TIBILIVE 2,5 mg

SCHEDULING STATUS S4

1. NAME OF THE MEDICINE
TIBILIVE 2,5 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 2,5 mg of tibolone.

TIBILIVE 2,5 mg contains sugar (lactose monohydrate each tablet contains 43,15 mg and mannitol 43,15 mg).

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Tablets.
White to off-white round uncoated tablets without any marking.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
TIBILIVE 2,5 mg is indicated for:
- symptomatic treatment of hot flushes and associated sweating resulting from natural or surgical menopause
- prevention of post-menopausal osteoporosis
- improvement of bone-mineral density in patients with established post-menopausal osteoporosis.

4.2 Posology and method of administration
Posology
The dosage is 1 tablet per day. A missed dose should be taken as soon as remembered, unless it is more than 12 hours overdue. In the latter case, the missed dose should be skipped and the next dose should be taken at the normal time.

Improvement of symptoms generally occurs within a few weeks but optimal results are obtained when therapy is continued for at least 3 months.

Starting TIBILIVE 2,5 mg
Women experiencing a natural menopause should commence treatment with TIBILIVE 2,5 mg at least 12 months after their last natural bleed. In case of a surgical menopause, treatment with TIBILIVE 2,5 mg may commence immediately.

Any irregular/unscheduled vaginal bleeding, either on or off hormone replacement therapy (HRT), should be fully investigated to exclude malignancy before starting TIBILIVE 2,5 mg.

Method of administration
Oral use.
TIBILIVE 2,5 mg should be swallowed whole with some water or other drink, preferably at the same time each day.

4.3 Contraindications
- hypersensitivity to tibolone or to any of the ingredients of TIBILIVE 2,5 mg
- known or suspected hormone-dependent tumours
- personal and family history of breast cancer, including suspected breast cancer
- previous idiopathic or current venous thromboembolism (deep venous thrombosis, (DVT) pulmonary embolism)
- known thrombophilic disorders e.g. protein C, protein S or antithrombin deficiency, including inherited thrombophilia (see section 4.4)
- active liver disease, severe liver disease, or a history of liver disease as long as liver function tests have failed to return to normal
- patients known with inherited genetic mutations: BRCA1 and BRCA2 genes
- early menstrual periods (before the age of 12 years)
- history of non-cancerous breast diseases (atypical hyperplasia or lobular carcinoma in situ)
- previous treatment using radiation therapy to the chest or breast
- previous exposure to diethylstilbestrol (DES)
- known or suspected oestrogen-dependent malignant tumours (e.g. endometrial cancer)
- vaginal bleeding of unknown etiology
- untreated endometrial hyperplasia
- cardiovascular or cerebrovascular disorders e.g. thrombophlebitis, thromboembolic processes or a history of these conditions
- any history of thromboembolic disease e.g. angina, myocardial infarction, stroke or transient ischaemic attack (TIA)
- porphyria
- pregnancy and lactation.

4.4 Special warnings and precautions for use
TIBILIVE 2,5 mg is not intended for contraceptive use.
TIBILIVE 2,5 mg is prescribed for the treatment of postmenopausal symptoms and should only be initiated for symptoms that adversely affect quality of life.

The use of TIBILIVE 2,5 mg should be avoided until 12 months after the last natural menstrual bleed. If TIBILIVE 2,5 mg is taken sooner than this, the frequency of irregular bleeding may be increased.

In the event that signs of thromboembolic processes occur, results of liver function tests become abnormal or if cholestatic jaundice appears, treatment with TIBILIVE 2,5 mg should be discontinued.

As a result of an apparently stimulated endometrium due to some oestrogen production, vaginal bleeding may occur during TIBILIVE 2,5 mg therapy. Normally such bleeding is of short duration. Bleedings commencing after 3 months of treatment, or recurrent or of longer duration should be investigated.

When changing to TIBILIVE 2,5 mg from any other form of hormonal substitution therapy, it is always advisable to induce a withdrawal bleeding with a progestogen before starting TIBILIVE 2,5 mg.
Tibolone, as in TIBILIVE 2,5 mg has been shown to be teratogenic in experimental animals, and should not be used in pre-menopausal women.

The risks of stroke, breast cancer and endometrial cancer (women with an intact uterus) for each woman should be carefully assessed, in the light of her individual risk factors and bearing in mind the frequency and characteristics of both cancers and stroke, in terms of their response to treatment, morbidity and mortality.

Medical examination/follow-up
Periodic examinations must be done for endometrial hyperplasia, as well as possible signs of virilisation.
Before initiating or reinstituting HRT or tibolone, as in TIBILIVE 2,5 mg, a complete personal and family medical history should be taken. Physical (including pelvic and breast) examination should be guided by this and by the contraindications and warnings for use.

During treatment, periodic check-ups are recommended of a frequency and nature adapted to the individual woman. Women should be advised that changes in their breasts should be reported to their doctor or nurse (see Breast cancer below). Investigations, including appropriate imaging tools, e.g. mammography, should be carried out in accordance with currently accepted screening practices, modified to the clinical needs of the individual.

Conditions which need supervision
If any of the following conditions are present, have occurred previously, and/or have been aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised. It should be taken into account that these conditions may recur or be aggravated during treatment with TIBILIVE 2,5 mg in particular:
- leiomyoma (uterine fibroids) or endometriosis
- history of, or risk factors for, thromboembolic disorders (see below)
- risk factors for oestrogen dependant tumours, e.g. 1st degree heredity for breast cancer
- hypertension
- liver disorders (e.g. liver adenoma)
- diabetes mellitus with or without vascular involvement
- cholelithiasis
- migraine or (severe) headache
- systemic lupus erythematosus
- history of endometrial hyperplasia (see below)
- epilepsy
- asthma
- otosclerosis.

Reasons for immediate withdrawal therapy:
TIBILIVE 2,5 mg therapy should be discontinued either in the case of a contraindication being discovered, or in any of the following situations:
- jaundice or deterioration in liver function
- significant increase in blood pressure
- new onset of migraine-type headache.

Endometrial hyperplasia and cancer
The available data from randomised controlled trials are conflicting, however observational studies have consistently shown that women who are prescribed tibolone, as in TIBILIVE 2,5 mg, in normal clinical practice are at an increased risk of having endometrial cancer diagnosed. In these studies, risk increased with increasing duration of use. Tibolone, as in TIBILIVE 2,5 mg increases endometrial wall thickness, as measured by transvaginal ultrasound.

The endometrial cancer risk is about 5 in every 1 000 women with a uterus not using HRT or tibolone, as in TIBILIVE 2,5 mg.

Break-through bleeding and spotting may occur during the first months of treatment (see section 4.3). Women should be advised to report any break-through bleeding or spotting if it is still present after 6 months of treatment, if it starts beyond that time or if it continues after treatment has been discontinued. The woman should be referred for gynaecological investigation, which is likely to include endometrial biopsy to exclude endometrial malignancy.

