Package leaflet: Information for the user
Intrarosa™ 6.5 mg pessary
prasterone

This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using 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 Intrarosa™ is and what it is used for

Intrarosa™ contains the active substance prasterone.

What Intrarosa™ is used for
Intrarosa™ is used to treat postmenopausal women having moderate to severe symptoms of vulvar and vaginal atrophy. It is used to relieve menopausal symptoms in the vagina such as dryness or irritation. It is caused by a drop in the levels of oestrogen in your body. This happens naturally after the menopause.

How Intrarosa™ works
Prasterone corrects the symptoms and signs of vulvar and vaginal atrophy by replacing the oestrogens which are normally produced before menopause by the ovaries of women. It is inserted into your vagina, so the hormone is released where it is needed. This may relieve discomfort in the vagina.

2. What you need to know before you use Intrarosa™
The use of HRT carries risks which need to be considered when deciding whether to start taking it, or whether to carry on taking it.

The experience in treating women with a premature menopause (due to ovarian failure or surgery) is limited. If you have a premature menopause the risks of using HRT may be different. Please talk to your doctor.

Before you start (or restart) HRT, your doctor will ask about your own and your family's medical history. Your doctor may decide to perform a physical examination. This may include an examination of your breasts and/or an internal examination, if necessary.

Once you have started on Intrarosa™ you should see your doctor for regular check-ups (at least every 6 months). At these check-ups, discuss with your doctor the benefits and risks of continuing with Intrarosa™.

Go for regular breast screening, as recommended by your doctor.

Do not take Intrarosa™
if any of the following applies to you. If you are not sure about any of the points below, talk to your doctor before taking Intrarosa™,
• If you have or have ever had **breast cancer**, or if you are suspected of having it;
• If you have **cancer which is sensitive to oestrogens**, such as cancer of the womb lining (endometrium), or if you are suspected of having it;
• If you have any **unexplained vaginal bleeding;**
• If you have **excessive thickening of the womb lining** (endometrial hyperplasia) that is not being treated;
• If you have or have ever had a blood clot in a vein (thrombosis), such as in the legs (deep venous thrombosis) or the lungs (pulmonary embolism);
• If you have a blood clotting disorder (such as protein C, protein S, or antithrombin deficiency);
• If you have or recently have had a disease caused by blood clots in the arteries, such as a heart attack, stroke or angina;
• If you have or have ever had a **liver disease** and your liver function tests have not returned to normal;
• If you have a rare blood problem called "porphyria" which is passed down in families (inherited);
• If you are **allergic** (hypersensitive) to **prasterone** or any of the other ingredients of Intrarosa™ (listed in section 6 Further information).

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

Warnings and precautions

When to take special care with Intrarosa™
Tell your doctor if you have ever had any of the following problems, before you start the treatment, as these may return or become worse during treatment with Intrarosa™. If so, you should see your doctor more often for check-ups:
• fibroids inside your womb;
• growth of womb lining outside your womb (endometriosis) or a history of excessive growth of the womb lining (endometrial hyperplasia);
• increased risk of developing blood clots (see "Blood clots in a vein (thrombosis)");
• increased risk of getting a oestrogen-sensitive cancer (such as having a mother, sister or grandmother who has had breast cancer);
• high blood pressure;
• a liver disorder, such as a benign liver tumour;
•diabetes;
• gallstones;
• migraine or severe headaches;
• a disease of the immune system that affects many organs of the body (systemic lupus erythematosus, SLE);

• epilepsy;
• asthma;
• a disease affecting the eardrum and hearing (otosclerosis);
• a very high level of fat in your blood (triglycerides);
• fluid retention due to cardiac or kidney problems.

Stop taking Intrarosa™ and see a doctor immediately
If you notice any of the following when taking HRT:
- any of the conditions mentioned in the 'DO NOT take Intrarosa™' section;
- yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a liver disease;
- if you become pregnant;
- a large rise in your blood pressure (symptoms may be headache, tiredness, dizziness);
- migraine-like headaches which happen for the first time;
- if you notice signs of a blood clot, such as:
  - painful swelling and redness of the legs;
  - sudden chest pain;
  - difficulty in breathing.

For more information, see 'Blood clots in a vein (thrombosis)'

Note: Intrarosa™ is not a contraceptive. If it is less than 12 months since your last menstrual period or you are under 50 years old, you may still need to use additional contraception to prevent pregnancy. Speak to your doctor for advice.

HRT and cancer
Intrarosa™ has not been studied in women with current or history of cancers.

Excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer)
Taking oestrogen-only HRT tablets for a long time can increase the risk of developing cancer of the womb lining (the endometrium). Intrarosa™ does not stimulate the endometrium as shown by atrophy of the lining of the womb in all women treated with Intrarosa™ for one year during the clinical trials.

