PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

PRIMOLUT N 5 mg tablets
Norethisterone
Contains lactose

Read all of this leaflet carefully before you start taking PRIMOLUT N

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse, or other health care provider.
- PRIMOLUT N has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What PRIMOLUT N is and what it is used for

PRIMOLUT N is a progestin, a synthetic hormonal product having properties in common with the natural female hormone progesterone. PRIMOLUT N also has a residual androgenic (male sex hormone) effect. PRIMOLUT N is used for timing of menstruation and to treat disturbances of the monthly bleeding (dysfunctional bleeding), absence of menstruation (primary and secondary amenorrhoea), and endometriosis (a disease leading to complaints caused by womb-lining tissue growing outside the womb).

2. What you need to know before you take PRIMOLUT N

Do not use PRIMOLUT N

- If you are hypersensitive (allergic) to norethisterone or any of the other ingredients of PRIMOLUT N (listed in section 6)
- If you are pregnant or think you might be pregnant
- If you are breastfeeding
- If you have (or have ever had) a heart attack or stroke (caused by a blood clot or a rupture of a blood vessel in the brain)
- If you have (or have ever had) a disease that can be an indicator (a) of a future heart attack (for example, angina pectoris which causes severe chest pain which may spread to the left arm) or (b) of a stroke (for example, a minor stroke with no residual effects, also called a transient ischaemic attack)
- If you have a severe or multiple risk factor(s) for blood clots
- If you have (or have ever had) a certain kind of migraine (with so-called focal neurological symptoms such as visual symptoms, speech disability, or weakness, or numbness in any part of your body)

- If you have diabetes with damaged blood vessels.
- If you have or have had a severe liver disease and have been told by your doctor that your liver function values have not yet returned to normal. Symptoms of a liver disease may be, for instance, yellowing of the skin and/or itching of the whole body.
- If you are taking any antiviral medicines which contain ombitasvir, paritaprevir, or dasabuvir, and combinations of these. These antiviral medicines are used to treat chronic (long-term) hepatitis C (an infectious disease that affects the liver, caused by the hepatitis C virus)
- If you have or have had a benign or malignant liver tumour.
- If you have or have had a malignant sex hormone-dependent tumour such as cancer of the breast or the genital organs.

If any of the above conditions appears for the first time while taking PRIMOLUT N, stop taking it at once and consult your doctor.

Warnings and precautions

Talk to your doctor or pharmacist before taking PRIMOLUT N.

The sexual steroid (progesterone) that is contained in this product is partly converted into estrogen. Therefore, the general warnings associated with the use of combined oral contraceptives should be considered in addition for PRIMOLUT N.

In some situations, you need to take special care while taking PRIMOLUT N, and your doctor may need to examine you regularly. Consult your doctor before starting to use PRIMOLUT N, if any of the following conditions apply to you or if any of them develop or worsen while you are taking PRIMOLUT N:

- if you smoke
- if you have diabetes (metabolic disease with elevated blood sugar levels)
- if you are seriously overweight
- if you have high blood pressure
- if you have a heart valve disorder or a certain heart rhythm disorder
- if you have had a thrombosis/embolism
- if anyone in your immediate family has had a thrombosis (venous thromboembolism in a sibling or a parent at a relatively early age), a heart attack or a stroke at a young age
- if you have an inflammation of your veins (superficial phlebitis)
- if you have varicose veins
- if anyone in your immediate family has had breast cancer
- if you have or have had chloasma (yellowish-brown pigmentation patches on the skin, particularly of the face); if so, avoid too much exposure to the sun or ultraviolet radiation
- if you have a history of depression
- if you suffer from migraine
- if you have epilepsy (see "Other medicines and PRIMOLUT N")
- if you or someone in your immediate family has ever had high blood levels of cholesterol or triglycerides (fatty substances)
- if you have a disease of the liver or gall bladder
- if you have Crohn's disease or ulcerative colitis (chronic inflammatory bowel disease)
- if you have systemic lupus erythematosus (or SLE, a disease of the immune system)
- if you have haemolytic uremic syndrome (or 'HUS', a disorder of blood coagulation causing failure of the kidneys)
- if you have sickle cell disease

- if you have a condition that occurred for the first time or worsened during pregnancy or previous use of sex hormones (e.g. hearing loss, a metabolic disease called porphyria, a skin disease called herpes gestationis, or a neurological disease called Sydenham's chorea)
- if you have hereditary angioedema. Consult your doctor immediately if you experience symptoms of angioedema such as swollen face, tongue or throat, and/or difficulty swallowing, or hives, together with difficulty breathing. Products containing estrogens may induce or worsen symptoms of angioedema

If any of the above conditions appears for the first time, recurs or worsen while using PRIMOLUT N, you should contact your doctor.

