PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

Novofem® film-coated tablets

Estradiol/norethisterone acetate.

Contains sugar:

Each red film-coated tablet contains 37,3 mg lactose monohydrate.

Each white film-coated tablet contains 36,8 mg lactose monohydrate.

Read all of this leaflet carefully before you start using Novofem®

Keep this leaflet. You may need to read it again.

If you have further questions, please ask your doctor or your pharmacist.

Novofem® 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 Novofem® is and what it is used for

Novofem® is a hormone replacement therapy (HRT). It contains two types of female hormones, an estrogen and a progestagen.

- Novofem® is indicated for the treatment of symptoms associated with estrogen deficiency in postmenopausal women with an intact uterus.
- Novofem® is also indicated to reduce the risk of bone loss in postmenopausal women.

The experience treating women over 65 years is limited.

Novofem® has no contraceptive effect.

2. What you need to know before you take Novofem®

Do not take Novofem® if you:

- Are hypersensitive (allergic) to estradiol or norethisterone acetate or any of the ingredients of Novofem® (see section 6).
- Have or suspect you have, or have had breast cancer;
- Have a family history of breast cancer;
- Have or suspect you have a hormone dependent tumour (e.g. cancer of the lining of the womb);
- Have abnormal vaginal bleeding;
- Have or have had deep vein thrombosis or pulmonary embolism of unknown origin (formation of blood clot in the blood vessels of your legs or your lungs);
- Have a blood clotting disorder (such as protein C, protein S or antithrombin deficiency).
- Have or have recently had a thrombosis (blood clot) (e.g. angina, myocardial infarction)
- Have an acute or active liver disease or a history of liver disease where your liver function tests have failed to return to normal;

- Have porphyria (metabolic disease with disturbed production of blood pigment);
- Have untreated endometrial hyperplasia (excessive growth of uterine mucosa);
- Are pregnant or suspect you are pregnant;
- Are breastfeeding your baby;
- Are known to have inherited genetic changes called BRCA1 and/or BRCA2 genes.
- Started your menstrual periods early (before the age of 12 years).
- Have a history of non-cancerous breast diseases such as atypical hyperplasia or lobular carcinoma *in situ*.
- Had any previous treatment using radiation therapy to the chest or breast.
- Have been treated or exposed while in your mother's womb to a medicine called diethylstilbestrol (DES).

Warnings and precautions

Medical examination/follow-up:

Before you start or re-start treatment with Novofem®, a complete medical history of you and your family should be taken. During treatment, you are recommended to have periodic check-ups. You are encouraged to report any changes in your breasts to your doctor or nurse.

Be sure to:

- Go for regular screening and cervical smear tests.
- Regularly check your breasts for any changes, such as dimpling of the skin, changes in the nipple, or any lumps you can see or feel.

- If you notice any changes in your breast, make an appointment to see your doctor as soon as possible.

Additionally, you are advised to join mammography screening programs when offered to you. For mammogram screening, it is important that you inform the nurse/health care provider who is actually taking the x-ray that you use Novofem®, as this medication may increase the density of your breasts which may affect the outcome of the mammogram. Where the density of
the breast is increased, mammography may not detect all lumps.

If you get breakthrough bleeding or spotting, it is usually nothing to worry about, especially during the first few months of therapy.

But if the bleeding or spotting:

- carries on for more than the first few months
- starts after you've been on Novofem® for a while
- carries on even after you've stopped taking Novofem®

make an appointment to see your doctor. It could be a sign that your endometrium has become thicker.

Ovarian cancer

Long-term (at least 5 years) use of HRTs, such as Novofem®, has been associated with an increased risk of ovarian cancer in some epidemiological studies.

Breast cancer

Breast cancer has been diagnosed slightly more often in women who use HRT than in women of the same age who do not use HRT. This slight increase in the number of breast cancer diagnoses gradually disappears during the course of the 10 years after stopping use of HRT. When you are using Novofem®, you must perform monthly breast self-examinations. Your doctor will advise you on when to report for breast examinations and any appropriate investigations.

Effects on your heart or circulation

Heart disease

Novofem® is not recommended for women who have heart disease, or have had heart disease recently. If you have ever had heart disease, talk to your doctor to see if you should be taking Novofem®.
Novofem® will not help to prevent heart disease.

Stroke

Recent research suggests that Novofem® increases the risk of having a stroke.

