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PROFESSIONAL INFORMATION

PATIENT INFORMATION LEAFLET

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SCHEDULING STATUS: S4

NUR-ISTERATE 200 mg/ml oily solution for injection
Norethisterone enantate
Sugar free.

Read all of this leaflet carefully before you are given NUR-ISTERATE.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.

What is in this leaflet

1. What NUR-ISTERATE is and what it is used for

NUR-ISTERATE is a hormonal contraceptive for intramuscular injection.

2. What you need to know before you are given NUR-ISTERATE

Do not use NUR-ISTERATE

Do not use NUR-ISTERATE if you have any of the conditions listed below. If any of these apply to you, tell your Healthcare Provider before using NUR-ISTERATE.

- If you are pregnant or think you might be pregnant.
- If you are suffering from or have a history of a thromboembolic disorder in your veins. Thrombosis is the formation of a blood clot. This may occur for example in the blood vessels of the legs (deep vein thrombosis) and the lungs (pulmonary embolism). See also the section "NUR-ISTERATE and thrombosis".
- If you have or have had a severe arterial, including cardiovascular, disease such as heart attack, stroke or ischaemic heart disease (angina pectoris). See also the section "NUR-ISTERATE and thrombosis".
- If you suffer from increased blood pressure requiring treatment.
- If you suffer or have suffered from a severe liver disease (as long as your liver function values have not 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 have or have had a benign or malignant liver tumour.
- If you suffer or have suffered from a malignant sex hormone-dependent tumour such as cancer of the breast or the genital organs.
- If you have diabetes mellitus with blood vessel damage.
- If you suffer from disturbances of your blood fat metabolism.
- If you are allergic to any of the ingredients of NUR-ISTERATE.
- If you have any unexplained vaginal bleeding.
- If you have an inherited disease called porphyria.

If any of these conditions appear for the first time while using NUR-ISTERATE, consult your Healthcare Provider because it may be necessary to discontinue NUR-ISTERATE. See also "General notes" in the next section.

Warnings and precautions

General notes

In this leaflet, several situations are described where use of NUR-ISTERATE should be discontinued, or where the reliability of NUR-ISTERATE may be decreased. In such situations you should not have sex, or you should take extra non-hormonal contraceptive precautions, e.g., use a condom or another barrier method. Do not use rhythm or temperature methods. These methods can be unreliable because NUR-ISTERATE alters the usual changes in temperature and cervical mucus that occur during the menstrual cycle.

NUR-ISTERATE does not protect against HIV infection (AIDS) or any other sexually transmitted disease.

The sexual steroid norethisterone that is contained in this product is partly converted by our body into an estrogen (ethinylestradiol), which is contained in products called combined hormonal contraceptives. The expected concentration of ethinylestradiol in your body is lower than after administration of combined hormonal contraceptives. Nevertheless, effects similar to those after administration of contraceptives containing a combination of hormones including ethinylestradiol cannot be excluded.

Take special care with NUR-ISTERATE

If NUR-ISTERATE is used in the presence of any of the conditions listed below you may need to be kept under close observation. Your Healthcare Provider can explain this to you. Therefore, if any of these apply to you, tell your Healthcare Provider before NUR-ISTERATE is started.

- you smoke;
- you have diabetes;
- you are overweight;
- you have had venous thromboembolism or anyone in your immediate family has had a thrombosis (venous thromboembolism in a sibling or a parent at a relatively early age);
- anyone in your immediate family has had breast cancer;
- you have high blood pressure;
- you suffer from migraine;
- you have haemolytic uremic syndrome (HUS; a disorder of blood coagulation causing failure of the kidneys);
- you have liver or gallbladder disease;
- you have experienced jaundice and/or itching all over your body during a pregnancy or during use of the Pill;
- you have experienced a depression;
- you have or have had chloasma (yellowish-brown pigmentation patches on the skin, particularly of the face);
- you have systemic lupus erythematosus (SLE; a disease affecting the skin all over the body);
- you have a neurological disease called Sydenham's chorea;
- you have had an extrauterine pregnancy (if the embryo had developed outside the womb) or an impairment of tube function (e.g. caused by inflammation of the tube).

