Package Leaflet: Information for the user

Tibolone 2.5 mg tablets
Tibolone

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. See section 4.

What is in this leaflet

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

1. What Tibolone tablets are and what they are used for

Tibolone tablets are a Hormone Replacement Therapy (HRT). They contain tibolone, a synthetic sex hormone. Tibolone is used in postmenopausal women with at least 12 months since their last natural period.

Tibolone is used for the relief of symptoms occurring after menopause
During the menopause, the amount of oestrogen produced by a woman's body drops. This can cause symptoms such as hot face, neck and chest ("hot flushes"). Tibolone alleviates these symptoms after the menopause. You will only be prescribed Tibolone if your symptoms seriously hinder your daily life.

2. What you need to know before you take Tibolone tablets

Medical History and regular check-ups
The use of HRT or Tibolone carries risks that 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 or Tibolone may be different. Please talk to your doctor.

Before you start taking (or restart) HRT or Tibolone, 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 Tibolone, 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 Tibolone.

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

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 medicine 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.

Do not take Tibolone tablets 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 Tibolone.

- 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 to tibolone or any of the other ingredients of these tablets (listed in section 6)
- If you are pregnant or think you might be pregnant
- If you are breastfeeding

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

Warnings and precautions
Talk to your doctor or pharmacist before taking Tibolone. Tell your doctor if you have or ever had any of the following problems, before you start the treatment, as these may return or become worse during treatment with Tibolone. If so, you should see your doctor more often for check-ups:
- fibroids inside your womb
- growth of the 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 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 (triglycerides) in your blood
- problems with your heart
- problems with your kidneys

Stop taking Tibolone and see a doctor immediately if you notice any of the following when taking HRT or Tibolone:
- any of the conditions mentioned in the "Do not take Tibolone " 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
- 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: Tibolone 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)
Observation studies have consistently shown that users of Tibolone have an increased risk for diagnosis of cancer of the lining of the womb. This risk rises with increasing duration of treatment.

Irregular bleeding
You may have irregular bleeding or drops of blood (spotting) during the first 3-6 months of taking Tibolone. But if the bleeding or spotting:
- Carries on for more than the first 6 months
- Starts after you have been taking Tibolone for more than 6 months
- Carries on even after you've stopped taking Tibolone

➔**See your doctor as soon as possible.**

Breast Cancer
Evidence shows that taking tibolone increases the risk of breast cancer. The extra risk depends on how long you use tibolone. In studies with HRT, after stopping HRT the extra risk decreased with time, but the risk may persist for 10 years or more when women have used HRT for more than 5 years. No data for persistence of risk after stopping are available for tibolone but a similar pattern cannot be ruled out.

Compare
Women taking Tibolone have a lower risk than women using combined HRT and a comparable risk with oestrogen-only HRT.

Regularly check your breasts. See your doctor if you notice any changes such as:
- Dimpling or sinking 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, 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).
With use of Tibolone , the increased risk of ovarian cancer is similar to other types of HRT.

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 apply to you:
- you use oestrogens
- 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'). The risk for a thromboembolic disease may be temporarily increased due to persistent immobilisation (such as being bedridden, leg in a cast), severe injuries or long-lasting surgery. In patients using HRT, like with all patients, precautionary actions after surgery should carefully be followed to prevent venous thromboembolic disease.
- 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 Tibolone and see a doctor immediately".

Compare
Of 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.
Of 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).

With use of Tibolone , the increased risk of getting a blood clot in a vein is lower than with other types of HRT.

Heart disease (heart attack)
There is no evidence that HRT or Tibolone will prevent a heart attack.
Women over the age of 60 who use oestrogen-progestogen HRT are slightly more likely to develop heart disease than those not taking any HRT. As the risk of heart disease strongly depends on age, the number of extra cases of heart disease is very low in healthy women close to menopause, but will rise with more advanced age.

There is no evidence to suggest that the risk of myocardial infarction with tibolone is different to the risk of other 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
Of women in their 50s who are not taking tibolone - on average, over a 5-year period, 3 in 1000 would be expected to have a stroke. Of women in their 50s who are taking tibolone, the figure would be 7 in 1000 (i.e. an extra 4 cases).

Of women **in their 60s** who are not taking tibolone – on average, over a 5-year period, **11 in 1000** would be expected to have a stroke.
Of women **in their 60s** who are taking tibolone, the figure would be **24 in 1000** (i.e. an extra 13 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.
- Treatment with tibolone results in changes in cholesterol values.
- Patients with cardiac or renal dysfunction: Oestrogens may cause fluid retention, and therefore patients with cardiac or renal dysfunction should be carefully observed.
- Patients with lipid metabolic disorder (hypertriglyceridaemia): Women with pre-existing hypertriglyceridaemia should be followed closely during therapy with tibolone, since rare cases of large increases of plasma triglycerides leading to pancreatitis have been reported with oestrogen therapy in this condition.