If you get:

- unexplained migraine-type headaches, with or without disturbed vision

see a doctor as soon as possible and do not take any more Novofem® until your doctor says you can. These headaches may be an early warning sign of a stroke.

Blood clots

Novofem® may increase the risk of **blood clots in the veins** (also called **deep vein thrombosis,** or **DVT**), especially during the first year of taking it.

You are more likely to get a blood clot:

- if you use estrogen-containing medicines
- if you are of older age
- if you are seriously overweight
- if you have had a blood clot before
- if any of your close family have had blood clots
- if you have had one or more miscarriages
- if you are pregnant or you just had a baby
- if you have cancer
- if you have any blood clotting problem that needs treatment with a medicine such as warfarin
- if you're off your feet for a long time because of major surgery, injury or illness
- if you have a rare condition called systemic lupus erythematosus. (a disease of the immune system that affects many organs of the body)

If any of the above-mentioned conditions apply to you, tell your doctor to see if you should take Novofem®.

If you get:

- painful swelling in your leg
- sudden chest pain
- difficulty breathing

see a doctor as soon as possible and **do not take any more Novofem®** until your doctor says you can. These may be signs of a blood clot.

If you're going to have surgery, make sure your doctor knows about it. You may need to stop taking Novofem® about 4 to 6 weeks before the operation, to reduce the risk of a blood clot. Your doctor will tell you when you can start taking Novofem® again.
It remains unclear if varicose veins play a role in VTE.

Other conditions you should be aware of:

- Novofem® may cause fluid retention, so if you have heart or kidney problems you should be carefully observed by your doctor. If you suffer from kidney failure you should be closely observed since it is expected that the levels of circulating active ingredients in Novofem® is increased.
- If you have asthma, epilepsy, or diabetes mellitus (high blood sugar) and these conditions have worsened during Novofem® treatment, your need for Novofem® should be reconsidered.
- If you are using Novofem® and are postmenopausal there is an increased risk of surgically confirmed gallbladder disease If you have a family history of high levels of triglycerides (fat) in your blood (familial hypertriglyceridaemia) you should know that there have been cases of serious elevations of plasma triglycerides, leading to pancreatitis (acute or chronic inflammation of the pancreas) and other complications due to estrogen therapy like Novofem®.

Conditions which need supervision

If you have (or have had) any of the following conditions, **tell your doctor.**

Your doctor may want to follow you more closely. These conditions may come back or get worse during treatment with Novofem®.

- Benign tumours of your womb (leiomyoma), deposition of uterine mucosa outside the womb (endometriosis), excessive growth of the womb lining (endometrial hyperplasia;
- History of venous thrombosis (blood clot formation) or embolisms (thromboembolic disorders) or presence of risk factors for such conditions;
- High blood pressure (hypertension);
- Liver disorders (e.g., liver adenoma - primary benign tumour of the liver);
- Diabetes with or without vascular involvement;
- Sudden hearing loss or otosclerosis;
- Migraine or (severe) headache;
- Systemic lupus erythematosus (autoimmune disease);
- Cholelithiasis (formation of stones in your gallbladder);
- Epilepsy fits) or asthma.

If you need a blood test, tell your doctor that you are taking Novofem® as estrogen can affect the results.

Tell your doctor before taking Novofem® that:

- You are on treatment for depression.
- You have had depression with previous use of estrogen and/or progesterone/progestogen-containing medicines.
- You have a substance abuse problem.

- You have an underlying psychiatric disorder such as post-traumatic stress disorder or bipolar disorder.
- You have a family history of mental disorders.
- You have a history of physical or sexual abuse.

Estrogen and/or progesterone/progestogen containing medicines, including Novofem®, may cause mood changes and depression, which may be severe. Severe depression is associated with a higher risk of suicidal thoughts/behaviour (e.g., talking about suicide, withdrawing from social contact, having mood swings, being preoccupied with death or violence, feeling hopeless about a situation, increasing use of alcohol/drugs, doing self-destructive things, personality changes) and suicide.

Stop taking Novofem® (reasons for immediate withdrawal of treatment)

If you are experiencing any of the following conditions below, stop taking Novofem®, and contact your doctor immediately:

- You notice signs of a blood clot, such as painful swelling and redness in your legs, sudden chest pain or difficulty in breathing.
- Yellowing of your skin or eyes (jaundice) or other liver problems. These may be signs of a liver disease.
- A large rise in your blood pressure while you are taking Novofem® (symptoms of high blood pressure include headache, tiredness and dizziness).
- Sudden or partial loss of your vision (eyesight).
- A migraine-type headache for the first time.
- You become pregnant.