Breast cancer
TIBILIVE 2,5 mg contains tibolone which has combined estrogenic and progestogenic effects and therefore, on prolonged use, may increase the risk of developing breast cancer. A meta-analysis of prospective epidemiological studies from 1992 to 2018 reported a significant increase in the risk of developing breast cancer in 55,575 women 40 - 59 years of age who used menopausal hormone therapy (MHT). The risk increased steadily with duration of use and was slightly greater for oestrogen-progestogen than oestrogen only preparations, and the risk persisted for more than 10 years after stopping the treatment. The relative risk (RR) to develop breast cancer for oestrogen-progestogen preparations was 1,60 at 1 - 4 years and RR = 2,08 at 5 - 14 years, while that for oestrogen only preparations was 1,17 at 1 - 4 years and 1,33 at 5 - 14 years. There was no risk to develop breast cancer in women who started MHT at 60 years of age.

All women on TIBILIVE 2,5 mg should receive yearly breast examinations by a healthcare provider and perform monthly breast self-examinations.
Mammography evaluations should be done based on patient age, risk factors, and prior mammogram results.

Ovarian cancer
Ovarian cancer is much rarer than breast cancer.
Long-term (at least 5 to 10 years) use of oestrogen-only HRT products has been associated with a slightly increased risk of ovarian cancer.
Some other studies suggest that the use of combined HRTs may be associated with a similar, or slightly smaller risk.
In one study it was shown that the relative risk for ovarian cancer with use of tibolone, as in TIBILIVE 2,5 mg was similar to the risk associated with use of other types of HRT.

Venous thromboembolism
Oestrogen or oestrogen-progestogen HRT is associated with a 1,3- to 3-fold risk of developing venous thromboembolism (VTE), i.e. deep vein thrombosis or pulmonary embolism. The occurrence of such an event is more likely in the first year of HRT than later (see section 4.8). In an epidemiological study using a UK database, the risk of VTE in association with tibolone was lower than the risk associated with conventional HRT, but only a small proportion of women were current users of tibolone and a small increase in risk compared with non-use cannot be excluded.

Patients with known thrombophilic states have an increased risk of VTE and HRT or tibolone, as in TIBILIVE 2,5 mg may add to this risk. HRT is therefore contraindicated in these patients (see section 4.3).

Generally recognised risk factors for VTE include use of oestrogens, older age, major surgery, prolonged immobilisation, obesity (BMI > 30 kg/m^2), pregnancy/postpartum period, systemic lupus erythematosus (SLE), and cancer. There is no consensus about the possible role of varicose veins in VTE. As in all postoperative patients, prophylactic measures need to be considered to prevent VTE following surgery. If prolonged immobilisation is to follow elective surgery, temporarily stopping HRT or tibolone 4 to 6 weeks earlier is recommended, if possible. Treatment should not be restarted until the woman is completely mobilised.
In women with no personal history of VTE but with a first degree relative with a history of thrombosis at young age, screening may be offered after careful counselling regarding its limitations (only a proportion of thrombophilic defects are identified by screening). If a thrombophilic defect is identified which segregates with thrombosis in family members or if the defect is 'severe' (e.g. antithrombin, protein S, or protein C deficiencies or a combination of defects) HRT or TIBILIVE 2,5 mg is contraindicated.

Women already on anticoagulant treatment require careful consideration of the benefit-risk of use of HRT or TIBILIVE 2,5 mg.

If VTE develops after initiating therapy, TIBILIVE 2,5 mg should be discontinued. Patients should be told to contact their doctors immediately when they are aware of a potential thromboembolic symptom (e.g. painful swelling of a leg, sudden pain in the chest, dyspnoea).

Coronary artery disease (CAD)
There is no evidence from randomised controlled trials of protection against myocardial infarction in woman with or without existing CAD who received combined oestrogen-progestogen or oestrogen-only HRT. In an epidemiological study using the General Practice Research Database (GPRD) no evidence was found of protection against myocardial infarction in post-menopausal women who received tibolone, as in TIBILIVE 2,5 mg.

Ischaemic stroke
TIBILIVE 2,5 mg increases the risk of stroke from the first year of treatment. The baseline risk of stroke is strongly age-dependent and so the effect of TIBILIVE 2,5 mg is greater with older age.

Risk of ischaemic stroke
- the relative risk of ischaemic stroke is not dependent on age or on duration of use, but as the baseline risk is strongly age-dependent, the overall risk of ischaemic stroke in women who use HRT or TIBILIVE 2,5 mg will increase with age
- a 2,9-year randomised, controlled study has estimated a 2,2-fold increase in the risk of stroke in women (mean age 68 years) who used 1,25 mg tibolone compared with placebo. The majority (80 %) of strokes were ischaemic
- the baseline risk of stroke is strongly age-dependent. Thus, the baseline incidence over a 5-year period is estimated to be 3 per 1,000 women aged 50 - 59 years and 11 per 1,000 women aged 60 - 69 years
- for women who use tibolone, as in TIBILIVE 2,5 mg for 5 years, the number of additional cases would be expected to be about 4 per 1000 users aged 50 - 59 years and 13 per 1000 users aged 60 - 69 years.

Other adverse reactions have been reported in association with oestrogen and oestrogen-progestogen treatment:
- long term use of oestrogen-only or combined oestrogen-progestogen HRT has been associated with an increased risk of ovarian cancer. In one study, 5 years of HRT resulted in 1 extra case per 2 500 users. This study showed that the relative risk for ovarian cancer with tibolone, as in TIBILIVE 2,5 mg, was similar to the risk with other types of HRT
- HRT is associated with a 1,3- to 3-fold risk increased relative risk of developing venous thromboembolism (VTE), i.e. deep vein thrombosis or pulmonary embolism. The occurrence of such an event is more likely in the first year of using HRT
- the risk of coronary artery disease is increased in users of combined oestrogen-progestogen HRT over the age of 60. There is no evidence to suggest that the risk of myocardial infarction with tibolone, as in TIBILIVE 2,5 mg is different to the risk with other HRT
- gall bladder disease
- skin and subcutaneous disorders: chloasma, erythema multiforme, erythema nodosum, vascular purpura
- probable dementia over the age of 65.

Other conditions
Treatment with tibolone, as in TIBILIVE 2,5 mg results in a marked dose-dependent decrease in HDL cholesterol (from -16,7 % with a 1,25 mg dose to -21,8 % for the 2,5 mg dose after 2 years). Total triglycerides and lipoprotein(a) levels were also reduced. The decrease in total cholesterol and VLDL-C levels was not dose-dependent. Levels of LDL-C were unchanged. The clinical implication of these findings is not yet known.

Oestrogens may cause fluid retention, and therefore patients with cardiac or renal dysfunction should be carefully observed.

