

PACKAGE LEAFLET: INFORMATION FOR THE USER
ZUMENON® 2MG TABLETS
(estradiol (as hemihydrate))

Your medicine is known as the above but will be referred to as Zumenon throughout the remainder of this leaflet.

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. 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 Zumenon is and what it is used for**
- 2. What you need to know before you use Zumenon**
- 3. How to use Zumenon**
- 4. Possible side effects**
- 5. How to store Zumenon**
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1. WHAT ZUMENON IS AND WHAT IT IS USED FOR

Zumenon is a Hormone Replacement Therapy (HRT). It contains the female hormone oestrogen. Zumenon is used in postmenopausal women with at least 6 months since their last natural period and women switching from standard (cyclic or sequential) HRT on the advice of their doctor.

Zumenon is used for:

Relief of symptoms occurring after menopause.

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").

Zumenon alleviates these symptoms after menopause. You will only be prescribed Zumenon 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 use Zumenon to prevent osteoporosis after menopause.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE ZUMENON

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.

Once you have started on Zumenon 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 Zumenon.

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

Do not take Zumenon

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 Zumenon, Do not take Zumenon

- 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 oestradiol or any of the other ingredients of Zumenon (listed in section 6 Further information)

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

When to take special care with Zumenon

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 Zumenon. 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
- hereditary and acquired angioedema

Stop taking Zumenon 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 Zumenon' section
- yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a liver disease
- swollen face, tongue and/or throat and/or difficulty swallowing or hives, together with difficulty breathing which are suggestive of an angioedema
- a large rise in your blood pressure (symptoms may be headache, tiredness, dizziness).
- migraine-like headaches which happen for the first time.
- 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: Zumenon 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).

Taking a progestogen in addition to the oestrogen for at least 12 days of each 28 day cycle protects you from this extra risk.

So your doctor will prescribe a progestogen separately if you still have your womb. If you have had your womb removed (a hysterectomy), discuss with your doctor whether you can safely take this product without a progestogen. 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.

Unexpected bleeding

You will have a bleed once a month (so-called withdrawal bleed) while taking Zumenon. But, if you have unexpected bleeding or drops of blood (spotting) besides your monthly bleeding, which:

- carries on for more than the first 6 months
- starts after you have been taking Zumenon more than 6 months
- carries on after you have stopped taking Zumenon

see your doctor as soon as possible

Breast cancer

Evidence shows that taking combined oestrogen-progestogen and or oestrogen-only hormone replacement therapy (HRT) increases the risk of breast cancer. The extra risk depends on how long you use HRT. The additional risk becomes clear within 3 years of use. After stopping HRT the extra risk will decrease with time, but the risk may persist for 10 years or more if you have used HRT for more than 5 years.

Compare

Women aged 50 to 54 who are not taking HRT, on average, 13 to 17 in 1000 will be diagnosed with breast cancer over a 5-year period.

For women aged 50 who start taking oestrogen-only HRT for 5 years, there will be 16-17 cases in 1000 users (i.e. an extra 0 to 3 cases).

For women aged 50 who start taking oestrogen-progestogen HRT for 5 years, there will be 21 cases in 1000 users (i.e. an extra 4 to 8 cases).

Women aged 50 to 59 who are not taking HRT, on average, 27 in 1000 will be diagnosed with breast cancer over a 10-year period.

For women aged 50 who start taking oestrogen-only HRT for 10 years, there will be 34 cases in 1000 users (i.e. an extra 7 cases).

For women aged 50 who start taking oestrogen-progestogen HRT for 10 years, there will be 48 cases in 1000 users (i.e. an extra 21 cases).

- **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.

Ovarian cancer

Ovarian cancer is rare - much rarer than breast cancer.

The use of oestrogen-only or combined oestrogen-progestogen 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, on average 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).

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 another organ
- you have systemic lupus erythematosus (SLE)
- you have cancer.

For signs of a blood clot, see "Stop taking Zumenon and see a doctor immediately".

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).

For women in their 50s who have had their womb removed and have been taking oestrogen-only HRT for over 5 years, there will be 5 to 8 cases in 1000 users (i.e. 1 extra case).

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.

For women who have had their womb removed and are 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.

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.

Other medicines and Zumenon

Some medicines may interfere with the effect of Zumenon.

This might lead to irregular bleeding. This applies to the following medicines:

- Medicines for **epilepsy** (such as phenobarbital, phenytoin and carbamazepine)
- Medicines for **tuberculosis** (such as rifampicin, rifabutin)
- Herbal remedies containing **St John's Wort** (Hypericum perforatum).