

Package leaflet: Information for the patient

Fematab 1mg & 2mg film-coated tablets

estradiol

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, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

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

1. What Fematab is and what it is used for

What Fematab is

The name of your medicine is Fematab. It belongs to a group of medicines called Hormone Replacement Therapy (HRT). Fematab contains a form of the female oestrogen hormone called estradiol.

What Fematab is used for

Fematab is used in postmenopausal women with at least 6 months since their last natural period.

• For the relief of the 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"). Fematab alleviates these symptoms after menopause. You will only be prescribed Fematab if your symptoms seriously hinder your daily life.

• To prevent thinning of the bones (osteoporosis) in post menopausal women

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 Fematab to prevent osteoporosis after menopause. Fematab is suitable for postmenopausal women, or if your doctor has advised you to switch from another type of HRT. It can not be used as a form of contraception. If you need to use contraception, you should use a non-hormonal method such as a condom or the coil.

How Fematab works

Fematab is known as an "oestrogen-only continuous" HRT product. This is because you are taking an oestrogen every day without a break. The oestrogen (estradiol) in Fematab replaces that which you produced in your ovaries from puberty until your menopause.

- The estradiol controls the signs of your menopause and gives protection against osteoporosis.
- Women who still have a womb should normally take some form of a progestagen hormone as well, because taking an oestrogen alone can cause problems due to a thickening of the womb lining. The progestagen prevents a build up of your womb lining.

2. What you need to know before you take Fematab

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 taking (or restart) HRT, your doctor should ask about you 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 Fematab, 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 to take Fematab.

Screening tests including appropriate imaging tools, such as mammography (an X-ray of the breasts), should be performed according to current medical recommendations. Your doctor will tell you how often these tests should be performed.

DO NOT take Fematab

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 Fematab:

- 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 **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 your legs (a deep vein thrombosis), or your 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 **angina, heart attack or stroke**

- 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 **estradiol** or any of the other ingredients of Fematab (listed in Section 6 Further information)

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

Warnings and Precautions

Tell your doctor if you have ever had any of the following problems, before you start the treatment, as this may return or become worse during treatment with Fematab. If so, you should see your doctor more often for check-ups:

- fibroids inside your womb
- growth of the womb lining outside the 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 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 Fematab 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 Fematab’ 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: Fematab 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 progestagen 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 progestagen 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 progestagen.

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

Unexpected bleeding (if you have a uterus and are also taking a progestagen)

You will have a bleed once a month (so-called withdrawal bleed) while taking Fematab and a progestagen. 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 Fematab more than 6 months
- carries on after you have stopped taking Fematab

see your doctor as soon as possible.

Unexpected bleeding (if you do NOT have a uterus)

You should not have any bleeding. But, if you do have any bleeding, **see your doctor as soon as possible.**

Breast cancer

Evidence shows that taking combined oestrogen-progestagen 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-progestagen 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-progestagen 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

Additionally, you are advised to join mammography screening programs when offered to you. For mammogram screening, it is important that you inform the nurse/healthcare professional who is actually taking the x-ray that you use HRT, 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.

Ovarian cancer

Ovarian cancer is rare – much rarer than breast cancer. The use of oestrogen-only or combined oestrogen-progestagen 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).

Make sure that you:

- go for regular cervical smear tests

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.

These blood clots can be serious and if one travels to the lungs (a pulmonary embolism or PE), 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 had a blood clot before
- 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 Fematab 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-progestagen 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-progestagen 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.

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.

Tell your doctor if you have or have had any of the following medical conditions. Your doctor will have to monitor you more closely:

- **heart disease**
- **kidney impairment**
- **higher than normal levels of certain blood fats (hypertriglyceridaemia)**

Other medicines and Fematab

Some medicines may interfere with the effect of Fematab. 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).
- Medicines for **HIV infections** (such as nevirapine, efavirenz, ritonavir and nelfinavir)
- Herbal medicines containing **St John's Wort** (*Hypericum perforatum*)
- Medicines for Hepatitis C virus (HCV) (such as combination regimen ombitasvir/paritaprevir/ritonavir with or without dasabuvir as well as a regimen with glecaprevir/pibrentasvir) may cause increases in liver function blood test results (increase in ALT liver enzyme) in women using CHCs containing ethinylestradiol. Fematab contains estradiol instead of ethinylestradiol. It is not known whether an increase in ALT liver enzyme can occur when using Fematab with this HCV combination regimen. Your doctor will advise you.