Women with pre-existing hypertriglyceridaemia should be followed closely during oestrogen replacement or hormone replacement therapy, since rare cases of large increases of plasma triglycerides leading to pancreatitis have been reported with oestrogen therapy in this condition.

Treatment with TIBILIVE 2,5 mg results in a very minor decrease of thyroid binding globulin (TBG) and total T4. Levels of total T3 are unaltered. TIBILIVE 2,5 mg decreases the level of sex-hormone-binding globulin (SHBG), whereas the levels of corticoid-binding globulin (CBG) and circulating cortisol are unaffected.

HRT does not improve cognitive function. There is some evidence of increased risk of probable dementia in women who start using continuous combined or oestrogen-only HRT after the age of 65.

TIBILIVE 2,5 mg contains lactose monohydrate. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, total lactose deficiency or glucose-galactose malabsorption should not take TIBILIVE 2,5 mg.

4.5 Interaction with other medicines and other forms of interaction
No examples of interaction between tibolone, as in TIBILIVE 2,5 mg and other medicines have been reported in clinical practice. However, the following potential interactions should be considered on a theoretical basis:
Since tibolone may increase blood fibrinolytic activity (lower fibrinogen levels; higher ATIII, plasminogen and fibrinolytic activity values), it may enhance the effect of anticoagulants. This effect has been demonstrated with warfarin.
Caution should therefore be exercised during the simultaneous use of TIBILIVE 2,5 mg and anticoagulants, especially when starting or stopping concurrent TIBILIVE 2,5 mg treatment. If necessary, the dose of warfarin should be adjusted.

There is limited information regarding pharmacokinetic interactions with tibolone. An *in vivo* study showed that simultaneous treatment of tibolone affects pharmacokinetics of the cytochrome P450 3A4 substrate midazolam to a moderate extent. Based on this, medicine interactions with other CYP3A4 substrates might be expected.

CYP3A4 enzyme-inducing medicines such as barbiturates, carbamazepine, hydantoins and rifampicin may enhance the metabolism of tibolone, as in TIBILIVE 2,5 mg, and thus decrease its therapeutic effect.

Herbal preparations containing St.John's wort *(Hypericum Perforatum)* may induce the metabolism of oestrogens and progestogens via CYP3A4. Clinically, an increased metabolism of oestrogens and progestogens may lead to decreased effect and changes in the uterine bleeding profile.

4.6 Fertility, pregnancy and lactation
Pregnancy
TIBILIVE 2,5 mg is contraindicated during pregnancy. If pregnancy occurs during medication with TIBILIVE 2,5 mg, treatment should be withdrawn immediately.
Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown.

Breastfeeding
TIBILIVE 2,5 mg is contraindicated during breastfeeding.

Fertility
In animal studies, tibolone, as in TIBILIVE 2,5 mg, had anti-fertility activities by virtue of its hormonal properties.

4.7 Effects on ability to drive and use machines
TIBILIVE 2,5 mg is not known to have any effects on alertness and concentration.

4.8 Undesirable effects
This section describes undesirable effects, which were registered in 21 placebo-controlled studies and during post-marketing surveillance.

Tabulated summary of adverse reactions

System Organ Class	Frequency	Side effects
Metabolism and nutrition disorders	*Less frequent*	Oedema
Psychiatric disorders	*Frequency unknown*	Depression
Nervous system disorders	*Frequency unknown*	Dizziness, headache, migraine
Eye disorders	*Frequency unknown*	Visual disturbances, blurred vision
Gastrointestinal disorders	*Frequent* *Less frequent*	Lower abdominal pain Gastrointestinal upset*, abdominal discomfort*
Hepato-biliary disorders	*Frequency unknown*	Changes in liver function parameters
Skin and subcutaneous tissue disorders	*Frequent* *Less frequent* *Frequency unknown*	Abnormal hair growth Acne, pruritis Rash, seborrheic dermatosis
Musculoskeletal, connective tissue and bone disorders	*Frequency unknown*	Arthralgia, myalgia
Reproductive system and breast disorders	*Frequent* *Less frequent*	Vaginal discharge, endometrial wall thickening, postmenopausal haemorrhage, breast tenderness, genital pruritus, vaginal candidiasis, vaginal haemorrhage, pelvic pain, cervical dysplasia, genital discharge, vulvovaginitis Breast discomfort, fungal infection, vaginal mycosis, nipple pain
Investigations	*Frequent* *Less frequent*	Weight increase, abnormal cervical smear* Amnesia

*The majority consisted of benign changes. Cervix pathology (cervical carcinoma) was not increased with tibolone compared to placebo.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the online service for adverse drug reaction reporting by following the link: https://www.sahpra.org.za/Publications/Index/8 or https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/
An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

4.9 Overdose
Signs and symptoms:
In cases of acute overdose nausea, vomiting and vaginal bleeding in females may occur.

Management of overdose:
No specific antidote is known. Symptomatic treatment can be given if necessary.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacological classification: A.21.13 Others
Pharmacotherapeutic group: Urogenital system (including sex hormones)
ATC code: G03CX01

Mechanism of action
Tibolone stabilises the hypothalamic-pituitary system after failure of ovarian function in the climacteric, which leads to the occurrence of vasomotor complaints as a result of the involvement of the thermoregulatory centre in the hypothalamus. The therapeutic central effect of tibolone is due to the combined estrogenic, progestogenic and weak androgenic activities of the medicine.

Tibolone has a moderate gonadotrophin suppressing effect in post-menopausal woman.
The peripheral effect of tibolone is the combination of hormonal activities which exerts a balanced effect and does not stimulate the endometrium in post-menopausal woman.

5.2 Pharmacokinetic properties
Absorption:
Following oral administration, tibolone is rapidly and extensively absorbed, appearing in the blood within 30 minutes of oral administration with peak levels between 1,5 and 4 hours. The consumption of foods has no significant effects on the extent of absorption.

Biotransformation:
Tibolone is metabolised in the liver and converted to metabolites. Some metabolites may contribute to the biological effects of the medicine. The elimination half-life of tibolone and active metabolites is less than 2 days, justifying once a day administration.

Elimination:
Excretion of tibolone is mainly in the form of conjugated (mostly sulphated) metabolites, which are excreted mainly in the faeces and to a lesser extent in the urine.

Pharmacokinetics in special patient groups
The pharmacokinetic parameters for tibolone and its metabolites were found to be independent of renal function.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Ascorbyl palmitate
Lactose monohydrate
Magnesium stearate
Mannitol
Potato starch

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Store at or below 30 °C.
Store in the original package in order to protect from light and moisture.

6.5 Nature and contents of container
TIBILIVE 2,5 mg tablets are packed in PVC/Aluminium foil blisters placed in an outer carton. Each carton contains 28 or 30 tablets.