Primolut N and depression

Some women using hormone-containing medicines including Primolut N have reported depression or depressed mood. Depression can be serious and may sometimes lead to suicidal thoughts. If you experience mood changes and depressive symptoms contact your doctor for further medical advice as soon as possible.

PRIMOLUT N and blood clots

A thrombosis is the formation of a blood clot which may block a blood vessel.

It has been concluded from epidemiological surveys that the use of oral estrogen/progestogen containing contraceptive pills increases a woman's risk of developing a venous thrombosis compared with a woman who does not take any (contraceptive) pill.

A thrombosis sometimes occurs in the deep veins of the legs (deep venous thrombosis). Venous thromboembolism (VTE) can develop whether or not you are taking the pill. It can also happen if you become pregnant. If a blood clot breaks away from the vein where it has formed, it may reach and block the arteries of the lungs, causing a so-called 'pulmonary embolism'. Blood clots can also occur very rarely in the blood vessels of the heart (causing a heart attack). Blood clots or a ruptured blood vessel in the brain may cause a stroke.

The risk of venous thromboembolism is highest during the first year of use. This increased risk is present after initially starting the combined pill or restarting (following a 4 week or greater pill free interval) the same or a different combined pill. Data from a large study suggest that this increased risk is mainly present during the first 3 months.

Overall the risk for venous thromboembolism in users of low estrogen dose (< 50 µg ethinylestradiol) pills is two to threefold higher than for non-users of combined oral contraceptives who are not pregnant and remains lower than the risk associated with pregnancy and delivery.

Venous thromboembolism, manifesting as deep venous thrombosis and/or pulmonary embolism, may occur during the use of all combined pills.

Rarely blood clots can occur in other parts of the body including the liver, gut, kidney, brain or eye.

The risk of thromboembolism is also increased shortly after childbirth.

Blood clots can also occur seldomly in the blood vessels of the heart (causing a heart attack) or the brain (causing a stroke).

WHEN SHOULD YOU CONTACT YOUR DOCTOR?

Regular check-ups

- When you are using PRIMOLUT N, your doctor will tell you to return for regular check-ups.

Contact your doctor as soon as possible if you:

- notice any changes in your health, especially involving any of the items mentioned in this leaflet (see "Do not use PRIMOLUT N" and "Warnings and precautions", do not forget about the items related to your immediate family);
- feel a lump in your breast;
- are going to use other medications (see "Other medicines and PRIMOLUT N");
- will have a prolonged period of immobilisation or will have surgery (consult your doctor at least six weeks in advance)
- have unusual, heavy vaginal bleeding.

Stop taking PRIMOLUT N and see your doctor immediately if you notice possible signs of thrombosis such as:

- coughing for no apparent reason;
- a feeling of pain and tightness in the chest which may reach the left arm;
- breathlessness;
- more frequent, unusually severe, or prolonged headache or a first migraine attack;
- partial or complete loss of vision, or double vision;
- slurring or speech disability;
- sudden changes to your hearing, sense of smell, or taste;
- dizziness or fainting;
- weakness or numbness in any part of your body;
- severe pain or swelling in either of your legs.

Also stop taking PRIMOLUT N and see your doctor immediately if you notice:

- jaundice (yellowish skin, whites of the eyes; this may be a sign of hepatitis)
- generalised severe itching (pruritus)
- high blood pressure
- that you are pregnant

The situation and symptoms mentioned above are described and explained in more detail elsewhere in this leaflet.

The risk of venous or arterial blood clots (e.g. deep venous thrombosis, pulmonary embolism, heart attack) or stroke increases:

- with age
- if you are overweight
- if anyone in your immediate family has ever had a blood clot (thrombosis in the leg, lung "pulmonary embolism", or elsewhere), a heart attack or a stroke at a young age, or if you or any of your relatives are known or suspected of having a hereditary blood clotting disorder increasing your risk for developing blood clots. In this case you should see a specialist before deciding about using any combined oral contraceptive. Certain blood factors that may suggest you have tendency for venous or arterial thrombosis include activated protein C (APC) resistance, hyperhomocysteinaemia, antithrombin-III deficiency, protein C deficiency, protein S deficiency, antiphospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant),
- with prolonged immobilisation (e.g. when you have your leg or legs in plaster or splints), major surgery, any surgery to the legs, or major trauma. In this situation it is better to stop taking PRIMOLUT N (if the surgery is planned you should stop at least four weeks before hand) and not to start again until two weeks after you are fully on your feet again.

