

NOVARTIS

Package leaflet: Information for the user

Climesse® 2 mg / 0.7 mg film-coated tablets
(Oestradiol valerate, norethisterone)

Read all of this leaflet carefully, before you start taking 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.

What is in this leaflet:

- 1. What Climesse is and what it is used for**
- 2. What you need to know before you take Climesse**
- 3. How to take Climesse**
- 4. Possible side effects**
- 5. How to store Climesse**
- 6. Content of the pack and other information**

1. What Climesse is and what it is used for

Climesse is a Hormone Replacement Therapy (HRT). It contains two types of female hormones, an oestrogen and a progestogen. Climesse is used in postmenopausal women with at least 12 months since their last natural period.

Oestradiol valerate is identical to the natural female hormone *oestrogen*. This hormone is produced by the ovaries before the menopause. Norethisterone belongs to the group of hormones known as *progestogens*. It has effects similar to the natural female hormone progesterone, also produced by the ovaries before the menopause.

Climesse is used for:

Relief of symptoms occurring after menopause

Menopause occurs naturally in all women, usually between the ages of 45 and 55 years. It occurs also in younger women who have their ovaries removed by surgery. During the menopause, the amount of the oestrogen produced by a woman's body drops. This can cause symptoms such as hot face, neck and chest ("hot flushes"), sleep problems, irritability and depression. Some women also have problems with urine control or dryness of the vagina, which may cause discomfort during or after sexual intercourse.

Climesse alleviates these symptoms after menopause. You will only be prescribed Climesse if your symptoms seriously hinder your daily life.

Prevention of osteoporosis

After the menopause some women may develop fragile bones (osteoporosis). You should discuss all available options with your doctor.

If you are at an increased risk of fractures due to osteoporosis and other medicines are not suitable for you, you can take Climesse to prevent osteoporosis after menopause.

2. What you need to know before you take Climesse

Medical history and regular check-ups

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. He/she should tell you what kind of changes in the breast you should look out for and may advise you to have a breast X-ray (a *mammogram*).

Once you have started on Climesse, you should see your doctor for regular check-ups (at least once a year). At these check-ups, discuss with your doctor the benefits and risks of continuing with Climesse.

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

Do not take Climesse

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 Climesse,

- 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 severe **kidney disease**;
- 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 oestradiol valerate or norethisterone or any of the other ingredients of Climesse (listed in section 6);
- if you are **pregnant**, or think you might be.

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

When to take special care with Climesse

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 Climesse. 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 an **oestrogen-sensitive cancer** (such as having a mother, sister or daughter or grandmother who has had breast cancer);
- **High blood pressure**

- **A liver disorder**, such as a benign liver tumour (*liver adenoma*)
- **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
- **Hypothyroidism** (a condition in which your thyroid gland fails to produce enough thyroid hormone and for which you are treated with thyroid hormone replacement therapy)
- **Hereditary angioedema** or episodes of rapid swelling of the hands, feet, face, lips, eyes, tongue, throat (airway blockage) or digestive tract.

Stop taking Climesse 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 Climesse' section
- Yellowing of your skin or the whites of your eyes (**jaundice**). These may be signs of a liver disease
- A large **rise in your blood pressure** (symptoms may be headache, tiredness, dizziness)
- Migraine-like headaches which happen for the first time, with or without disturbed vision. Headaches like these can be an early sign of a stroke. If you have already had a stroke, talk with your doctor about whether the benefits of the treatment outweigh the possibly increased risk.
- If you get pain in your chest that spreads to your arm or neck. This pain may be a sign of heart disease.
- If you become pregnant
- 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: Climesse 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

Excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer)

Taking oestrogen-only HRT will increase the risk of excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the womb lining (endometrial cancer).

The progestogen in Climesse protects you from this extra risk.

In women who still have a womb and who are not taking HRT, on average, 5 in 1000 will be diagnosed with endometrial cancer between the ages of 50 and 65.

For women aged 50 to 65 who still have a womb and who take oestrogen-only HRT, between 10 and 60 women in 1000 will be diagnosed with endometrial cancer (i.e. between 5 and 55 extra cases), depending on the dose and for how long it is taken.

Irregular bleeding

You may have irregular bleeding or drops of blood (spotting) during the first 3-6 months of taking Climesse. However, if the irregular bleeding:

- carries on for more than the first 6 months
- starts after you have been taking Climesse for more than 6 months
- carries on after you have stopped taking Climesse
- if you have painful menstrual periods

See your doctor as soon as possible.