6.6 Special precautions for disposal
No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION
Pharma Dynamics (Pty) Ltd
1st Floor Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, Cape Town
7945, South Africa

8. REGISTRATION NUMBER
A52/21.13/0078

9. DATE OF FIRST AUTHORISATION
19 April 2022

10. DATE OF REVISION OF THE TEXT
07 November 2022

PATIENT INFORMATION LEALFET

SCHEDULING STATUS S4

TIBILIVE 2,5 mg tablets
Tibolone
TIBILIVE 2,5 mg contains sugar (lactose monohydrate 43,15 mg and mannitol 43,15 mg)

Read all of this leaflet carefully before you start taking TIBILIVE 2,5 mg
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- TIBILIVE 2,5 mg has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What TIBILIVE 2,5 mg is and what it is used for
TIBILIVE 2,5 mg 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 and also in women who had their ovaries removed.

Unlike some other medicines used for hormone replacement therapy, TIBILIVE 2,5 mg does not stimulate the lining of the womb. Treatment with TIBILIVE 2,5 mg therefore does not lead to monthly vaginal bleeding.

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"). TIBILIVE 2,5 mg 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)
- improvement of bone-mineral density in post-menopausal osteoporosis:
  If you are at an increased risk of fractures due to osteoporosis and other medicines are not suitable for you, you can use TIBILIVE 2,5 mg to prevent fractures after menopause.

2. What you need to know before you take TIBILIVE 2,5 mg
Do not take TIBILIVE 2,5 mg:
- if you are hypersensitive (allergic) to tibolone, or to any of the ingredients of TIBILIVE 2,5 mg
- if you, or anyone in your family have or have ever had breast cancer, or if you are suspected of having it
- if you have or have ever had a blood clot in a vein (thrombosis), such as in the legs (deep venous thrombosis – DVT) or the lungs (pulmonary embolism)
- if you have a blood clotting disorder (such as protein C, protein S, or antithrombin deficiency), including an inherited disorder that makes your blood more likely to clot
- if you have or have ever had a liver disease and your liver function tests have not returned to normal
- if you have inherited genetic mutations: BRCA1 and BRCA2 genes, as you have a higher risk of developing cancer
- in the case of early menstrual periods (before the age of 12 years)
- if you have ever had other non-cancerous breast diseases such as atypical hyperplasia (a precancerous condition that affects cells in the breast) or lobular carcinoma in situ (abnormal cells growing in the lining of the milk glands)
- if you have ever had treatment using radiation therapy to the chest or breast
- if you have ever been exposed to diethylstilbestrol (DES), a synthetic oestrogen medicine
- 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 recently have had a disease caused by blood clots in the arteries, such as a heart attack, stroke or angina
- if you have a rare blood problem called "porphyria" which is passed down in families (inherited)
- if you are pregnant, think you might be pregnant or are breastfeeding your baby.

Warnings and precautions
Take special care with TIBILIVE 2,5 mg:
TIBILIVE 2,5 mg 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.

If you have started menopause you should not take TIBILIVE 2,5 mg until 12 months after your last natural period. If you take it sooner than this you may have irregular bleeding.

Stop taking TIBILIVE 2,5 mg and see a doctor immediately if any of the following occur:
- 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.

Medical check-up
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 TIBILIVE 2,5 mg therapy, 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 TIBILIVE 2,5 mg.
Go for regular breast screening and cervical smear tests, as recommended by your doctor.
Regularly check your breasts for any changes such as dimpling of the skin, changes in the nipple, or any lumps you can see or feel.

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 TIBILIVE 2,5 mg. 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) below)
- 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 or a very high level of fat in your blood (triglycerides)
- 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).

Hormone Replacement Therapy (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 TIBILIVE 2,5 mg. 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 months of taking TIBILIVE 2,5 mg. Talk to your doctor if the bleeding or spotting:
- carries on for more than the first 3 months
- starts after you have been taking TIBILIVE 2,5 mg for more than 3 months
- carries on even after you've stopped taking TIBILIVE 2,5 mg.

Breast cancer
TIBILIVE 2,5 mg contains tibolone which has combined estrogenic and progestogenic effects and therefore, on prolonged use, may increase the risk of developing breast cancer.

The risk is steadily increased with duration of use, and women taking TIBILIVE 2,5 mg have a lower risk than women using combined menopausal hormone therapy (MHT) and a comparable risk with oestrogen-only MHT.

All women on TIBILIVE 2,5 mg should receive yearly breast examinations by a healthcare provider and perform monthly breast self-examinations. 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. A slightly increased risk of ovarian cancer has been reported in women taking hormone replacement therapy for at least 5 to 10 years.
With use of TIBILIVE 2,5 mg, 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/m^2)
- you have systemic lupus erythematosus (SLE)
- you have cancer
- 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.

For signs of a blood clot, see the section above: Stop taking TIBILIVE 2,5 mg and see a doctor immediately.

You may need to stop taking TIBILIVE 2,5 mg about 4 to 6 weeks before you have an operation to reduce the risk of a blood clot.

Heart disease (heart attack)
There is no evidence that HRT or TIBILIVE 2,5 mg will prevent a heart attack.

Stroke
Recent research suggests that HRT and TIBILIVE 2,5 mg slightly increases the risk of having a stroke. The increased risk is seen mainly in post-menopausal women over 60 years old.

Other conditions
Oestrogens may cause fluid retention, and therefore patients with heart or kidney disease should be carefully observed.

If you have high levels of fats called triglycerides in your blood (hypertriglyceridaemia), your doctor will closely monitor this condition as there is a risk of developing pancreatitis during TIBILIVE 2,5 mg therapy.

If you need a blood test, tell your doctor or the laboratory staff that you are taking TIBILIVE 2,5 mg, because it can affect the results of some tests.

TIBILIVE 2,5 mg 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 TIBILIVE 2,5 mg
Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

Some medicines may interfere with the effect of TIBILIVE 2,5 mg. This might lead to irregular bleeding. This applies to the following medicines:
- medicines against blood clotting (such as warfarin)
- medicines for epilepsy (such as phenobarbitone, phenytoin and carbamazepine)
- medicines for tuberculosis (such as rifampicin)
- herbal remedies containing St John's Wort *(Hypericum perforatum).*

If you are going to have an operation, make sure your doctor knows about it. You may need to stop taking HRT about 4 to 6 weeks before the operation, to reduce the risk of a blood clot. Your doctor will tell you when you can start taking HRT again.

TIBILIVE 2,5 mg with food and drink
TIBILIVE 2,5 mg can be taken with or without food.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking TIBILIVE 2,5 mg.

TIBILIVE 2,5 mg should not be used during pregnancy. Stop taking TIBILIVE 2,5 mg if you suspect or find out you are pregnant.

TIBILIVE 2,5 mg is contraindicated in breastfeeding.