Dangerously high blood levels of the following medicines may occur when you take Fematab:

- tacrolimus and cyclosporine – used, for example, for organ transplants
- fentanyl – a painkiller
- theophylline – used for asthma and other breathing problems

Therefore, careful drug monitoring for quite some time and a dosage decrease may become necessary.

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.

Laboratory tests

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

Fematab with food and drink

Fematab can be taken with or without food.

Pregnancy and breast-feeding

Fematab is for use in postmenopausal women only. If you become pregnant, stop taking Fematab and contact your doctor.

Driving and using machines

The effect of Fematab on driving or using machinery has not been studied. An effect is unlikely.

Fematab contains lactose (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

This includes some rare disorders passed down in families that affect how the body uses lactose (such as total lactase deficiency or glucose-galactose malabsorption).

3. How to take Fematab

Always take this medicine exactly as your doctor 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 symptoms for as short as necessary. Speak to your doctor if you think this dose is too strong or not strong enough.

When to start taking Fematab

You can start taking Fematab on any convenient day if:

- you are currently not taking any other HRT product
- you are switching from a "continuous combined" HRT product. This is when you take a tablet or use a patch every day that contains both an oestrogen and a progestagen.

You start taking Fematab the day after you finish the pack for your current progestagen phase if:

- you are switching from a "cyclic" or "sequential" HRT product. This is where you take an oestrogen tablet or use a patch for the first part of your cycle, followed by both an oestrogen and a progestagen for up to 14 days.

Unexpected bleeding (if you have a uterus and are also taking a progestagen)

You may have irregular bleeding or drops of blood (spotting) during the first 3-6 months of taking Fematab and a progestagen.

However, if the irregular bleeding:

- carries on for more than the first 6 months
- starts after you have been taking Fematab for more than 6 months
- carries on after you have stopped taking Fematab you must see your doctor.

Unexpected bleeding (if you do NOT have a uterus)

You should not have any bleeding. But, if you do have any bleeding, you must see your doctor.

Taking this medicine

Generally, your doctor will start you on the 1mg tablet and then move you up to the 2mg tablet if necessary.

- Swallow the tablet with water.
- You can take your tablet with or without food.
- Try to take your tablet at the same time each day.

This will make sure that there is a constant amount of the medicine in your body. This will also help you remember to take your tablets.

Women who still have their womb should also normally take a progestagen hormone for up to 14 days of each month.

- Take one tablet every day, without a break between packs. The blisters are marked with the days of the week to make it easier for you to remember when to take your tablets.

How much to take

If you are taking Fematab to prevent osteoporosis, your doctor will adjust the dose to suit you. It will depend on your bone mass.

If you need to have surgery

Tell your doctor if you are going to have surgery and tell your surgeon that you are taking Fematab. You may need to stop taking Fematab 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 Fematab again.

If you take more Fematab than you should

If you (or someone else including a child) take too many Fematab tablets, you may feel sick (nauseous), sleepy, dizzy or be sick (vomit).

If you are a woman taking Fematab then you may experience withdrawal bleeding. Treatment should be symptomatic. If you are worried, talk to your doctor for advice.

If you forget to take Fematab

- If you forget to take today's tablet and it is less than 12 hours late, take it as soon as you remember. Take the next day's tablet at the normal time.
- If it is more than 12 hours since you should have taken your tablet, miss this tablet out. Take the next day's tablet at the usual time and continue taking your tablets as normal.
- Do not take a double dose to make up for a forgotten dose.
- If you miss a tablet, it is more likely that you will have irregular bleeds.

If you stop taking Fematab

Do not stop taking/using Fematab without first talking to your doctor.

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

4. Possible side effects

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

Stop taking Fematab and see a doctor straight away or go to hospital, if you notice or suspect any of the following.

You may need urgent medical treatment:

- swollen face, lips or tongue often with breathing problems (angioedema)
- if you get painful swelling in your leg, sudden chest pain or have difficulty breathing. These could be signs of a blood clot
- an unexpected headache, which could be a sign of high blood pressure
- sudden problems with your vision or an unexpected migraine
- breast cancer (you may notice dimpling of the skin, changes in the nipple or lumps that you can see or feel)
- abnormal or unexpected vaginal bleeding (for more details on what bleeding might be expected please read "Endometrial cancer" in "Safety of HRT"). These could be signs of a thickening of the lining of the womb (endometrial hyperplasia)
- angina, heart attack or stroke
- persistent pelvic and abdominal pain and bloating, difficulty eating, feeling full quickly which could be signs of ovarian cancer
- yellowing of the skin or eyes (jaundice) or other liver changes
- you become pregnant.

