



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

1. What Tibolone is and what it is used for

This medicine is a Hormone Replacement Therapy (HRT). It contains tibolone, a substance that has favourable effects on different tissues in the body, such as brain, vagina and bone. This medicine is used in postmenopausal women with at least 12 months (1 year) since their last natural period.

This medicine 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"). Tibolone alleviates these symptoms after menopause. You will only be prescribed this medicine 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 Tibolone to prevent osteoporosis after menopause.

In section 6, 'Contents of the pack and other information' you can find more information about Tibolone and what it is used for.

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

Regular check-ups

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.

Some women should not take Tibolone

Do not take Tibolone

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 this medicine (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, pharmacist or nurse before taking Tibolone

If you have ever had any of the following problems, tell your doctor 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 in your blood (triglycerides)
- fluid retention due to cardiac or kidney problems

Stop taking Tibolone and see a doctor immediately

- If you notice any of the following when taking 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)

There have been reports of an increased cell growth or cancer of the lining of the womb in women using Tibolone. The risk of cancer of the lining of the womb increases the longer you take the medicine.

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:**
 - o dimpling or sinking of the skin
 - o changes in the nipple
 - o 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-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).

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 are **pregnant** or recently had a baby
- 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)
- 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 Tibolone 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).

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 due to use of oestrogen-progestogen HRT 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

Recent research suggests that HRT and Tibolone slightly increases the risk of having a stroke. The increased risk is seen mainly in women over 60 years old.

Compare

Looking at 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.

For women in their 50s who are taking **Tibolone**, the figure would be 7 in 1000 (i.e. an extra 4 cases).

Looking at 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.

For 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.

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 against **blood clotting** (such as warfarin)
- Medicines for **epilepsy** (such as phenobarbital, phenytoin and carbamazepin)

- Medicines for **tuberculosis** (such as rifampicin)
- Herbal remedies containing **St John's Wort** (Hypericum perforatum).

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, herbal medicines or other natural products.

Tibolone with food and drink

You can eat or drink normally while you are taking **Tibolone**

Pregnancy and breast-feeding

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

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

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

Tibolone contains Lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before using Tibolone.

3. How to take Tibolone

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Tibolone is administered orally.

The recommended dose is one tablet every day. Take this dose unless your doctor or pharmacist told you to do something different.

Press the tablet so that it comes through the foil. Swallow the tablet with some water or other drink, without chewing.

Take Tibolone at the same time each day.

The strips of tablets are marked with the days of the week. Start by taking a tablet marked with the current day. For example, if it is Monday, take a tablet marked Monday on the top row of the strip. Follow the arrows until the strip is empty. Start the next strip the next day. Do not leave a break between strips or packs.

You should not take Tibolone until 12 months after your last natural menstruation. If Tibolone is taken before this period of time, the likelihood of irregular vaginal hemorrhaging may be increased.

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.

If you take more **Tibolone** than you should
It is unlikely that taking more than one tablet will do you any harm, but you may feel sick, be sick or have some vaginal bleeding. If you take more Tibolone than you should, you should see a doctor or pharmacist immediately. If you have taken too much Tibolone, immediately contact your doctor, pharmacist or Poison control center.

If you forget to take Tibolone

If you forget to take a tablet, take it as soon as you remember, unless you are more than 12 hours late. If you are more than 12 hours late, just skip it, and take your next tablet at the usual time. Don't take a double dose.

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 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 Tibolone again.

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. **Most side effects are mild.**

Other side effects

Common (may affect up to 1 in 10 women):

- breast pain • stomach or pelvic pain
- unusual hair growth
- vaginal bleeding or spotting.
- vaginal problems such as more secretions, itching, irritation and thrush
- weight gain.

Uncommon (may affect up to 1 in 100 women):

- swollen hands, ankles or feet – a sign of fluid retention
- stomach upset • acne
- painful nipples or breasts feeling uncomfortable
- vaginal infections

Rare (may affect up to 1 in 1000 women):

- itchy skin

Some women taking Tibolone have also reported:

- depression, dizziness, migraine, headache
- joint pain or muscle pain
- skin problems such as rash or itching
- loss of vision or blurred vision
- Gastrointestinal disorders
- changes in liver tests
- Water retention

There have been reports of breast cancer and of an increased cell growth or cancer of the lining of the womb in women using Tibolone.