It is uncertain whether a risk exists with Intrarosa™ used for long term (more than one year) treatments. However, Intrarosa™ has been shown to have very low absorption into the blood, therefore the addition of a progestagen is not necessary.

If you get bleeding or spotting, it's usually nothing to worry about, but you should make an appointment to see your doctor. It could be a sign that your endometrium has become thicker.

The following risks apply to HRT medicines which circulate in the blood. However Intrarosa™ is for local treatment in the vagina and the absorption into the blood is very low. It is less likely that the conditions mentioned below will get worse or come back during treatment with Intrarosa™, but you should see your doctor if you are concerned.

Breast cancer
Evidence suggests that taking combined oestrogen-progestogen and possibly also oestrogen-only HRT increases the risk of breast cancer. The extra risk depends on how long you take HRT. The additional risk becomes clear within a few years. However, it returns to normal within a few years (at most 5) after stopping treatment.

• **Regularly check your breasts. See your doctor if you notice any changes such as:**
  • dimpling of the skin;
  • changes in the nipple;
  • any lumps you can see or feel.

Additionally, you are advised to join mammography screening programs when offered to you.

Ovarian cancer
Ovarian cancer is rare - much rarer than breast cancer. The use of oestrogen-only HRT has been associated with a slightly increased risk of ovarian cancer.

The risk of ovarian cancer varies with age. For example, in women aged 50 to 54 who are not taking HRT, about 2 women in 2000 will be diagnosed with ovarian cancer over a 5-year period. For women who have been taking HRT for 5 years, there will be about 3 cases per 2000 users (i.e. about 1 extra case).
Cases of ovarian and breast cancer have rarely been reported in women treated with 6.5 mg of prasterone for 52 weeks.

Effect of HRT on heart and circulation
Intrarosa™ has not been studied in women with history of thromboembolic diseases, uncontrolled hypertension or heart disease.

Blood clots in a vein (thrombosis)
The risk of blood clots in the veins is about 1.3 to 3-times higher in HRT users than in non-users, especially during the first year of taking it.

Blood clots can be serious, and if one travels to the lungs, it can cause chest pain, breathlessness, fainting or even death.

You are more likely to get a blood clot in your veins as you get older and if any of the following applies to you. Inform your doctor if any of these situations applies to you:
  • you are unable to walk for a long time because of major surgery, injury or illness (see also section 3, If you need to have surgery);
  • you are seriously overweight (BMI >30 kg/m^2);
  • you have any blood clotting problem that needs long-term treatment with a medicine used to prevent blood clots;
  • if any of your close relatives has ever had a blood clot in the leg, lung or another organ;
  • you have systemic lupus erythematosus (SLE);
  • you have cancer.

For signs of a blood clot, see “Stop taking Intrarosa™ and see a doctor immediately”.
In clinical trials, no deep vein thrombosis has been observed with intravaginal prasterone while one case of pulmonary embolism which corresponds to an incidence lower with Intrarosa™ than in the placebo group.

Compare
Looking at women in their 50s who are not taking HRT, on average, over a 5-year period, 4 to 7 in 1000 would be expected to get a blood clot in a vein.

Heart disease (heart attack) / Hypertension
For women taking oestrogen-only therapy there is no increased risk of developing a heart disease.

Stroke
The risk of getting stroke is about 1.5 times higher in HRT users than in non-users. The number of extra cases of stroke due to use of HRT will increase with age.
No case of stroke has been observed with Intrarosa™ during clinical trials.
Compare
Looking at women in their 50s who are not taking HRT, on average, 8 in 1000 would be expected to have a stroke over a 5-year period. For women in their 50s who are taking HRT, there will be 11 cases in 1000 users, over 5 years (i.e. an extra 3 cases).

Other conditions
• HRT will not prevent memory loss. There is some evidence of a higher risk of memory loss in women who start using HRT after the age of 65. Speak to your doctor for advice;
• You may have vaginal discharge due to melting of the 'hard fat base' which adds to increased vaginal secretions due to treatment. If vaginal discharge occurs, it is not required to stop Intrarosa™.
• Intrarosa™ may weaken condoms, diaphragms and cervical caps made of latex.
• If you have a vaginal infection you will need a course of antibiotics before taking Intrarosa™.

Children and adolescents

Intrarosa™ is only used in adult women.

Other medicines and Intrarosa™

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

No data on efficacy and safety are available in women currently treated with hormonal therapy such as: androgens, hormone replacement therapy (oestrogen alone or combined with progestogens).

The use of Intraorsa in combination with hormone replacement therapy (oestrogen-only or oestrogen-progestagen combination or androgen treatment) or vaginal oestrogens is not recommended.

Pregnancy, breast feeding and fertility

Pregnancy and breast feeding
Intrarosa™ is for use in postmenopausal women only. If you become pregnant, stop taking Intrarosa™ and contact your doctor.