- If you experience mood changes and depression contact your doctor for advice.

Other medicines and Novofem®

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

The following medicines may interfere with the effect of Novofem® and might lead to irregular bleeding:

- Medicines used for epilepsy (such as anticonvulsants e.g., phenobarbitone, phenytoin and carbamazepine)
- Medicines used for tuberculosis (such as rifampicin, rifabutin)
- Medicines used for HIV infections (such as nevirapine, efavirenz, ritonavir, nelfinavir)
- Medicines used to treat hepatitis C (such as telaprevir)
- Herbal products with St John's wort (*Hypericum perforatum*)
- Medicine used to treat depression (such as imipramine)
- Medicine used to treat fungal infections (such as ketoconazole).

HRT can affect the way some other medicines work:

- A medicine for epilepsy (lamotrigine), as this could increase frequency of seizures

Novofem® may have an impact on a concomitant treatment with ciclosporin (medicine used after transplant procedures).

If you have diabetes your requirement for insulin or oral anti-diabetic medicines may be increased when taking Novofem®.

Novofem® with food, drink and alcohol

See section 3.

Pregnancy, breastfeeding and fertility

Do not take Novofem® if you are pregnant or breastfeeding.

If you are pregnant or breastfeeding, think you may be pregnant or planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking Novofem®.

Driving and using machines

Novofem® can cause side effects, such as dizziness, and may affect your ability to drive or use machinery. Make sure that you know how Novofem® affects you before you drive a vehicle or operate machinery.

Novofem® contains lactose monohydrate

Novofem® tablets contain lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking Novofem®.

3. How to take Novofem®

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

Always take Novofem® as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

If you are not switching from another hormone replacement therapy you can start treatment with Novofem® on any convenient day. If you are switching

from another hormone replacement therapy ask your doctor when you should start treatment with Novofem®.

Take one tablet once a day at about the same time each day. Take the tablet in the following order:

One red tablet once a day for 16 days followed by one white tablet once a day for 12 days until all 28 tablets of a calendar pack are used. After taking the last white tablet, treatment is continued with the first red tablet of a new pack on the next day without interruption.

A menstruation-like bleeding usually occurs at the beginning of a new pack.

Take the tablet with a sufficient quantity of liquid (e.g. one glass of water).

You can take Novofem® with or without food.

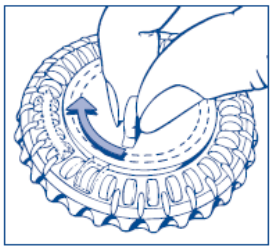
If the treatment is not giving you symptom relief after you have taken the tablet for three months you should contact your doctor.

Do not exceed the recommended dosage.

If you have the impression that the effect of Novofem® is too strong or too weak, tell your doctor or pharmacist.

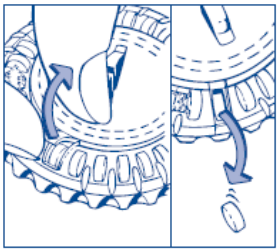
Instructions for use of the calendar pack

1. **Set the day reminder:**



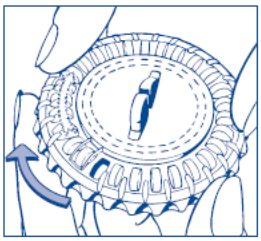
Turn the inner disc to set the day of the week opposite the little plastic tab.

2. How to take the first tablet:



Break the plastic tab and tip out the first tablet.

3. Every day:



Simply move the transparent dial clockwise one space as indicated by the arrow. Tip out the next tablet.

The transparent dial can only be turned after the tablet in the opening has been removed.

If you take more Novofem® than you should

Overdose of Novofem® could cause breast tenderness, irregular bleeding, nausea and vomiting.

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

If you forget to take Novofem®

Do not take a double dose to make up for a forgotten individual dose.

If you forget to take a tablet on one day discard the tablet and continue treatment as before. Forgetting a dose may increase the likelihood of breakthrough bleeding and spotting.

If you stop taking Novofem®

If you would like to discontinue your treatment with Novofem® for any reason, please discuss your decision with your doctor. He will explain the effects of the withdrawal of treatment and discuss other possibilities of treatment with you.