Driving and using machines
TIBILIVE 2,5 mg has no known effect on the ability to drive or use machines.
It is not always possible to predict to what extent TIBILIVE 2,5 mg may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which TIBILIVE 2,5 mg affects them.

TIBILIVE 2,5 mg contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking TIBILIVE 2,5 mg.

3. How to take TIBILIVE 2,5 mg
Do not share medicines prescribed for you with any other person. Always use TIBILIVE 2,5 mg exactly as your doctor has instructed. You should check with your doctor or pharmacist if you are unsure.

Adults:
The usual dose is one tablet daily, preferably at the same time each day. Swallow the tablet whole with a little water.

Natural menopause:
Wait for 12 months after your last period before you start taking TIBILIVE 2,5 mg.

Menopause as a result of surgery:
If you have had a hysterectomy or you are being treated for endometriosis you can start taking TIBILIVE 2,5 mg immediately.

Your doctor will tell you how long your treatment with TIBILIVE 2,5 mg will last. Do not stop treatment early because your symptoms may return.
If you have the impression that the effect of TIBILIVE 2,5 mg is too strong or too weak, tell your doctor or pharmacist.

If you take more TIBILIVE 2,5 mg than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

Symptoms of overdose may include:
- nausea, vomiting and vaginal bleeding.

take this leaflet and the rest of the remaining TIBILIVE 2,5 mg with you so the doctor will know what you have taken.

If you forget to take TIBILIVE 2,5 mg
If you forget to take TIBILIVE 2,5 mg, take as soon as you remember on the same day, unless you are more than 12 hours late. If you are more than 12 hours late, just skip it, and take your next tablet the next day. Do not take a double dose to make up for forgotten individual doses.

4. Possible side effects
TIBILIVE 2,5 mg can have side effects.
Not all side effects reported for TIBILIVE 2,5 mg are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using TIBILIVE 2,5 mg, please consult your healthcare provider for advice.

If any of the following happens, stop using TIBILIVE 2,5 mg and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to TIBILIVE 2,5 mg. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- your blood pressure rises
- your skin or the whites of your eyes go yellow (jaundice)
- you suddenly have migraine-type headaches (see section 2 above)
- you have signs of a blood clot (painful swelling and redness of the legs, sudden chest pain, difficulty in breathing)
- stroke (pressuring with symptoms such as trouble walking, speaking and understanding as well as paralysis or numbness of the face, arm or leg).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
- lower abdominal pain
- abnormal hair growth
- vaginal problems such as discharge, itching, irritation, vaginal bleeding or spotting, breast tenderness, pelvic pain, thickening of the lining of the womb or the lining of the cervix
- weight increase, abnormal pap-smear test results.

Less frequent side effects:
- fluid retention (swollen hands, ankles or feet)
- acne, itchy skin
- gastrointestinal upset, abdominal discomfort
- breast discomfort, fungal infection, vaginal thrush (yeast infection), nipple pain
- memory loss.

The following side effects have been reported but the frequency for them to occur is not known:
- depression
- dizziness, headache, migraine
- visual disturbances, blurred vision
- liver problems
- skin problems such as rash or itching, scaly patches and red skin
- joint pain, muscle pain.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report any side effects to SAHPRA via the online service for adverse drug reaction reporting by following the link: https://www.sahpra.org.za/Publications/Index/8 or https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/.
By reporting side effects, you can help provide more information on the safety of TIBILIVE 2,5 mg. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

5. How to store TIBILIVE 2,5 mg
Store all medicines out of reach of children.
Store at or below 30 °C.
Store in the original package in order to protect from light and moisture.
Do not use after the expiry date stated on the carton.
Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What TIBILIVE 2,5 mg contains:
Each tablet contains 2,5 mg of tibolone.

The other ingredients are:
Tablet cores:
Ascorbyl palmitate, lactose monohydrate, magnesium stearate, mannitol, potato starch.

What TIBILIVE 2,5 mg looks like and contents of the pack
White to off-white round uncoated tablets without any marking.

TIBILIVE 2,5 mg tablets are packed in PVC/Aluminium foil blisters placed in outer carton. Each carton contains 28 or 30 tablets.

Holder of Certificate of Registration
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PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS S4

TIBILIVE 2,5 mg tablette
Tiboloon
TIBILIVE 2,5 mg bevat suiker (laktosemonohidraat 43,15 mg en mannitol 43,15 mg)

Lees hierdie hele inligtingsblad deeglik deur, voordat u begin om TIBILIVE 2,5 mg te gebruik
- Hou hierdie inligtingsblad. Dit mag nodig wees vir u om dit weer te lees.
- Indien u verdere vrae het, vra asseblief u dokter, apteker, verpleegkundige, of ander gesondheidsorgverskaffer.
- TIBILIVE 2,5 mg is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit mag skadelik wees vir hulle, selfs al is hulle simptome dieselfde as u eie.

Wat hierdie inligtingsblad bevat

1. Wat TIBILIVE 2,5 mg is en waarvoor dit gebruik word
TIBILIVE 2,5 mg is 'n hormoonvervangingsterapie (HVT). Dit bevat tiboloon, 'n bestanddeel, wat 'n voordelige uitwerking op verskeie liggaamsweefsels, soos die van die brein, vagina en been, uitoefen. Die medisyne word gebruik deur postmenopousale vroue wie 'n natuurlike menstruasie ten minste 12 maande (1 jaar) gelede ondervind het, en ook deur die wie se ovaria verwyder is.

TIBILIVE 2,5 mg, anders as ander medisyne wat vir hormoonvervangingsterapie gebruik word, stimuleer nie die baarmoederwand nie. Behandeling met TIBILIVE 2,5 mg lei dus nie na maandelikse vaginale bloeding nie.

Hierdie medisyne word gebruik vir:
- verligting van simptome wat volg na menopouse: Tydens menopouse, verlaag die hoeveelheid estrogeen wat deur 'n vrou se liggaam vervaardig word. Dit lei tot simptome soos 'n warm gesig, nek en bors ("warm gloede"). TIBILIVE 2,5 mg verlig hierdie simptome wat volg na menopouse. Hierdie medisyne sal slegs aan u voorgeskryf word, indien u simptome u daaglikse leefwyse ernstig verhinder
- voorkoming van osteoporose: Na menopouse, mag sommige vroue bros bene ontwikkel (osteoporose)
- verbetering van beenmineraal-digtheid by postmenopousale osteoporose: Indien u 'n verhoogde risiko vir frakture weens osteoporose toon en ander medisyne is nie gepas vir u nie, mag u TIBILIVE 2,5 mg gebruik, om frakture na menopouse te verhoed.

