Nor 5 mg exactly according to your doctor's instructions. You should check with your doctor or pharmacist if you are unsure.
The usual dose is:
▶ dysfunctional bleeding
Take 1 Primolut Nor 5 mg tablet thrice daily for 10 days. Bleeding from the vagina, which is not caused by organic disturbances, will stop within 1 to 3 days in the majority of cases. In order to guarantee success of the treatment, you will still have to take Primolut Nor 5 mg for the entire length of 10 days. A withdrawal bleed will occur approximately 2 to 4 days after the end of treatment, which is comparable to normal menstruation with respect to intensity and duration.

▶ *light bleeding while taking the tablets*
Occasionally, more light bleeding can occur after bleeding has initially been stopped. Even in these cases, you should not interrupt or stop taking the tablets.

▶ *Bleeding has not been stopped, strong break-through bleeding*
If vaginal bleeding does not stop despite your having taken the tablets correctly, an organic cause or factor must be considered, which is not related, as such, to the reproductive organs (such as polyps, carcinoma of the uterine cervix or of the endometrium, myoma (benign tumour of muscle fibres), residue of a miscarriage, an abdominal pregnancy or coagulopathy), which then require other measures for the most part. The same also applies in the event that relative strong bleeding returns after having been stopped initially.
Route of administration:
You should take the tablets whole (do not chew) with sufficient liquid (preferably with a glass of drinking water).
If you have the impression that the effect of Primolut Nor 5 mg is too strong or too weak, talk to your doctor.
If you take more Primolut Nor 5 mg than you should:
Animal experimental studies on acute toxicity, that were conducted with Norethisterone acetate, showed no indication of any risk of acute undesirable effects in the event of accidentally taking several times the therapeutic daily dose.
There are no particular measures to recommend in the event of overdosing other than to stop taking the product or to reduce the dose. Severe intoxication is not to be expected, when children accidentally take Primolut Nor 5 mg tablets.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Primolut Nor 5 mg can cause side effects, although not everybody gets them.
The following incidence rating is used to evaluate the frequency of side effects:

Very common:	more than 1 out of 10 treated
Common:	less than 1 out of 10, but more than 1 out of 100 treated
Uncommon:	less than 1 out of 100, but more than 1 out of 1,000 treated
Rare:	less than 1 out of 1,000, but more than 1 out of 10,000 treated
Very rare:	less than 1 out of 10,000 treated or unidentified

Possible adverse reactions:
Adverse reactions are more frequent in the first months of using Primolut preparations and become less frequent during the course of therapy. In addition to the adverse reactions listed in the section, 'Take special care with Primolut Nor 5 mg', there have been other reports of undesired effects amongst the users of Primolut preparations, although a causal connection could not always be established.
Adverse reactions are listed in the following Table according to the MedDRA System Organ Classes (MedDRA SOCs). The incidence rates are based on data from post-authorisation surveillance and from publications.

System Organ Class	Common	Uncommon	Rare	Very rare
Immune system disorders			Hypersensitivity reactions	
Nervous system disorders	Headaches	Migraine		
Eye disorders				Visual disturbances
Respiratory, thoracic and mediastinal disorders				shortness of breath with respiratory distress (dyspnoea)
Gastrointestinal disorders	Nausea			
Skin and subcutaneous tissue disorders			Hives (Urticaria) rash	
General disorders and administration site conditions	Fluid retention in tissue (oedema)			

Adverse reactions descriptions, their synonyms and related conditions are the most suitable representation within the MedDRA terminology.
Intermenstrual bleeding of varying intensity is common.
Premenstrual tension (e.g. breast tension), painful menstruation (dysmenorrhoea), tension in the breast (mastodynia), depression, tiredness and weight gain are uncommon.
Signs of virilisation (such as acne) are uncommon. In isolated cases, there can be voice changes in women with particular sensitivity to androgenic impulses. Above all in women with singing or speaking professions, the consideration has to be weighed, whether or not to discontinue treatment at the first signs of voice change (slight tiredness of the voice, roughness, hoarseness).
In rare cases, glucose tolerance can be impaired; there can be changes in the liver function, biliary stasis with and without jaundice (cholestasis with and without icterus), an increase in clotting factors and in blood pressure.
There can also be changes in various clinical-chemical serum parameters, which do not, however, have any direct pathological significance.
There can be unwanted changes in blood lipid levels, when using higher (5 mg and more).
It has been observed in scientific investigations that there is a statistic association between the use of oestrogen / progestogen combinations and the occurrence of thromboembolic disease, such as venous inflammation with blood clot formation (thrombophlebitis), pulmonary embolism, blood clot in the brain (cerebral thrombosis) and blood clot formation (thrombosis).
Although Primolut Nor 5 mg does not contain any oestrogen, maybe patients being treated with progestogen alone should also be closely monitored as a precautionary measure.
There have been rare, isolated cases observed, in which thromboembolic diseases, such as deep vein thrombosis, were associated with the use of Primolut Nor 5 mg. Consequently, the risk / benefit assessment for this product should include a possibly increased risk of thrombosis, especially if there are thromboembolic diseases in the medical history.
In rare cases following the use of hormones, to which the active substance contained in Primolut Nor 5 mg also belongs, benign hepatic changes and, even less frequently, malignant hepatic changes have been observed, which, in isolated cases, have caused life-threatening bleeding into the abdominal cavity. For this reason, you are well advised to inform your doctor, if you experience unusual complaints in the epigastric region, that do not go away on their own after a while.
For reasons to stop taking Primolut Nor 5 mg, see the section entitled 'Take special care with Primolut Nor 5 mg'.
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. STORING PRIMOLUT NOR 5 mg

Keep out of the reach and sight of children.
Do not use after the expiry date stated on the outer carton.
Store below 30°C.

6. FURTHER INFORMATION

What Primolut Nor 5 mg contains:
The active substance is Norethisterone acetate.
1 tablet contains 5 mg Norethisterone acetate.
The other constituents are:
lactose, maize starch, polyvidone 25,000, talc and magnesium stearate.
What Primolut Nor 5 mg looks like and contents of the pack:
Primolut Nor 5 mg tablets are packaged in blister packs made of transparent polyvinyl chloride film and aluminium foil.
Tablets for oral administration
12 tablets
20 tablets
50 tablets
Manufacturer:
Schering GmbH & Co. Produktions KG
D-99427 Weimar, Germany.
a subsidiary of
Bayer Pharma AG
D-13342 Berlin, Germany.
This leaflet was last approved in October 2007

Special references
More detailed Information, needed by the doctor, can be found in special publications concerning this product.