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.

Compare

Women aged 50 to 79 who are not taking HRT, on average, 9 to 17 in 1000 will be diagnosed with breast cancer over a 5-year period. For women aged 50 to 79 who are taking oestrogen-progestogen HRT over 5 years, there will be 13 to 23 cases in 1000 users (i.e. an extra 4 to 6 cases).

Regularly check your breasts. See your doctor if you notice any changes such as:

- dimpling of the skin
- change in the nipple
- any lump you can see or feel

Ovarian cancer

Ovarian cancer is rare. A slightly increased risk of ovarian cancer has been reported in women taking HRT for at least 5 to 10 years.

Women aged 50 to 69 who are not taking HRT, on average about 2 women in 1000 will be diagnosed with ovarian cancer over a 5-year period. For women who have been taking HRT for 5 years, there will be between 2 and 3 cases per 1000 users (i.e. up to 1 extra case).

Effect of HRT on heart and circulation

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/m²)
- 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 an other organ
- you have systemic lupus erythematosus (SLE)
- you have cancer.

For signs of a blood clot, see “Stop taking Climesse and see a doctor immediately”.

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.

For women in their 50s who have been taking oestrogen-progestogen HRT for over 5 years, there will be 9 to 12 cases in 1000 users (i.e. an extra 5 cases).

Heart disease (heart attack)

There is no evidence that HRT will prevent a heart attack.

Women over the age of 60 years who use oestrogen-progestogen HRT are slightly more likely to develop heart disease than those not taking any HRT.

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.

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.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription, herbal medicines or other natural products. Some medicines may interfere with the effect of Climesse. This might lead to irregular bleeding. This applies to the following medicines:

- medicines for **epilepsy** (such as phenobarbital, phenytoin, carbamazepine),
- medicines for **tuberculosis** (such as rifampicin, rifabutin),
- medicines for **HIV infection** (such as nevirapine, efavirenz, ritonavir, teleprevir, nelfinavir),
- herbal remedies containing **St John's wort** (*Hypericum perforatum*).

Laboratory tests

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

Pregnancy and breast-feeding

Climesse is for use in postmenopausal women only. If you become pregnant, stop taking Climesse and contact your doctor. Do not take Climesse if you are pregnant or while you are breast-feeding.

Driving and using machines

Climesse has no known effects on the ability to drive and use machines.

Climesse contains lactose

Lactose is a form of sugar. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking Climesse.

3. How to take Climesse

Always use this medicine exactly as your doctor has told you. 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. During the treatment your doctor may adjust the dose according to your individual needs.

When to start treatment

Climesse is a continuous combined HRT. This means that *oestrogen* and *progestogen* are given continuously.

- **If you are not currently taking HRT, or if you have been using a continuous combined HRT** (in which *oestrogen* and *progestogen* are given every day without interruption), you can start to take Climesse on any convenient day.
- **If you are changing from a sequential HRT or cyclic HRT** (in which the *progestogen* is added for 12-14 days of the cycle), you should complete your treatment cycle and then start taking Climesse immediately.

How to take Climesse

Take one tablet each day by following the sequence of numbers and arrows on the calendar pack.

Swallow your tablets whole with a glass of water.

The pack has been designed specifically to help you take the tablets correctly.

Write the name of the day you take your first tablet in the box below. For example, if you start your tablets on a Wednesday, then write “Wednesday” in the box. This day will also be the day on which you will take **tablets 8, 15 and 22**. This will help you check that you have taken each tablet on the right day.

| |
|----------------------------|
| Write your start day here: |
|----------------------------|

When you finish one blister pack, start the new one the next day whether or not you experience bleeding. This will normally be the same day of the week as you started the previous blister pack. Do not take a break between blister packs unless your doctor tells you.

The tablets are best taken at the same time every day; try to get into a routine.

Follow your doctor’s instructions as to how and when you should take Climesse tablets and never change the dose yourself, however well you feel.

If you are unsure about how much medicine to take or when to take it, ask your doctor or pharmacist.

How long to take Climesse

From time to time, you will need to discuss with your doctor the possible risks and benefits associated with Climesse and whether you still need the treatment. It is important that you take the lowest possible effective dose and only for as long as needed.

If you have taken more Climesse than you should

Contact your doctor or pharmacist immediately if you have taken too much Climesse.

If you forget to take Climesse

If you forget to take a tablet at your usual time, try to take it within 12 hours. If this is not possible, leave the forgotten tablet and continue to take the remaining tablets at the usual time.

