SELECT THE REQUIRED INFORMATION

PROFESSIONAL INFORMATION

PATIENT INFORMATION LEAFLET

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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.
- NUR-ISTERATE 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.

SCHEDULING STATUS: S4

NAME OF THE MEDICINAL PRODUCT:

NUR-ISTERATE

Oily solution for intramuscular injection

1. WHAT NUR-ISTERATE CONTAINS:

1 ml contains norethisterone enantate 200 mg.
Other ingredients are: castor oil for injection, benzyl benzoate.

2. WHAT NUR-ISTERATE IS USED FOR:

NUR-ISTERATE is a hormonal contraceptive for intramuscular injection.

3. BEFORE YOU USE NUR-ISTERATE:

3.1 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 Professional 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 later in this leaflet called “Hormonal contraceptives and thrombosis”.
- If you have or have had a severe arterial, including cardiovascular, disease such as heart attack, stroke or ischemic heart disease (angina pectoris). See also the section "Hormonal contraceptives 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 tumor.
- If you suffer or have suffered from a malignant sex hormone-dependent tumor 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.
- In porphyria NUR-ISTERATE should be used only after careful consideration of the benefits and risks.

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

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.

3.2 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 Professional can explain this to you. Therefore, if any of these apply to you, tell your Healthcare Professional 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 hemolytic 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 you 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 Professional.

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 Professional well in advance (as soon as you get to know) of any expected hospitalization or surgery. Your Healthcare Professional may tell you that NUR-ISTERATE needs to be discontinued before surgery or at the time of immobilization. Your Healthcare Professional 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 Professional immediately (See also "When should you contact your Healthcare Professional?").

NUR-ISTERATE and cancer:

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

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

Reduced efficacy:

The efficacy of NUR-ISTERATE may be reduced in the event of e.g. prolonged injection intervals (See "If you forget to get your next NUR-ISTERATE injection:") or concomitant medication (See "Using other medicines”).

Reduced cycle control:

- Menstrual bleeding
  Individually different cycle disturbances may occur during the treatment. In case of questions please ask your Healthcare Professional 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). A tendency for the cycle to stabilize is observed with increasing duration of use.

- 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 Professional 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 Professional because pregnancy must be ruled out by means of a suitable test.

WHEN SHOULD YOU CONTACT YOUR HEALTHCARE PROFESSIONAL?

Regular check-ups

- When you are using NUR-ISTERATE, your Healthcare Professional will tell you to return for regular check-ups.

Contact your Healthcare Professional as soon as possible if:

- you notice any changes in your own health, especially involving any of the items mentioned in this leaflet (see also: "Before you use NUR-ISTERATE/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 "Using other medicines");
- you are to be immobilized or are to have surgery (consult your Healthcare Professional 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 Professional 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 Professional 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 Professional **immediately** because an extra-uterine pregnancy must be considered.

See your Healthcare Professional immediately if you notice possible signs of thrombosis:

- 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.

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

3.3 Pregnancy and breastfeeding:

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

3.4 Taking other medicines with 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 Professional, for advice.

Some medicines may stop NUR-ISTERATE from working properly. These include medicines that increase the metabolism of NUR-ISTERATE, e.g. some of those are used for the treatment of epilepsy (e.g. primidone, phenytoin, barbiturates, carbamazepine and oxcarbazepine); tuberculosis (e.g. rifampicin and rifabutin); antibiotics (e.g. griseofulvin) for some other infectious diseases and the herbal remedy St. John's Wort (primarily used for the treatment of depressive moods). NUR-ISTERATE may also interfere with the working of other medicines (e.g. cyclosporin). Always tell the Healthcare Professional who prescribes NUR-ISTERATE which medicines you are already using. Also tell any other Healthcare Professional or dentist who prescribes another medicine (or the dispensing pharmacist) that you use NUR-ISTERATE. They can tell you if you need to take additional contraceptive precautions and if so, for how long.

Laboratory tests:

If you need a blood test, tell your Healthcare Professional or the laboratory staff that you are using NUR-ISTERATE, because it can affect the results of some tests.

4. 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 Professional 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.

4.1 Starting NUR-ISTERATE:

When no hormonal contraceptive has been used in the past month:
NUR-ISTERATE should be administered within the first 5 days of your natural cycle, i.e. the first 5 days of the menstrual bleeding.

When changing from a combined oral contraceptive (COC or the combined "Pill"):
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.

When changing from another progestogen-only method ("Minipill", injection, implant) or from a progestogen releasing intrauterine device (IUS):
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.

Following abortion:
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 "Breastfeeding".

4.2 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 Professional 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.

4.3 If you use more NUR-ISTERATE than you should:

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

4.4 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 Professional as soon as possible and use non-hormonal methods of contraception (e.g. condoms) in the meantime.

4.5 Effects when treatment with NUR-ISTERATE is stopped:

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 Professional.

5. POSSIBLE SIDE EFFECTS:

Not all side effects reported for NUR-ISTERATE are included in this leaflet. Should your general health worsen while taking NUR-ISTERATE, please consult your doctor, pharmacist or other Healthcare Professional for advice.

Below is the list of side effects by the parts of the body they affect and by how common they are:

Very common means 10 or more in every 100 people are likely to get these.

Reproductive system and breast disorders:
- Uterine/Vaginal bleeding including spotting (light bleeding from the vagina similar to, but lighter than, a period).
- Short lasting absence of monthly bleeding (amenorrhoea).

Common: between 1 and 10 in every 100 people are likely to get these.

Immune system disorders:
- Hypersensitivity reaction

Metabolism and nutrition disorders:
- Weight increase

Nervous system disorders:
- Dizziness
- Headache

Gastrointestinal disorders:
- Nausea

Skin and subcutaneous tissue disorders:
- Skin disorder such as rashes.

General disorders and administration site conditions:
- Injection site reaction

Uncommon: between 1 and 10 in every 1000 people are likely to get these.

*Psychiatric disorders**:***
- Depressed mood

Experience has shown that the short-lasting reactions (urge to cough, coughing fits, difficulties in breathing) which occur in isolated cases during or immediately after the injection of oily solutions can be avoided by injecting the solution extremely slowly.

6. STORING AND DISPOSING OF 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.

7. PRESENTATION OF NUR-ISTERATE:

1 ampoule of 1 ml.
100 ampoules of 1 ml each.

8. IDENTIFICATION OF NUR-ISTERATE:

Clear, yellowish, oily solution.

9. REGISTRATION NUMBER:

J/21.8.2/136

10. NAME AND ADDRESS OF REGISTRATION HOLDER:

Bayer (Pty) Ltd
Reg. No.: 1968/011192/07
27 Wrench Road
Isando
1609

11. DATE OF PUBLICATION:

15 April 2011