PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

LIVIFEM® Tablets

Read all of this leaflet carefully before you start taking LIVIFEM.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- LIVIFEM has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

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

1. WHAT LIVIFEM CONTAINS

The name of your medicine is LIVIFEM. Each tablet contains 2,5 mg tibolone as the active ingredient. LIVIFEM also contains the following inactive ingredients: Potato starch, magnesium stearate, ascorbyl palmitate and lactose.

Contains lactose.

2. WHAT LIVIFEM IS USED FOR

During and after the menopause, the production of sex hormones by the body decreases. Women may then suffer from complaints such as hot flushes, night sweats, vaginal irritation, depression and loss of sexual desire. In addition, the menopause may cause thinning of the

bones (osteoporosis).

LIVIFEM contains tibolone, a substance that can replace the natural sex hormones after the menopause. LIVIFEM can relieve menopausal complaints, also in women who have had their ovaries removed; prevent bone loss and improve bone mineral density in established post-menopausal osteoporosis. Relief of symptoms usually starts within a few weeks, but optimal results are obtained after at least 3 months of treatment. LIVIFEM is not intended for contraceptive use.

Unlike some other preparations used for hormone replacement therapy, LIVIFEM does not stimulate the lining of the womb. Treatment with LIVIFEM therefore does not lead to monthly vaginal bleeding.

3. BEFORE YOU TAKE LIVIFEM

LIVIFEM may not be suitable for you if you suffer from certain medical conditions.

If any of the following applies to you or if you are not sure about any of the points below, **talk to your doctor** before taking LIVIFEM.

Do not take LIVIFEM

- If you are **pregnant** or think you may be pregnant.
- If you are **breastfeeding**.
- If you have or have ever had **breast cancer**, or if you are suspected of having it.
- If you have **cancer which is sensitive to oestrogens**, such as cancer of the womb lining (endometrium), or if you are suspected of having it.
- If you have any **unexplained vaginal bleeding.**

- If you have **excessive thickening of the womb lining** (endometrial hyperplasia) that is not being treated.
- If you have or have ever had a **blood clot in a vein** (thrombosis), such as in the legs (deep venous thrombosis) or the lungs (pulmonary embolism).
- If you have a **blood clotting disorder** (such as protein C, protein S or antithrombin deficiency).
- If you have or recently have had a disease caused by blood clots in the arteries, such as a **heart attack**, **stroke** or **angina**.
- If you have or have ever had a **liver disease** and your liver function tests have not returned to normal.
- If you have a rare blood problem called “porphyria” which is passed down in families (inherited).
- If you are **allergic** (hypersensitive) to **tibolone** or any of the other ingredients of LIVIFEM.

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

Take special care with LIVIFEM

Tell your doctor if you have ever had any of the following problems, before you start the treatment, as these may return or become worse during treatment with LIVIFEM. 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

- 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 LIVIFEM and see a doctor immediately

If you notice any of the following when taking LIVIFEM:

- any of the conditions mentioned in **"Do not take LIVIFEM"**
- 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.

Caution: Before taking LIVIFEM it is important to tell your doctor if you have or have ever had too much cholesterol or other fatty substances in the blood. Also tell your doctor if you have been treated with other sex hormones recently.

During long-term treatment with LIVIFEM annual medical checks are recommended.

LIVIFEM 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 and studies of an increased cell growth or cancer of the lining of the womb in women using LIVIFEM. The risk of cancer of the lining of the womb increases with the duration of use.

Irregular bleeding

You may have irregular bleeding or drops of blood (spotting) during the first 3 to 6 months of taking LIVIFEM.

However, if the irregular bleeding:

- carries on for longer than the first 6 months
- starts after you have been taking LIVIFEM for longer than 6 months
- carries on after you have stopped taking LIVIFEM.

Consult your doctor as soon as possible.

Breast cancer

Evidence suggests that taking combined oestrogen-progestogen and possibly also oestrogen-only hormone replacement therapy increases the risk of breast cancer. The extra risk depends on how long you take hormone replacement therapy. The additional risk

becomes clear within a few years. However, it returns to normal within a few years (at most 5) after stopping treatment.

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. A slightly increased risk of ovarian cancer has been reported in women taking hormone replacement therapy for at least 5 to 10 years.

Effect of LIVIFEM 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 hormone replacement therapy 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
- 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 LIVIFEM and see a doctor immediately"** above.

Heart disease (heart attack)

There is no evidence that LIVIFEM will prevent a heart attack.

Stroke

Recent research suggests that hormone replacement therapy and LIVIFEM increases the risk of having a stroke. This increased risk has mainly been observed in elderly post-menopausal women above 60 years of age.