→Tell your doctor if any of the above mentioned side effects continues or becomes troublesome.

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)
 - "Purpura vascular" - small haemorrhagic points on the skin

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 Yellow Card Scheme Website: 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

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 carton after 'EXP'. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

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 contains

The active substance is tibolone.
The other ingredients are potato starch, lactose monohydrate, ascorbyl palmitate, anhydrous lactose and magnesium stearate.

What Tibolone looks like and the contents of the pack

Tibolone tablets are White to off white, circular with flat face beveled edge, uncoated tablet debossed with 'TO above 2' on one side and plain on other side. Approximate Diameter 6.00±0.20 mm.

Tibolone tablets are packaged in blisters consisting of a transparent polyvinyl chloride film and an aluminium blister foil. The following packages are available: Carton packs containing 1, 3 blisters of 28 tablets and Carton packs containing 2,3 blisters of 10 tablets.

The Marketing Authorisation Holder and Manufacturer:

Strides Pharma UK Ltd,
Unit 4, The Metro Centre,
Dwight Road, Watford
WD18 9SS,
United Kingdom

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More about Tibolone

In women, the most important sex hormones are estrogens and progestagens. These hormones are necessary for the normal sexual development of women and have an important role in regulating the menstrual cycle. Estrogens play an important role in the formation of bones. The bones are formed during youth and the peak of bone mass is reached between the 20-30 years of age. After this age, the bone mass decreases, first slowly, but in later ages the loss of bone mass is accelerated, especially after menopause. The period in which this happens (usually around the age of 50) is called climacteric or menopause. If the ovaries are removed surgically (ovariectomy) before menopause, the decrease in hormone production will occur very abruptly.

In many cases, this decrease in hormone production leads to well-known menopausal complaints, such as hot flashes and night sweats. Lack of sex hormones can also cause the vaginal wall to become thinner and drier. For this reason, intercourse can become painful and vaginal infections may be more frequent. In many women, these physical problems are accompanied by mood swings, nervousness, depression, irritability, and loss of sexual desire.

One problem that often goes unnoticed is the rapid bone loss that occurs in many women after menopause. For this reason, the bones become brittle and can break easily (osteoporosis), especially the spine, hip and wrists. Osteoporosis can also cause back pain, weight loss and back curvature.

Tibolone contains tibolone, a substance that has beneficial effects of sex hormones on different tissues of the body such as brain, vagina and bone. This results in Tibolone relieving menopausal complaints, such as hot flashes and night sweats.

This medicine also has a stimulating effect on the inner lining of the vagina, and a favourable effect on mood and sexual desire. Tibolone stops and also treats the osteoporosis process, i.e. the bone loss that occurs after menopause, in the spine, hip and wrists. Unlike other medications used in hormone replacement therapy, Tibolone does not stimulate the lining of the uterus (endometrium). Therefore, treatment with Tibolone does not cause monthly vaginal bleeding.

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180 x 600 mm

Front Side

180 x 600 mm

Back Side

10201



CMO - ARTWORK DETAIL LABEL

10202



		MFG. LOCATION	NAARI PHARMA	
PRODUCT	Tibolone 2.5 mg tablets			
BUYER/COUNTRY	SPUK	COMPONENT	Pack Insert	
DIMENSION	180 x 600 mm	PACK	--	
NEW ITEM CODE	1048158	OLD ITEM CODE	1041604	
COLOUR SHADES	Black	No. of Colours	1	
Change Control No.	Record No.: 367602	Artwork Version	3.0	
Design/Style	Front & Back Printing. To be supplied in the folded size: 70 x 35 mm.			
Substrate	60 GSM Paper.			
Special Instructions	PRINTING CLARITY TO BE CLEAR AND SHARP			
Autocartanator Requirements	NA			
Caution to the printer: Before processing, please ensure that the ARTWORK received for printing is exactly in line with APPROVED ARTWORK provided to you. In case of any FONTS/DESIGN are Mismatching with the APPROVED ARTWORK, please inform SCM / PD for further action. DO NOT MAKE ANY CHANGE TO THE ARTWORK WITHOUT WRITTEN INSTRUCTIONS FROM SCM / PD.				

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