If any of the above conditions appear for the first time, recur, or worsen while using NUR-ISTERATE, you should contact your Healthcare Provider.

NUR-ISTERATE and thrombosis

Thrombosis is the formation of a blood clot which may block a blood vessel.
Thrombosis sometimes occurs in the deep veins of the legs (deep venous thrombosis). If this blood clot breaks away from the veins where it is formed, it may reach and block the arteries of the lungs, causing a so-called "pulmonary embolism". Deep venous thrombosis is a rare occurrence. It can develop whether or not you are using NUR-ISTERATE. It can also happen if you become pregnant.
It is generally recognized that the risk for venous thromboembolism increases for example with increasing age, if you are overweight, if you have had venous thromboembolism or if anyone in your immediate family has had a thrombosis (venous thromboembolism in a sibling or a parent at a relatively early age). The risk of having deep venous thrombosis is temporarily increased as a result of an operation or immobilization (for example, when you have your leg or legs in plaster or splints). In women who use hormonal contraceptives such as NUR-ISTERATE the risk may be yet higher. Tell your Healthcare Provider well in advance (as soon as you get to know) of any expected hospitalization or surgery. Your Healthcare Provider may tell you that NUR-ISTERATE needs to be discontinued before surgery or at the time of immobilization. Your Healthcare Provider will also tell you when NUR-ISTERATE can be started again after you are back on your feet.

The risk of thromboembolism is also increased shortly after childbirth. See also "After having a baby" (in the section "Starting NUR-ISTERATE").

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

If you develop high blood pressure while using NUR-ISTERATE, you may be told to stop using it.
If you notice possible signs of a thrombosis, consult your Healthcare Provider immediately (See also "When should you contact your Healthcare Provider?").

NUR-ISTERATE and cancer

In rare cases benign liver tumours and even more rarely, malignant liver tumours have been reported in users of hormonal contraceptives. These tumours may lead to internal bleeding.

Contact your Healthcare Provider immediately if you have severe pain in your abdomen.

NUR-ISTERATE and depression

Some women using hormonal contraceptives including NUR-ISTERATE 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.

Reduced efficacy

The efficacy of NUR-ISTERATE may be reduced in the event of e.g. prolonged injection intervals (See "If you forget to use NUR-ISTERATE") or concomitant medication (See "Other medicines and NUR-ISTERATE").

Reduced cycle control

Menstrual bleeding
Individually different cycle disturbances may occur during the treatment. In case of questions please ask your Healthcare Provider for advice before the start of the treatment. These disturbances are rarely a reason for the discontinuation of NUR-ISTERATE.

In general, the cycle under NUR-ISTERATE does not change significantly in about 50 to 70 % of the women (bleeding intervals between 26 and 35 days, duration of bleeding 1 to 7 days).

Procedure in the event of intermenstrual bleeding
Intermenstrual bleeding of varying intensity may occur, particularly during the first few months. These disturbances need not concern you and do not impair the contraceptive reliability. Treatment is usually unnecessary and normally, NUR-ISTERATE does not need to be discontinued. However, you should inform your Healthcare Provider in any case because it may be necessary for him to rule out other potential causes.

Absence of withdrawal bleeding
Absence of the withdrawal bleeding occurred in 8 to 25 % of the women during clinical investigations. It was generally of short duration and disappeared again in the further course of treatment. The rate of missed bleedings did not increase with prolonged use.
In any case, if no withdrawal bleeding has occurred within the preceding 10 weeks, contact your Healthcare Provider because pregnancy must be ruled out by means of a suitable test.