- if you smoke (the risk increases the more you smoke and the older you get, especially in women over 35 years of age). When using PRIMOLUT N you should stop smoking, especially if you are older than about 35 years of age.
- if you or someone in your immediate family has or has ever had high blood levels of cholesterol or triglycerides (fatty substances)
- if you have high blood pressure. If you develop high blood pressure while using PRIMOLUT N, you may be told to stop using it.
- if you suffer from migraine
- if you have a heart valve disorder or a certain heart rhythm disorder

Very occasionally thrombosis may cause serious permanent disabilities or may even be fatal.

If you notice possible signs of a thrombosis, stop taking PRIMOLUT N and consult your doctor immediately.

PRIMOLUT N and cancer

Breast cancer has been observed slightly more often in women using combined pills, but it is not known whether this is caused by the treatment itself. For example, it may be that more tumours are detected in women on combined pills because they are examined by their doctor more often. The risk of breast tumours becomes gradually less after stopping the combined hormonal contraceptive. It is important to regularly check your breasts and you should contact your doctor if you feel any lump.

In rare cases benign liver tumours and even more rarely, malignant liver tumours have been reported in users of hormonal substances such as the one contained in PRIMOLUT N. These tumours may lead to internal bleeding.

The most important risk factor for cervical cancer is persistent Human Papilloma Virus (HPV) infection. Some studies suggest that long-term use of the pill increase a woman's risk of developing cervical cancer. However, it is not clear to what extent sexual behaviour or other factors such as Human Papilloma Virus increases this risk.

The afore mentioned tumours may be life-threatening or may have fatal outcome.

Contact your doctor immediately if you have severe pain in your abdomen.

Other medicines and PRIMOLUT N

Always tell your health care provider if you are taking other medicine. This includes all complementary or traditional medicines.

Some medicines
- can have an influence on the blood levels of PRIMOLUT N
- can make it less effective
- can cause unexpected bleeding.

These include:
- medicines used for the treatment of:
    - epilepsy (e.g. phenytoin, barbiturates, primidone, carbamazepine, oxcarbamazepine, topiramate, felbamate)
    - tuberculosis (e.g. rifampicin)
    - HIV and Hepatitis C Virus infections (so-called protease inhibitors and nonnucleoside reverse transcriptase inhibitors)

  - fungal infections (griseofulvin, azole antifungals, e.g. 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)
- the herbal remedy St. John's wort (primarily used for the treatment of depressive moods).
- grapefruit juice.

PRIMOLUT N may influence the effect of other medicines, e.g.:
- ciclosporin
- lamotrigine
- midazolam
- theophylline
- melatonin
- tizanidine

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Laboratory tests

If you need a blood test, tell your doctor or the laboratory staff that you are taking PRIMOLUT N, because it can affect the results of some tests.

PRIMOLUT N with food and drink

The tablets are to be swallowed whole with some liquid.

Pregnancy and breast feeding

You must not use PRIMOLUT N if you are pregnant or think you might be pregnant.
You must not use PRIMOLUT N during breastfeeding.

Driving or using machines

There are no known effects.

PRIMOLUT N contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take PRIMOLUT N

Do not share medicines prescribed for you with any other person.

If you have sexual intercourse, you should use non-hormonal methods (for example a condom) of contraception instead of taking a contraceptive pill. If you think you might have become pregnant despite the protective measures, the treatment must be interrupted until the situation has been clarified by your doctor.

The following dosages are recommended:

- Dysfunctional bleeding

Take one tablet of PRIMOLUT N 5 mg 3 times daily for 10 days. In the majority of cases this will stop bleeding from the womb (uterine bleeding) that is not caused by organic defects within 1 to 3 days, nevertheless to ensure treatment success PRIMOLUT N 5 mg tablets must be taken for the full 10 days. About 2 to 4 days after completion of the treatment, withdrawal bleeding will occur with the intensity and duration of normal menstruation.

Occasionally, slight bleeding may occur after the initial cessation of bleeding. Do not stop or interrupt tablet intake if this occurs.

If vaginal bleeding does not stop although you have taken your tablets correctly, an organic or extra-genital cause must be considered, which, if so, will mostly require other measures. This also applies when after an initial cessation of bleeding, fairly heavy bleeding reoccurs during tablet intake.

If this happens you should contact your doctor.