2. Wat u nodig het om te weet, voordat u TIBILIVE 2,5 mg gebruik
Moet nie TIBILIVE 2,5 mg neem:
- indien u hipersensitief (allergies) is vir tiboloon, of vir enige van die ander bestanddele van TIBILIVE 2,5 mg nie
- indien u, of enige iemand in u familie ooit vantevore borskanker gehad het, of daar 'n vermoede is dat u dit het nie
- indien u 'n bloedklont in aar (trombose), soos in die bene (diep veneuse trombose – DVT) of die longe (pulmonêre embolisme) het, of ooit gehad het nie
- indien u 'n bloedstollingsversteuring (soos proteïen-C-, proteïen-S-, of 'n antitrombientekort), insluitend 'n oorerflike versteuring, wat u bloed meer geneig maak om te stol, het nie
- indien u 'n lewersiekte het, of ooit gehad het nie en u lewerfunksietoetse het nie na normaal teruggekeer nie
- indien u oorerflike genetiese mutasie het nie: BRCA1- en BRCA2-gene, aangesien u 'n hoër risiko vir die ontwikkeling van kanker het
- in die geval van vroeë menstruale siklusse (voor die ouderdom van 12 jaar oud) nie
- indien u ooit ander nie-kwaadaardige borstesiektes, soos atipiese hiperplasie ('n pre-kwaadaardige toestand wat selle in die borste aantas), of lobulêre karsinoom in situ (abnormale selle wat in die wand van die melkkliere groei), gehad het nie
- indien u ooit bestralingsbehandeling vir die bors of borste ondergaan het nie
- indien u ooit blootgestel is aan diëtielstilbestrol (DES), 'n sintetiese estrogeenmedisyne nie
- indien u aan kanker ly wat sensitief vir estrogene is nie, soos kanker van die baarmoederwand (endometrium), of daar vermoed word dat u daaraan ly nie
- indien u onverklaarbare vaginale bloeding ervaar nie
- indien u 'n uitermatige verdikking van die baarmoederwand het, wat nie behandel word nie (endometriale hiperplasie)
- indien u 'n siekte wat veroorsaak word deur bloedklonte in die arterie (soos 'n hartaanval, beroerte, of angina), het of onlangs gehad het nie
- indien u aan 'n skaars bloedprobleem, wat "porfirie"genoem word en deur families oorgedra word (oorgeërf), ly nie
- indien u swanger is, vermoed dat u swanger mag wees, of u baba borsvoed nie.

Waarskuwings en voorsorgmaatreëls
Neem spesiale sorg met TIBILIVE 2,5 mg:
TIBILIVE 2,5 mg is nie 'n voorbehoedmiddel nie. Indien u minder as 12 maande gelede u laaste menstruasie ondervind het, of indien u jonger as 50 jaar oud is, mag dit steeds nodig wees vir u om bykomende voorbehoedmaatreëls te tref, om swangerskap te verhoed.

Indien u die menopouse-stadium betree, moet u nie TIBILIVE 2,5 mg gebruik, totdat 12 maande verstryk het na u laaste natuurlike menstruasie nie. Indien u dit vroeër sou gebruik, mag u onreëlmatige bloeding ervaar.

Staak die gebruik van TIBILIVE 2,5 mg en raadpleeg 'n dokter onmiddellik, indien enige van die volgende voorkom:
- vergeling van u vel en die wit gedeeltes van u oë (geelsug). Hierdie mag tekens van 'n lewersiekte wees
- 'n aansienlike verhoging in u bloeddruk (simptome mag hoofpyn, moegheid en duiseligheid insluit)
- migraine-soortige hoofpyne, wat vir die eerste maal manifesteer
- indien u swanger sou raak
- indien u enige tekens van 'n bloedklont opmerk, soos:
  - pynlike swelling en rooiheid van die bene
  - skielike borspyn
  - problematiese asemhaling.

Mediese ondersoek
U dokter sal navraag doen aangaande u eie en u familie se mediese geskiedenis. U dokter mag besluit om 'n fisiese ondersoek uit te voer. Dit mag, indien nodig, 'n ondersoek van u borste en/of 'n interne ondersoek, insluit.
Sodra u TIBILIVE 2,5 mg behandeling begin, moet u u dokter vir gereelde opvolgondersoeke besoek (ten minste een keer per jaar). Bespreek die voordele en risiko's vir die voortdurende behandeling met TIBILIVE 2,5 mg tydens hierdie opvolgondersoeke, met u dokter.
Gaan vir gereelde siftingstoetse vir u borste asook servikale smeertoetse, soos deur u dokter aanbeveel word.
Ondersoek u borste gereeld vir enige veranderinge soos kuiltjies in die vel, veranderinge in die tepel, of enige knoppe wat u kan sien of voel.

Indien u ooit enige van die volgende probleme ervaar, vertel u dokter voordat u met die behandeling begin, aangesien dit mag terugkeer, of vererger tydens behandeling met TIBILIVE 2,5 mg. Indien dit wel die geval is, moet u u dokter meer gereeld besoek vir opvolgondersoeke:
- fibroïede aan die binnekant van die baarmoeder, groeisel aan die buitekant van die baarmoederwand (endometriose), of 'n geskiedenis van 'n uitermatige groeisel van die baarmoederwand (endometriale hiperplasie)
- verhoogde risiko vir die ontwikkeling van bloedklonte (sien Bloedklonte in 'n vena (trombose), onder)
- verhoogde risiko vir estrogeen-sensitiewe kanker (soos om 'n moeder, suster, of ouma te hê wie borskanker gehad het)
- hoë bloeddruk
- 'n lewerversteuring, soos 'n nie-kwaadaardige gewas
- diabetes
- galstene, of 'n baie hoë vetvlak in u bloed (trigliseriede)
- migraine of erge hoofpyne
- 'n siekte van die immuunstelsel, wat verskeie organe in die liggaam aantas (sistemiese lupus erythematosus, SLE)
- epilepsie
- asma
- 'n siekte wat die oordrom en gehoor aantas (otosklerose).

Hormoonvervangingsterapie (HVT) en kanker:
Uitermatige verdikking van die baarmoederwand (endometriale hiperplasie) en kanker van die baarmoederwand (endometriale kanker):
Daar is aanmeldings van 'n verhoogde selgroei, of kanker van die baarmoederwand by vroue wie TIBILIVE 2,5 mg gebruik. Die risiko vir kanker van die baarmoederwand neem toe, hoe langer u die medisyne gebruik.

Onreëlmatige bloeding
U mag onreëlmatige bloeding of druppels bloed (bloedvlekke) tydens die eerste maande van TIBILIVE 2,5 mg gebruik ervaar. Praat met u dokter indien die bloeding of bloedvlekke:
- vir langer as 3 maande volhou
- begin nadat u TIBILIVE 2,5 mg vir langer as 3 maande gebruik het
- voortduur selfs nadat u TIBILIVE 2,5 mg gebruik gestaak het.