4. Possible side effects

Novofem® can have side effects.

Not all side-effects reported for Novofem® are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while taking Novofem®, please consult your doctor, pharmacist or other health care provider for advice.

If any of the following happens, stop taking Novofem® and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of your hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing; low blood pressure (paleness and coldness of skin, rapid heartbeat), feeling dizzy, sweating;
- hives, rash or itching;
- fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to Novofem®. 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:

Less frequent:

- Peripheral embolism and thrombosis (formation of blood clot)

Frequency unknown:

- Stroke (sudden weakness in your face, arm or leg, especially on one side of your body, confusion, difficulty speaking, blurred vision)
- Myocardial infarction (heart attack – death of segment of heart muscle)

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent:

- Headache and breast tenderness
- Vaginal candidiasis with fungus
- Dizziness, sleeplessness, depression
- Increased blood pressure, aggravated hypertension (high blood pressure)
- Dyspepsia (indigestion), abdominal pain, flatulence (excessive wind), nausea
- Vaginal bleeding, aggravated uterine fibroids (benign tumour of the womb)
- Oedema
- Weight increased

Less frequent:

- Migraine (severe headache)
- Changes in libido (sexual drive)
- Vomiting
- Gallbladder disease, gallstones
- Hair loss
- Muscle cramps
- Breast cancer (see below)
- Nervousness
- Vertigo (spinning feeling in your head, dizziness)
- Diarrhoea
- Bloating
- Acne
- Uterine fibroid (growth of your womb)

Frequency unknown:

- Endometrial cancer (cancer of the lining of the womb).
- Anxiety
- Visual disturbances
- Greasiness of the skin on your face (seborrhoea).
- Vaginal and genital itching.
- Endometrial hyperplasia (excessive growth of the lining of
- the womb)
- Hirsutism (excessive hair growth in areas usually not hairy)
- Decreased weight.

The following side effects have been seen in women treated with active ingredients similar to the two ingredients in Novofem®:

- Venous thromboembolism (blood clot in leg vein or pelvic vein and artery conveying blood from the heart to the lungs).
- Skin disorders: Chloasma (exceptional cases of skin pigmentation in the face), erythema multiforme, erythema nodosum (acute inflammatory skin disease), haemorrhagic eruption (severe skin disease) and vascular purpura (severe skin disease).
- Probable dementia (brain disorder) in patients over the age of 65.
- Suicidal thoughts/behaviour and suicide.

If you notice any of these side effects also those 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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
By reporting side effects, you can help provide more information on the safety of Novofem®.

5. How to store Novofem®

- Store at or below 25 ˚C.
- Store in a dry place, protected from light.
- Keep the container in the outer carton until required for use.
- Keep the container in the outer carton until required for use.
- Keep all medicines out of the reach of children.
- Do not use Novofem® after the expiry date stated on the label of the calendar dial pack and/or outer carton.
- Return all unused medicine to your pharmacist.

- Do not dispose of unused medicine in drains and sewerage systems (e.g., toilets).

6. Contents of the pack and other information

What Novofem® contains

The red film-coated tablets contain: anhydrous estradiol 1 mg (as estradiol hemihydrate).

The white film-coated tablets contain: anhydrous estradiol 1 mg (as estradiol hemihydrate) and norethisterone acetate 1 mg.

The other ingredients are:

hydroxypropylcellulose, lactose monohydrate, magnesium stearate (E572), maize starch, and talc (E553b).

Red film-coated tablets also contain: hypromellose, propylene glycol, red iron oxide (E172), talc (E553b), and titanium dioxide (E171).

White film-coated tablets also contain: hypromellose, talc (E553b), and triacetin (E1518).

What Novofem® looks like and contents of the pack

Each red tablet is film-coated, biconvex and engraved with NOVO 282.

Each white tablet is film-coated, biconvex and engraved with NOVO 283.

Novofem® is supplied in a calendar dial pack with 28 tablets.

The calendar dial pack consists of the following three parts:

- The base of coloured non-transparent polypropylene;
- The ring-shaped lid made of transparent polystyrene;
- The centre dial made of coloured non-transparent polystyrene.

Holder of certificate of registration

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This leaflet was last revised in

Date on the registration certificate: 29 July 2005

Date of text revision: 26 August 2025

Registration number

37/21.8.2/0297