Other medicines and Tibolone
Some medicines may interfere with the effect of Tibolone. This might lead to irregular bleeding. This applies to the following medicines:
- Medicines to prevent blood clotting (such as warfarin)
- Medicines for epilepsy (such as phenobarbital, phenytoin and carbamazepine)
- Medicines for tuberculosis (such as rifampicin or rifabutin)
- Herbal remedies containing St John's Wort (Hypericum perforatum)

HRT can affect the way some other medicines work: Concomitant use with tibolone can increase the effect of anticoagulants (medicines against blood clotting).

The concomitant use with tibolone can have an influence on medicines with active substances (e.g. midazolam) that are metabolised by certain enzymes (so called cytochrome-P450-enzymes).

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. Your doctor will advise you.

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

Pregnancy and breast-feeding
Don't take Tibolone when you are pregnant or breastfeeding.

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

Driving and using machines
Tibolone has no known effect on the ability to drive or use machines.

Tibolone tablets contain lactose monohydrate
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Tibolone tablets

Always take Tibolone exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

How much Tibolone should you take and how often
Your doctor will aim to prescribe the lowest dose to treat your symptoms for as short a time as necessary. Speak to your doctor if you think this dose is too strong or not strong enough.

Unless otherwise prescribed by the doctor, the usual dose is: One tablet daily after a meal, preferably at the same time each day.

Do not take a progestogen medicine in addition to Tibolone.

How to take Tibolone
You should take the tablets with a little water or other beverage, preferably at the same time every day.

What to take into account when you start treatment with Tibolone
If your menopause occurred naturally, you should start taking Tibolone at the earliest 1 year after your last natural monthly bleeding. If your ovaries have been removed by surgery, you can start taking Tibolone immediately.

If you wish to start taking Tibolone and have had irregular or unexpected vaginal bleeding, please ensure that you contact the doctor who is treating you before starting Tibolone treatment, so that any malignant disease can be excluded.

If you wish to switch over to Tibolone from a medicine that contains an oestrogen and a progestogen, please ask your doctor what you should take into account.

How long should you take Tibolone
Your doctor will aim for the treatment to be as short as possible.

Usually, an improvement of symptoms is achieved within a few weeks.

If you take more Tibolone tablets than you should
If you have taken more Tibolone than you should, please contact your doctor or pharmacist immediately.

Toxic symptoms are unlikely even if several tablets are taken at the same time. In case of acute overdose, nausea, vomiting and withdrawal bleeding may occur. Contact your doctor so that these symptoms can be treated.

If you forget to take Tibolone tablets
If you forget to take a tablet at the usual time, you should take it as soon as possible unless more than 12 hours have passed since the time at which it was due. In this case, skip the missed tablet and take the next tablet at the usual time. Do not take a double dose to make up for a forgotten tablet.

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

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

4. Possible side effects

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

Serious side effects
Stop taking Tibolone and see a doctor immediately if you notice any of the following when taking HRT or Tibolone:
- any of the conditions mentioned in the "Do not take Tibolone " section (section 2 above)
- 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
- 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)" in section 2 above.

Other side effects

Common side effects that were observed in clinical studies (may affect up to 1 in 10 women):
- vaginal bleeding or spotting
- stomach pain
- weight gain
- breast pain
- unusual hair growth
- vaginal problems such as more secretions, itching and irritation
- thickening of the lining of the womb
- vaginal infection with fungi (e.g. candidiasis)
- pelvic pain
- tissue changes of the cervix
- inflammation of labia and vagina (so called 'vulvovaginitis')
- abnormalities in the smear of the cervix.

Uncommon side effects (may affect up to 1 in 100 women):
- acne
- painful nipples or breasts
- infections with fungi.

Other side effects that were reported with Tibolone since marketing:
- dizziness, headache, migraine
- depression
- skin problems such as rash or itching
- loss of vision or blurred vision
- tummy or intestinal upset
- fluid retention
- joint pain or muscle pain
- changes in liver tests.

There have been reports of cancer of the lining of the womb, breast cancer and stroke in women using Tibolone (see "Warnings and precautions" in section 2).

The following 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 "What you need to know before you take Tibolone".

The following side effects have been reported with other HRTs:
- gall bladder disease
- various skin disorders:
  - discolouration 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)
  - skin haemorrhages (vascular purpura)

Talk to your doctor if you have irregular vaginal bleeding or spotting or if you get one of the side effects mentioned above or if they get worse.

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Tibolone tablets

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

Do not use Tibolone after the expiry date which is stated on the carton/blister pack after EXP: The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions. Do not use this medicine if you notice the blister pack is damaged.
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 Tibolone tablets contain
The active substance is tibolone.
One film-coated tablet contains 2.5 mg tibolone.

The other ingredients are:
Potato starch, lactose monohydrate, magnesium stearate [vegetable origin], palmitoyl ascorbic acid.

What Tibolone tablets look like and contents of the pack
Tibolone tablets are white to whitish, flat round tablets of approximately 6 mm diameter.

Tibolone tablets are available in packs of 1 x 28 tablets and 3 x 28 tablets.
Not all pack sizes may be marketed.

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ARISTO

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