Borskanker
TIBILIVE 2,5 mg bevat tibiloon met gekombineerde estrogeniese en progestogeniese uitwerking en dus mag langdurige gebruik, die risiko om borskanker te ontwikkel, verhoog.
Hierdie risiko neem geleidelik toe met die tydsduur van gebruik. Vroue wie TIBILIVE 2,5 mg neem, het 'n laer risiko as vroue wie gekombineerde menopousale hormoonterapie (MHT) gebruik en 'n vergelykbare risiko met estrogeen-alleenlik MHT.

Alle vroue wie TIBILIVE 2,5 mg gebruik, moet jaarlikse borste-ondersoeke deur 'n gesondheidsorgverskaffer ontvang en moet maandelikse borste-selfondersoeke uitvoer. Besoek u dokter indien u enige veranderinge opmerk, soos:
- dimpelvorming of induiking van die vel
- veranderinge in die tepel
- enige knoppe wat u kan sien of voel.

Ovariale kanker
Ovariale kanker is skaars – meer skaars as borskanker. 'n Effense toename in die risiko vir ovariale kanker is aangemeld by vroue wie hormoonvervangingsterapie vir ten minste 5 tot 10 jaar gebruik.
Die verhoging in risiko vir ovariale kanker met die gebruik van TIBILIVE 2,5 mg, is soortgelyk aan ander tipes HVT.

Effek van HVT op die hart en sirkulasie
Bloedklonte in 'n vena (trombose)
Die risiko vir bloedklonte in die vena is ongeveer 1,3- tot 3-keer hoër by HVT gebruikers as by nie-gebruikers, veral tydens die eerste jaar van gebruik.
Bloedklonte mag ernstig wees en sou een die longe bereik, kan dit borspyn, asemnood, floute en selfs sterfte veroorsaak.

U is meer geneig om 'n bloedklont in u vena te ontwikkel soos wat u ouer word en indien enige van die volgende op u van toepassing is. Raadpleeg u dokter indien enige van die volgende op u van toepassing is:
- u is swanger of het onlangs aan 'n baba geboorte geskenk
- u gebruik estrogene
- u is nie in staat om te loop vir 'n lang tydperk weens 'n groot operasie, besering, of siekte nie (sien ook afdeling 3, indien u 'n operasie benodig)
- u is ernstig oorgewig (BMI > 30 kg/m^2)
- u ly aan sistemiese lupus erythematosus (SLE)
- u het kanker
- u het 'n bloedstollingsprobleem wat langtermynbehandeling vereis met 'n medisyne wat bloedklonte verhoed
- indien u of enige van u naasbestaandes ooit 'n bloedklont in die been, long, of ander orgaan ontwikkel het.

Vir tekens van 'n bloedklont, verwys na die afdeling bo: Staak die gebruik van TIBILIVE 2,5 mg en besoek onmiddellik 'n dokter.

Dit mag nodig wees vir u om TIBILIVE 2,5 mg vir ongeveer 4 tot 6 weke voor u 'n operasie ondergaan te staak, om die risiko vir 'n bloedklont, te verlaag.

Hartsiekte (hartaanval)
Daar is geen bewyse dat HVT of TIBILIVE 2,5 mg, 'n hartaanval sal voorkom nie.

Beroerte
Onlangse navorsing dui aan dat HVT en TIBILIVE 2,5 mg die risiko vir 'n beroerte, slegs effens verhoog. Die verhoogde risiko kom hoofsaaklik voor by postmenopousale vroue ouer as 60 jaar.

Ander toestande
Estrogene mag vloeistofretensie veroorsaak en pasiënte met hart- of niersiekte, moet dus noukeurig waargeneem word.

Indien daar hoë vetvlakke in u bloed voorkom, wat trigliseriede genoem word (hipertrigliseridemie), sal u dokter hierdie toestand noukeurig monitor, aangesien daar 'n risiko vir die ontwikkeling van pankreatitis mag voorkom tydens TIBILIVE 2,5 mg behandeling.

Vertel u dokter, of die laboratoriumpersoneel dat u TIBILIVE 2,5 mg gebruik indien u 'n bloedtoets benodig, aangesien dit die resultate van sommige toetse mag beïnvloed.

TIBILIVE 2,5 mg sal nie geheueverlies voorkom nie. Daar is bewyse van 'n hoër risiko vir geheueverlies by vroue wie HVT begin gebruik na die ouderdom van 65 jaar. Raadpleeg u dokter vir advies.

Ander medisyne en TIBILIVE 2,5 mg
Vertel altyd u gesondheidsorgverskaffer indien u enige ander medisyne neem. (Dit sluit aanvullende en tradisionele medisyne in).

Sommige medisyne mag inmeng met die werking van TIBILIVE 2,5 mg.
Dit mag lei tot onreëlmatige bloeding. Dit is van toepassing op die volgende medisyne:
- medisyne teen bloedstolling (soos warfarien)
- medisyne vir epilepsie (soos fenobarbitoon, fenitoïen en karbamasepien)
- medisyne vir tuberkulose (soos rifampisien)
- kruiemiddels wat Johanneskruid *(Hypericum perforatum)* bevat.

Indien u binnekort 'n operasie ondergaan, maak seker dat u dokter daarvan bewus is. Dit mag nodig wees dat u die gebruik van HVT vir ongeveer 4 tot 6 weke voor die operasie staak, om die risiko vir 'n bloedklont te verlaag. U dokter sal aandui wanneer u weer u HVT mag begin gebruik.

TIBILIVE 2,5 mg saam met kos en drinkgoed
TIBILIVE 2,5 mg mag saam met, of sonder kos geneem word.

Swangerskap, borsvoeding en fertiliteit
Indien u swanger is of borsvoed, vermoed dat u swanger is, of 'n baba beplan, raadpleeg asseblief u dokter, apteker, of ander gesondheidsorgverskaffer vir advies, voordat u TIBILIVE 2,5 mg gebruik.

TIBILIVE 2,5 mg moet nie tydens swangerskap gebruik word nie. Staak die gebruik van TIBILIVE 2,5 mg indien u vermoed dat u swanger is, of reeds swanger is.

TIBILIVE 2,5 mg word teenaangedui tydens borsvoeding.

Bestuur en die hantering van masjiene
TIBILIVE 2,5 mg toon geen bekende uitwerking op u vermoë om te bestuur, of masjiene te hanteer nie.
Dit is nie altyd moontlik om te voorspel tot watter mate TIBILIVE 2,5 mg met die daaglikse aktiwiteite van 'n pasiënt mag inmeng nie. Pasiënte moet nie by bogenoemde aktiwiteite betrokke raak, totdat hulle bewus is hoe TIBILIVE 2,5 mg hulle aantas nie.

TIBILIVE 2,5 mg bevat laktose
Indien u dokter aangedui het, dat u 'n onverdraagsaamheid teenoor sekere suikers toon, raadpleeg u dokter, voordat u TIBILIVE 2,5 mg gebruik.