To prevent the recurrence of dysfunctional bleeding (in case you do not have menstrual cycles with ovulation) your doctor may decide that you should take PRIMOLUT N 5 mg tablets as a prophylaxis (1 tablet 1 to 2 times daily from the 16th to the 25th day of the cycle (1st day of the cycle = 1st day of the last bleeding). Withdrawal bleeding occurs a few days after the last tablet intake.

- Primary and secondary amenorrhea

Hormone treatment of secondary amenorrhea can be carried out only after pregnancy is ruled out. Primary or secondary amenorrhea is sometimes caused by a prolactinoma (an alteration of a gland in the brain producing increased amounts of a hormone-like substance) which needs to be excluded by your doctor before starting treatment with PRIMOLUT N.

Your doctor will prescribe you an estrogen (e.g. for 14 days) before you start with PRIMOLUT N 5 mg. Thereafter you take 1 tablet of PRIMOLUT N 5 mg 1 to 2 times daily for 10 days. Withdrawal bleeding occurs within a few days of intake of the last tablet.

If sufficient estrogen production in your body has been achieved, an attempt can be made to stop the estrogen treatment and to trigger cyclical bleeding by administering 1 tablet of PRIMOLUT N 5 mg twice daily from the 16th to the 25th day of the cycle.

- Premenstrual syndrome, cyclical mastopathy

One tablet of PRIMOLUT N 5 mg taken 1 to 3 times daily during the 2nd half (luteal phase) of the cycle, may relieve or improve premenstrual symptoms such as headaches, depressive moods, water retention, and a feeling of tension in the breasts.

- Timing of menstruation

Monthly menstrual bleeding can be postponed with administration of PRIMOLUT N 5 mg. However, this method should be used by you only if you are not at risk of pregnancy during the treatment cycle.

Take 1 tablet PRIMOLUT N 5 mg 2 to 3 times daily for no longer than 10 to 14 days, beginning about 3 days before the expected menstruation. Bleeding will occur 2 to 3 days after medication has been stopped.

- Endometriosis

Start treatment between the first and 5th day of the cycle with 1 tablet PRIMOLUT N 5 mg twice daily. If spotting occurs, the dose can be increased to 2 tablets twice daily. If bleeding ceases, you may consider returning to the initial dose. Continue treatment for at least 4 to 6 months. With uninterrupted daily intake, ovulation and menstruation do not usually occur. After stopping the hormone treatment withdrawal bleeding will occur.

If you take more PRIMOLUT N than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital of poison centre.

There have been no reports of serious harmful effects from taking too many PRIMOLUT N tablets at one time. If you have taken several tablets at a time, you may experience nausea, vomiting or vaginal bleeding.

If you forget to take PRIMOLUT N

If you forget a dose, wait until it is time to take your next prescribed dose. Do not take the missed dose.
Do not take a double dose to make up for forgotten individual doses.

If you stop taking PRIMOLUT N

There are no specific withdrawal symptoms if you stop PRIMOLUT N but there is the possibility that the original complaints re-occur.

4. Possible side effects

PRIMOLUT N can have side effects.
Not all side-effects reported for PRIMOLUT N are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking PRIMOLUT N, please consult your health care provider for advice.

Side effects are more common during the first months of treatment with PRIMOLUT and disappear with continued treatment. In addition to the side effects listed in the section entitled “Warnings and precautions” the following side effects have been reported in users of PRIMOLUT preparations, although PRIMOLUT could not always be confirmed as the cause. Below we list possible side effects by the parts of the body they affect and by how common they are:

Frequent
- Uterine/Vaginal bleeding including Spotting*
- Weak periods (Hypomenorrhea)*
- Headache
- Nausea
- Absence of periods (Amenorrhea)*
- Generalised swelling (Oedema)

Less frequent
- Migraine
- Hypersensitivity reactions
- Nettle rash (Urticaria)
- Rash
- Visual disturbances
- Shortness of breath (Dyspnoea)

* if taken for Endometriosis

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

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of PRIMOLUT N.

5. How to store PRIMOLUT N

Store at or below 30 °C.
Keep in well closed containers and protect from light.
Store all medicines out of reach of children.
Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What PRIMOLUT N contains

- The active substance is norethisterone.
- The other ingredients are lactose monohydrate, maize starch, magnesium stearate.

What PRIMOLUT N looks like and contents of the pack

White, round tablet, biconvex, imprinted with "AN" in a regular hexagon on one side.

Brown glass bottles with tamperproof polyethylene closures in a carton, or aluminium/PVC blisters in a carton.

Contents of the pack:
30 or 150 tablets.

Holder of Certificate of Registration

Bayer (Pty) Ltd
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