If you need to have surgery

If you are going to have surgery, tell the surgeon that you are taking Climesse. You may need to stop taking Climesse 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 Climesse again.

If you stop taking Climesse

Stopping Climesse may increase the risk of breakthrough bleeding or spotting. If this occurs after you stop treatment, contact your doctor immediately. Your doctor will need to work out the reason for this. After a long treatment break, consult your doctor before starting to take Climesse again.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

The following diseases are reported more often in women using HRT compared to women not using HRT:

- breast cancer
- abnormal growth or cancer of the lining of the womb (endometrial hyperplasia or cancer)
- ovarian cancer
- blood clots in the veins of the legs or lungs (venous thromboembolism)
- heart disease
- stroke
- probable memory loss if HRT is started over the age of 65

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

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

Some effects could be serious

These symptoms need immediate medical attention:

- Unexpected vaginal bleeding or spotting (breakthrough bleeding) after taking Climesse for some time, or after you stop treatment
- Painful menstrual periods
- Painful swelling and redness of the legs
- Sudden chest pain
- Difficulty in breathing
- Pain in your chest that spreads to your arm or neck
- Yellowing of the eyes and face (jaundice)
- Rapid increase in your blood pressure
- Unexplained migraine-like headaches
- Breast changes, including dimpling of the breast skin, changes in the nipple, lumps that you can see or feel.

Stop taking Climesse and tell your doctor immediately if you get any of the effects mentioned above.

Check the risks to be aware of with HRT in general in section 2, *When to take special care with Climesse*.

Other side effects

In addition, the following side effects have been reported with Climesse:

- Breast tension and pain, enlargement of the breasts, breast cancer.
- Discharge from the vagina, irregular bleeding or spotting.
- Headache, dizziness, vertigo, tiredness or irritability, changes in sexual desire, depression.
- Increased blood pressure, palpitations (sensation of fluttering in the chest), tender or painful veins (signs of thrombophlebitis), fluid retention, nose bleeds.
- Indigestion, wind, nausea, vomiting, abdominal pain and bloating, problems with your gall bladder (biliary stasis).
- General itching, hair loss, hives and skin rash, acne.
- Glucose intolerance which can make you sweat or feel faint after eating.
- Weight gain, leg cramps.
- Fibroids (benign growth in the uterus).
- Pain in extremity

The following side effects have been reported with other HRTs:

- gallbladder disease,
- various skin disorders:
 - discoloration of the skin specially of face or neck known as “pregnancy patches” (chloasma)
 - painful reddish skin nodules (erythema nodosum)
 - rash with target-shaped reddening or sores (erythema multiforme)
- decline in memory or mental ability
- diarrhoea
- dry eyes and contact lens discomfort

If you get any side effects talk to your doctor or pharmacist. This includes any side effects not listed in this leaflet.

5. How to store Climesse

- Keep out of the sight and reach of children.
- Do not take this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
- Do not store above 25°C.
- Store in the original package.
- Do not throw away any medicine via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. This measure will help to protect the environment.

6. Contents of the pack and other information

What Climesse contains

- The active substances are 2 mg oestradiol valerate (equivalent to 1.528 mg oestradiol) and 0.7 mg norethisterone.
- The other ingredients are lactose monohydrate, maize starch, povidone, purified water, talc, magnesium stearate, hypromellose, polyethylene glycol, iron oxide red (E172), titanium dioxide (E171).

What Climesse looks like and contents of the pack

The Climesse 2 mg/0.7 mg film-coated tablets are pink tablets with “OG” on one side and “CG” on the other.

Climesse is available in cartons of 28 tablets (1 blister pack), 84 tablets (3 blisters packs) or 98 tablets. Not all pack sizes may be marketed in your country.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Novartis Pharmaceuticals UK Ltd, Frimley Business Park, Frimley, Camberley, Surrey GU16 7SR.

Manufacturer

Novartis Pharmaceuticals UK Ltd, Wimblehurst Road, Horsham, West Sussex, RH12 5AB
United Kingdom and Frimley Business Park, Frimley, Camberley, Surrey, GU16 7SR, England, United Kingdom.

This medicinal product is authorised in the Member States of the EEA under the following name

Germany: Merigest

United Kingdom: Climesse

This leaflet was revised in February 2014.

If you would like any more information, or would like the leaflet in a different format, please contact Medical Information at Novartis Pharmaceuticals UK Ltd, telephone number 01276 698370

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