3. Hoe om TIBILIVE 2,5 mg te gebruik
Moet nie medisyne wat vir u voorgeskryf is met enige ander persoon deel nie. Gebruik TIBILIVE 2,5 mg altyd presies soos deur u dokter aanbeveel word. U moet u dokter of apteker raadpleeg, indien u onseker is.

Volwassenes:
Die gewone dosis is een tablet daagliks, verkieslik op dieselfde tydstip elke dag. Sluk die tablet heel, met 'n bietjie water.

Natuurlike menopouse:
Wag vir 12 maande, na u laaste menstrusie voordat u begin om TIBILIVE 2,5 mg te neem.

Menopouse as gevolg van 'n operasie:
Indien u 'n histerektomie gehad het, of u tans behandel word vir endometriose, kan u TIBILIVE 2,5 mg dadelik begin gebruik.

U dokter sal u vertel vir hoe lank u behandeling met TIBILIVE 2,5 mg sal duur. Moet nie behandeling vroegtydig staak nie, aangesien u simptome mag terugkeer.
Indien u onder die indruk is dat die uitwerking van TIBILIVE 2,5 mg té sterk of té swak is, vertel u dokter, of apteker.

Indien u meer TIBILIVE 2,5 mg neem as wat u behoort
In die geval van oordosering, raadpleeg u dokter of apteker. Indien beide nie beskikbaar is nie, kontak u naaste hospitaal of gifbeheersentrum.

Simptome van oordosering mag die volgende insluit:
- naarheid, braking en vaginale bloeding.

Neem hierdie inligtingsblad en die oorblywende TIBILIVE 2,5 mg tablette saam met u, sodat die dokter weet wat u geneem het.

Indien u vergeet om TIBILIVE 2,5 mg te neem
Indien u vergeet om TIBILIVE 2,5 mg te neem, neem dit so gou as wat u onthou op dieselfde dag, tensy daar meer as 12 ure verstryk het. Indien daar meer as 12 ure verstryk het, slaan die vergete dosis oor en neem u tablet die volgende dag. Moet nie 'n dubbeldosis neem, om op te maak vir die vergete individuele doserings nie.

4. Moontlike newe-effekte
TIBILIVE 2,5 mg kan newe-effekte hê.
Nie alle newe-effekte wat vir TIBILIVE 2,5 mg aangemeld is, word in hierdie inligtingsblad ingesluit nie. Sou u algemene gesondheid versleg, of indien u enige ongewenste effekte ervaar terwyl u TIBILIVE 2,5 mg gebruik, raadpleeg asseblief u gesondheidsorgverskaffer vir advies.

Indien enige van die volgende gebeur, staak die gebruik van TIBILIVE 2,5 mg en vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal:
- swelling van die hande, voete, enkels, gesig, lippe, mond, of keel, wat sluk of asemhaling mag bemoeilik
- uitslag of gejeuk
- floute.

Hierdie is alles baie ernstige newe-effekte. Indien u dit het, kon u 'n ernstige allergiese reaksie vir TIBILIVE 2,5 mg gehad het. U mag dringende mediese aandag, of hospitalisasie benodig.

Vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal, indien u enige van die volgende opmerk:
- u bloeddruk verhoog
- u vel of die wit gedeeltes van u oë word geel (geelsug)
- u ervaar skielik migraine-tipe hoofpyne (sien afdeling 2 bo)
- u tekens van 'n bloedklont opmerk (pynlike swelling en rooiheid van die bene, skielike borspyn, moeilike asemhaling)
- beroerte (met simptome soos, sukkel om te loop, praat en verstaan, asook verlamming of gevoelloosheid in die gesig, arm, of been).

Hierdie is alles ernstige newe-effekte. U mag dringende mediese aandag benodig.

Vertel u dokter indien u enige van die volgende opmerk:
Newe-effekte wat dikwels voorkom:
- lae buikpyn
- abnormale haargroei
- vaginale probleme soos, afskeiding, gejeuk, irritasie, vaginale bloeding, of vlekking, teerheid van die borste, bekkenpyn, verdikking van die baarmoederwand, of servikale wand
- gewigstoename, abnormale papsmeertoetsresultate.

Minder algemene newe-effekte:
- vloeistofretensie (geswelde hande, enkels of voete)
- aknee, jeukerige vel
- gastroïntestinale versteuring, abdominale ongemak
- borsongemak, swaminfeksie, vaginale sproei (swaminfeksie), tepelpyn
- geheueverlies.

Die volgende newe-effekte is aangemeld maar die frekwensie van voorkoms is onbekend:
- depressie
- duiseligheid, hoofpyn, migraine
- sigsteurnisse, wasige sig
- lewerprobleme
- velprobleme soos uitslag, gejeuk, skubberige vlekke en rooi vel
- gewrigspyn, spierpyn.

Indien u enige newe-effekte opmerk, wat nie in hierdie inligtingsblad genoem word nie, raadpleeg asseblief u dokter, of apteker.

Aanmelding van newe-effekte
Indien u newe-effekte ervaar, praat met u dokter, apteker of verpleegkundige. U kan ook newe-effekte by SAHPRA via die aanlynskakel vir ongewenste geneesmiddelreaksie rapporteer: https://www.sahpra.org.za/Publications/Index/8 of https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/. Deur die aanmelding van newe-effekte, kan u help om meer inligting aangaande die veiligheid van TIBILIVE 2,5 mg in te win.
U kan ook 'n epos direk na die maatskappy stuur, pharmacovigilance@pharmadynamics.co.za om veiligheid van die produk te verseker.

5. Hoe om TIBILIVE 2,5 mg te bewaar
Bewaar alle medisyne buite die bereik van kinders.
Bewaar teen of benede 30 °C.
Bewaar in die oorspronklike verpakking om te beskerm teen lig en vogtigheid.
Moet nie gebruik na die vervaldatum wat op die kartonhouer aangedui word nie.
Neem alle ongebruikte medisyne na u apteker terug.
Moet nie ongebruikte medisyne in dreine of rioolstelsels (bv. toilette), weggooi nie.

6. Verpakkingsinhoud en ander inligting
Wat TIBILIVE 2,5 mg bevat:
Elke tablet bevat 2,5 mg tiboloon.

Die ander bestanddele is:
Tabletkerne:
Aartappelstysel, askorbielpalmitaat, laktosemonohidraat, magnesiumstearaat, mannitol.

Hoe TIBILIVE 2,5 mg lyk en die verpakkingsinhoud
Wit tot naaswit onbedekte tablet, sonder enige identifiseringsmerke op die tablette.

TIBILIVE 2,5 mg tablette word verpak in PVC/Aluminiumfoelie-stulpstroke. Stulpstroke word in 'n kartonhouer met 28 or 30 tablette geplaas.

Eienaar van die Registrasiesertifikaat
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Hierdie inligtingsblad was voorheen hersien
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