Other medicines and NUR-ISTERATE

If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of NUR-ISTERATE with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other Healthcare Provider for advice. They can tell you if you need to take additional contraceptive precautions (for example condoms) and if so, for how long, or, whether the use of another medicine you need must be changed.

Some medicines can have an influence on the blood levels of NUR-ISTERATE and can make it less effective in preventing pregnancy, or can 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, rifabutin),
  - HIV and Hepatitis C Virus infections (so-called protease inhibitors and non-nucleoside reverse transcriptase inhibitors),
  - fungal infections (griseofulvin, azole antifungals, e.g. fluconazole, itraconazole, ketoconazole, voriconazole),
  - bacterial infections (macrolide antibiotics, e.g. clarithromycin, erythromycin)
  - certain heart diseases, high blood pressure (calcium channel blockers, e.g. verapamil, diltiazem),
- the herbal remedy St. John's wort (primarily used for the treatment of depressive moods),
- grapefruit juice.

NUR-ISTERATE may influence the effect of other medicines, e.g.
- ciclosporin,

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 or other laboratory test, tell your Healthcare Provider or the laboratory staff that you are using NUR-ISTERATE, because it can affect the results of some tests.

NUR-ISTERATE with food and drink

Not applicable.

Pregnancy and breastfeeding

The administration of NUR-ISTERATE during pregnancy is contraindicated. If pregnancy occurs during treatment, further injections must not be given.

If you are pregnant or breastfeeding, think you may be pregnant, or are planning to have a baby, please consult your doctor, pharmacist, or other healthcare provider for advice before using this medicine.

Driving and using machines

There are no observed effects. However, in the adverse effects section Dizziness and Effects on vision are stated as potential side effects.
It is not always possible to predict to what extent NUR-ISTERATE may interfere with the daily activities of a patient. Patients should ensure that they do not perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision e.g. driving, riding, flying, sailing, operating machines/equipment until they are aware of the measure to which NUR-ISTERATE affects them.

3. How to use NUR-ISTERATE

NUR-ISTERATE, when used correctly, has a failure rate of approximately 1 % per year. The failure rate may increase when intervals between injections are prolonged.

Your Healthcare Provider will administer NUR-ISTERATE as a deep intramuscular injection (preferably into the buttocks muscles, alternatively into the upper arm). The injection will be administered very slowly (see section "Possible side effects"). It is advisable to place a plaster over the injection site after the injection to prevent any reflux of the NUR-ISTERATE solution.

Starting NUR-ISTERATE

<u>When no hormonal contraceptive has been used in the past month</u>

NUR-ISTERATE should be administered within the first 5 days of your natural cycle, i.e. the first 5 days of the menstrual bleeding.

<u>When changing from a combined oral contraceptive (COC or the combined "Pill")</u>

Preferably, NUR-ISTERATE should be started immediately on the day after the last active tablet of your previous COC. When starting later you should additionally use a barrier method (e.g. a condom) for the first 7 days after injection.

<u>When changing from another progestogen-only method ("Minipill", injection, implant) or from a progestogen releasing intrauterine device (IUS)</u>

You may switch any day from the Minipill without break (from an implant or an IUS on the day of its removal, from another injectable when the next injection would be due), but should in all of these cases use a barrier method (e.g. a condom) for the first 7 days after injection. If you are not sure about the type of method you have used, contact your doctor or pharmacist.

<u>Following abortion</u>

NUR-ISTERATE may be started immediately as long as there are no medical objections.

After having a baby

NUR-ISTERATE may be started immediately as long as there are no medical objections. If you are breastfeeding see section "Pregnancy and breastfeeding".

Management of next injections

The next three injections are to be given in intervals of 8 weeks, after which a further injection is required every 12 weeks (84 days). If the injection interval is extended beyond, no adequate contraceptive protection will be available from the 13th week onwards and your Healthcare Provider will advise you accordingly to use additional contraceptive measures.
Should technical reasons make it impossible to maintain the 84-day injection interval, a 2-month regimen can alternatively be adopted.