If you notice or suspect any of the above, stop taking Fematab and see a doctor straight away or go to hospital.

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.

The following side effects may happen with this medicine:

Common (may affect up to 1 in 10 patients)

- weight changes (up or down)
- headache
- abdominal pain
- feeling sick (nausea)
- rash, itching
- abnormal uterine bleeding
- vaginal bleeding or spotting

Uncommon (may affect up to 1 in 100 people)

- vaginal thrush
- hypersensitivity (allergic) reaction such as skin rash, itching, skin redness
- feeling depressed

- feeling dizzy
- visual disturbances
- palpitations – heart pounding and racing
- indigestion
- gall bladder disease
- painful, reddish skin nodules (erythema nodosum)
- hives
- painful or tender breasts
- your body holding onto more water than usual (fluid retention).

Rare (may affect up to 1 in 1,000 people)

- anxiety
- change in your sex drive
- migraine
- not being able to wear your contact lenses
- feeling bloated
- being sick (vomiting)
- excessive hair growth on face or body
- acne
- muscle cramps
- painful periods
- a change in your vaginal discharge
- pre-menstrual tension (PMT)
- swollen breasts
- tiredness

The following side effects have been reported with other oestrogen-only HRTs:

- breast cancer
- benign or malignant tumours which may be affected by levels of oestrogens such as cancer of the womb lining, ovarian cancer (see section 2 for more information)
- increase in size of uterine fibroids (leiomyoma)
- worsening of fits (epilepsy)
- probable increase in dementia over the age of 65. HRT will not prevent dementia (the gradual loss of mental abilities such as thinking, remembering and reasoning). In one study of women who started using “combined” HRT after the age of 65, there was a small increase in the risk of dementia.
- muscle twitches you cannot control (chorea)
- stroke
- blood clots in the arteries (arterial thromboembolism) such as angina or heart attack (myocardial infarction)
- blood clots in the veins (venous thromboembolism) such as in your legs (a deep vein thrombosis) or your lungs (pulmonary embolism)
- inflammation of the pancreas (pancreatitis) in women with pre-existing high levels of certain blood fats (hypertriglyceridaemia)
- a condition where gastric juices, containing acid, travel back from the stomach into the oesophagus (gastroesophageal reflux disease) symptoms include heartburn
- liver disorders, sometimes with yellowing of the skin (jaundice)
- swelling of the skin around the face and the throat. This may cause difficulty in breathing (angioedema)
- various skin disorders: purplish patches or spots on the skin (vascular purpura), discoloration of the skin known as “pregnancy patches” (chloasma), rash with target-shaped reddening or sores (erythema multiforme)
- urinary incontinence
- painful/lumpy breasts (fibrocystic breast changes)

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects:

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Website: www.hpra.ie
By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Fematab

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 outer carton and blister strip. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

You should keep the blister strip in the outer carton.

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 Fematab contains

The active substance is estradiol hemihydrate.

Fematab 1mg: Each tablet contains 1mg of estradiol (as the hemihydrate)

Fematab 2mg: Each tablet contains 2mg of estradiol (as the hemihydrate)

The other ingredients in the tablet core are lactose monohydrate, hypromellose, maize starch, colloidal anhydrous silica and magnesium stearate.

The ingredients in the coating used in the 1mg tablet are titanium dioxide (E171), hypromellose, macrogol 400.

The ingredients in the coating used in the 2mg tablet are titanium dioxide (E171), yellow, black and red iron oxides (E172), hypromellose, macrogol 400 and talc.

What Fematab looks like and contents of the pack

The 1mg tablets are white and the 2mg tablets are brick red. Both tablets have '379' marked on one side. Fematab is available as a one month calendar pack (28 tablets).

Marketing Authorisation Holder and Manufacturer

The Marketing Authorisation Holder is:

Mylan IRE Healthcare Limited, Unit 35/36, Grange Parade, Baldoyle Industrial Estate, Dublin 13.

Fematab is made by:

Abbott Biologicals BV, 8121 AA Olst, The Netherlands.

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