Other conditions

Hormone replacement therapy like LIVIFEM will not prevent memory loss. There is some evidence of a higher risk of memory loss in women who start using hormone replacement therapy, like LIVIFEM, after the age of 65 years. Speak to your doctor for advice.

LIVIFEM should not be taken until 12 months after your last natural menstrual bleed. If LIVIFEM is taken sooner than this, the risk of irregular menstrual bleeding may be increased.

Taking other medicines with LIVIFEM

Some medicines may interfere with the effect of LIVIFEM. 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 carbamazepine)

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

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other health professional for advice before taking LIVIFEM.

Ability to drive or operate machinery. As far as is known LIVIFEM has no adverse effect on alertness and concentration.

Important information about some of the ingredients of LIVIFEM

LIVIFEM tablets contain lactose. If you have been told by your doctor that you have intolerance to some sugars contact your doctor before taking this medicinal product.

4. HOW TO TAKE LIVIFEM

Take LIVIFEM as directed by your doctor.
You should always read the instructions on the label of your medicine.
If you are not sure how to take LIVIFEM, ask your doctor, pharmacist or other healthcare professional.

The usual dosage is one tablet daily, preferably at the same time each day. Swallow the tablet whole without chewing, using some water or other fluid. The LIVIFEM pack contains 28 white tablets. The first tablet should be taken from the upper row of the pack marked with the corresponding day of the week. You should then follow the direction of the arrows and continue taking one tablet each day until the pack is empty.

What to do if you miss a dose

Take the missed dose as soon as you remember unless you are more than 12 hours late. If you are more than 12 hours late, do not take the missed dose and just carry on with the next dose as normal.

What to do in the case of an overdose

If someone has taken several tablets at once, there is no need for great concern. However, you should consult your doctor. Symptoms that may arise are nausea and vomiting and in females vaginal bleeding may occur after a few days.

General instructions

1. This medicine has been prescribed only for your current medical condition. Do not use it for other medical problems.
2. Do not allow other people to use your medicines and do not use medicines meant for other people.
3. Tell any doctor treating you what medicines you are taking. Always carry a medical information card stating which medicines you are using. This can be very important in case you are involved in an accident.
4. Return unused medicines to the pharmacy for disposal.
5. Make sure that other people you live with or who look after you read this information.

5. POSSIBLE SIDE EFFECTS

The following diseases are reported more often in women using hormone replacement therapy compared to women not using hormone replacement therapy:

- 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 hormone replacement therapy is started over the age of 65 years.

LIVIFEM may have side effects. Most of these side effects are mild.

Common side effects observed in clinical studies (occurring in 1 to 10 % of the women using LIVIFEM) were:

- vaginal bleeding or spotting
- abdominal pain
- weight gain
- breast pain
- unnatural hair growth
- vaginal symptoms such as discharge, itching and irritation.

An uncommon side effect (occurring in 0,1 to 1 % of the women using LIVIFEM) was acne.

Other side effects observed with LIVIFEM in market use were:

- dizziness, headache, migraine, depression
- rash or itching
- visual disturbances
- gastrointestinal upset
- fluid retention
- joint pain, muscle pain
- changes in liver function.

In some women, vaginal bleeding or spotting may occur, mainly during the first months of treatment. Other side effects may occasionally occur, such as headache, swollen feet and lower legs, dizziness, itching, weight gain, nausea, abdominal pain, rash and depression.

Tell your doctor if vaginal bleeding or spotting occurs or if any side effects become troublesome or continue. It is also important to tell your doctor or pharmacist if you experience any other unusual or unexpected symptoms during treatment with LIVIFEM.

You should stop taking LIVIFEM if you experience any signs of thrombosis (headache or pain elsewhere in your body, dizziness, fainting, disturbances in vision, swollen ankles) or jaundice (yellowing of the eyes or skin).

Not all side effects reported for LIVIFEM are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking LIVIFEM, please consult your doctor, pharmacist or other healthcare professional for advice. Tell your doctor if any side effect becomes troublesome or continues.

6. STORING AND DISPOSING OF LIVIFEM

Store at or below 25 °C, and protect from light and moisture. Keep your LIVIFEM in the original container in a safe place. Store all medicines out of reach of children.
The expiry date (sometimes written as “EXP.:”) is printed on the strip of tablets. Do not use LIVIFEM after this date.

7. PRESENTATION OF LIVIFEM

Press-through strips with 28 tablets, in a carton.

8. IDENTIFICATION OF LIVIFEM

A white, round, flat tablet with bevelled edges, coded MK above 2 on the one side and Organon and a star on the reverse side.

9. REGISTRATION NUMBER

V/21.5.4/55

10. NAME AND BUSINESS ADDRESS OF REGISTRATION HOLDER

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11. DATE OF PUBLICATION

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