Fertility

Intrarosa™ is not meant for women with child-bearing potential. It is not known if this medicine affects fertility.

Driving and using machines

Intrarosa™ does not affect your ability to drive and use machines.

3. How to use Intrarosa™

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

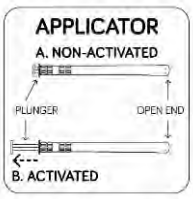
Your doctor will aim to prescribe the lowest dose to treat your symptom for as short as necessary. Speak to your doctor if you think this dose is too strong or not strong enough.

How much to use
Use one pessary once a day, at bedtime.

How to use
Insert the pessary into the vagina with your finger or with an applicator provided in the pack.

Before you start
• Empty your bladder and wash your hands before handling the pessary and applicator.
• Tear off one wrapped pessary from the 7-pessary strip.

A. Using the applicator



STEP 1
• 1A. Remove 1 applicator from the package.
• 1B. Pull back on the plunger until it stops to activate the applicator. The applicator must be activated before use. Place the applicator on a clean surface.

STEP 2
• Slowly pull the plastic tabs on the pessary away from eac h other while keeping the pessary still between your fingers.
• Carefully remove the pessary from the plastic wrap.
• If a pessary falls on an unsanitary surface, replace it with a new one.

STEP 3
• Place the flat end of the pessary into the open end of the activated applicator as shown. You are now ready to insert the pessary into your vagina.

STEP 4
• Hold the applicator between your thumb and middle finger.
• Leave your index (pointer) finger free to press the applicator plunger after the applicator is inserted into your vagina.

STEP 5
• Select the position for insertion of the pessary that is most comfortable for you.

5a. Lying position

5b. Standing position

STEP 6
• Gently slide the pessary end of the applicator into your vagina as far as it will comfortably go.

Do not use force.

STEP 7
• Press the applicator plunger with your index (pointer) finger to release the pessary.
• Remove the applicator. Wash it or throw it away after using for one week (see details in section 3 - "How to use Intrarosa™")

B. Using the finger
Follow the above instructions of Step 2, and then insert the pessary into the vagina with your finger as far as it can comfortably go. **Do not use force.**

How long to use
After initial use, see your doctor at least every 6 months to check if you need to keep using Intrarosa™.

If you use more Intrarosa™ than you should

Vaginal douching is recommended.

If you forget to use Intrarosa™

If you forget to use a pessary, insert one as soon as you remember. However, if the next dose is due in less than 8 hours, skip the missed pessary.

Do not use two pessaries to make up for a forgotten dose.

If you need to have surgery

If you are going to have surgery, tell the surgeon that you are taking Intrarosa™. You may need to stop taking Intrarosa™ about 4 to 6 weeks before the operation to reduce the risk of a blood clot (see section 2, Blood clots in a vein). Ask your doctor when you can start taking Intrarosa™ again.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following diseases are reported more often in women using HRT medicines which circulate in the blood compared to women not using HRT. These risks apply less to vaginally administered oestrogen treatments:
- breast cancer;
- ovarian cancer;
- blood clots in the veins of the legs or lungs (venous thromboembolism);
- stroke;
- probable memory loss if HRT is started over the age of 65.

For more information about these side effects, see section 2.

The side effect the most frequently reported in the clinical studies was vaginal discharge. This is likely due to melting of the hard fat added to an expected increase in vaginal secretions due to treatment. Vaginal discharge does not require to stop Intrarosa™.

The following adverse effects were also reported:
− with a common frequency (may affect up to 1 in 10 people): abnormal Pap smear (mostly ASCUS or LGSIL), weight fluctuations (either increase or decrease);

− with a uncommon frequency (may affect up to 1 in 100 people): benign cervical or uterine polyps, benign breast mass.

The following side effects have been reported with HRT containing estrogens but not with Intrarosa™ during clinical trials:
• gall bladder disease
• various skin disorders:
- discoloration of the skin especially of the face or neck known as “pregnancy patches” (chloasma);
- painful reddish skin nodules (erythema nodosum);
- rash with target-shaped reddening or sores (erythema multiforme).

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. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5.How to store Intrarosa™

Keep this medicine out of the sight and reach of children.

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

Do not store above 30 °C.

Do not freeze.

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 Intrarosa™ contains
- The active substance is prasterone. Each pessary contains 6.5 mg of prasterone.
- The only other ingredient is the hard fat (adeps solidus).

What Intrarosa™ looks like and contents of the pack

Intrarosa™ is a white to off-white, bullet-shaped pessary approximately 28 mm long and 9 mm in diameter at its widest end.

The applicator is made of LDPE and 1% colorant (Titanium dioxide).

It is available in blister packs of 28 pessaries with 6 applicators.

Marketing Authorisation Holder

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