In any case, if no withdrawal bleeding has occurred within the preceding 10 weeks, pregnancy must be ruled out by means of a suitable test.

If you use more NUR-ISTERATE than you should

Administration by your Healthcare Provider of this single use injectable minimises the risk of overdose. There have been no reports of serious side effects from overdose.

If you forget to use NUR-ISTERATE

If you do not get your next injection on the due date, you run an increased risk of an unwanted pregnancy. Contact your Healthcare Provider as soon as possible and use non-hormonal methods of contraception (e.g. condoms) in the meantime.

If you stop using NUR-ISTERATE

If you stop getting further NUR-ISTERATE injections, for example because you want to get pregnant, the normal ability to conceive usually returns after 4 to 5 months after the last injection. If you do not get the usual monthly bleedings within this period of time, please contact your Healthcare Provider.

4. Possible side effects

NUR-ISTERATE can have side effects.

Not all side effects reported for NUR-ISTERATE are included in this leaflet. Should your general health worsen or if you experience any untoward effects while using NUR-ISTERATE, please consult your doctor, pharmacist, or other Healthcare Provider for advice.

If any of the following happens, stop using NUR-ISTERATE and tell your doctor immediately or go to the casualty department at your nearest hospital:

- an unusual cough;
- severe pain in the chest which may reach the left arm;
- breathlessness;
- any unusual, severe, or prolonged headache or 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 in your abdomen;

- severe pain or swelling in either of your legs.

These are all very serious side effects and may indicate thrombosis. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- you notice any changes in your own health, especially involving any of the items mentioned in this leaflet (see also "Do not use NUR-ISTERATE" and "Take special care with NUR-ISTERATE"; do not forget about the items related to your immediate family);
- you feel a lump in your breast;
- you are going to use other medications (see also "Other medicines and NUR-ISTERATE");
- you are to be immobilized or are to have surgery (consult your Healthcare Provider when you get to know about this because NUR-ISTERATE may have to be discontinued in advance);
- you have unusual, heavy vaginal bleeding;
- you miss your period within 10 weeks after the last menstrual bleeding or suspect you are pregnant (inform your Healthcare Provider because NUR-ISTERATE needs to be discontinued in case of pregnancy);
- you experience a recurrence of jaundice and/or pruritus which occurred first during pregnancy or previous use of sex steroids, like the Pill (your Healthcare Provider may decide to discontinue NUR-ISTERATE in this case);
- you experience a recurrence of earlier depression;
- you experience unexplained complaints in the lower part of your stomach together with an irregular cycle pattern (no monthly bleeding or no monthly bleeding followed by persistent bleeding), you should contact your Healthcare Provider **immediately** because an extrauterine pregnancy must be considered.

Tell your doctor if you notice any of the following:

Frequent side effects

- uterine/vaginal bleeding including spotting (light bleeding from the vagina similar to, but lighter than, a period)
- short lasting absence of monthly bleeding (amenorrhoea).
- increased weight
- dizziness
- headache
- nausea
- skin disorder such as rashes
- injection site reaction

Less frequent side effects

- depressed mood

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, Pharmacist or other Health Care Provider. 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 NUR-ISTERATE.

5. How to store NUR-ISTERATE

Keep out of the reach and sight of children.
Do not use NUR-ISTERATE after the expiry date which is stated on the pack.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.
Store at or below 30 °C.
Protect from light.

6. Contents of the pack and other information

What NUR-ISTERATE contains

The active substance is norethisterone enantate. 1 ml NUR-ISTERATE contains 200 mg norethisterone enantate.
The other ingredients are castor oil for injection and benzyl benzoate.

What NUR-ISTERATE looks like and contents of the pack

Clear, yellowish, oily solution.

Ampoule of 1 ml, glass type I
Pack sizes: 1 x 1 ml; 100 x 1 ml

Holder of Certificate of Registration

Bayer (Pty) Ltd
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