

Livial®

USER PACKAGE LEAFLET

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

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine 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.

In this leaflet:

1. What Livial is and what it is used for
2. Before you take Livial
3. How you take Livial
4. Possible side effects
5. Storing Livial
6. More about Livial

Livial, 2.5 mg, tablet

- The active substance is: tibolone.
- The other ingredients are: potato starch, lactose, ascorbyl palmitate, and magnesium stearate.
- Livial 2.5 mg tablets are white and marked 'MK2' on one side and 'Organon' on the other side. They come in cardboard boxes containing one or three packs of 28 tablets.

1. What Livial is and what it is used for

At the time of the menopause (or after an operation to remove the ovaries), a woman's body stops producing the female hormone, estrogen. Women may then suffer from symptoms such as hot flushes, night sweats, vaginal irritation, depression, and loss of sexual desire. Too little sex hormones may also cause thinning of the bones (osteoporosis). Livial belongs to the group of medicines called Hormone Replacement Therapy (HRT). It relieves menopausal symptoms and stops the process of thinning of the bones. Relief of symptoms usually starts within a few weeks, but optimal results are obtained after at least three months of treatment. In Section 6 you can find more information about how Livial works and what it is used for.

2. Before you take Livial

Do not take Livial if you

- are pregnant or think you may be pregnant.
- are breast feeding
- have or have had breast cancer, or if breast cancer is suspected
- have or if it is suspected that you have an estrogen-dependent tumor, such as cancer of the lining of the womb
- have abnormal vaginal bleeding, which has not been evaluated by your doctor
- have abnormal growth of the lining of your womb (endometrial hyperplasia)
- have or have had a blood circulation disorder such as blood clots (in the veins of the legs or the lungs)
- have had a heart condition such as angina or a heart attack
- have or have had liver disease as long as the liver function has not returned to normal
- have had an allergic reaction to tibolone, or any of the other ingredients in Livial
- have porphyria (an inherited disorder)

Take special care with Livial

As well as benefits, hormone replacement therapy (HRT) has some risks which you need to consider when you're deciding whether to take it, or whether to carry on using it.

Medical check-ups

Before you start taking HRT, your doctor should ask about your own and your family's medical history. Your doctor may decide to examine your breasts and/or your abdomen, and may do an internal examination. You will also get periodic check-ups, especially examinations of the breasts.

Once you've started on HRT, you should see your doctor for regular check-ups (at least once a year). At these check-ups, your doctor may discuss with you the benefits and risks of continuing to take HRT. Certain conditions may be made worse by HRT. If you have or have had any of the following conditions inform your doctor who will monitor you closely: uterine fibroids, endometriosis, a history of clots in the blood vessels, if anyone in your family has ever had an estrogen-dependent cancer, such as a close relative who has had breast cancer, high blood pressure, liver disorders, diabetes, gallstones, migraine or (severe) headache, systemic lupus erythematosus, a history of endometrial hyperplasia, epilepsy, asthma, otosclerosis (inherited deafness). Tell your doctor if you notice any change in your condition whilst using Livial.

HRT can sometimes cause fluid retention.

Livial is not a contraceptive and will not stop you getting pregnant.

Reasons for immediately stopping Livial:

- jaundice (your skin goes yellow)
- a sudden increase in blood pressure
- if you get migraine, or severe headaches, for the first time

Effects on your risk of developing cancer

Endometrial cancer

Taking estrogen-only HRT for a long time can increase the risk of an increased cell growth or cancer of the lining of the womb (the endometrium). Taking a progestogen as well as the estrogen helps to lower this risk.

Because Livial is slightly different to most HRT you don't need to add a separate progestogen when you are taking Livial. There have been reports of an increased cell growth or cancer of the lining of the womb in women using Livial. The risk of cancer of the lining of the womb increases with the duration of use.

If you get breakthrough bleeding or spotting, it's usually nothing to worry about, especially during the first few months of taking HRT. But if the bleeding or spotting:

- carries on for more than 6 months
- starts after you've been on HRT for a while
- carries on even after you've stopped taking HRT

Make an appointment to see your doctor. It could be a sign that your endometrium has become thicker.

Breast cancer

Women who have breast cancer, or have had breast cancer in the past, should not take HRT.

Taking estrogen, estrogen-progestogen combined HRT or tibolone for several years slightly increases the risk of breast cancer. The risk increases with the duration of HRT use and returns to normal within about five years after stopping HRT. Women using Livial have a lower risk than women using combined HRT but have a greater risk of developing breast cancer than women using estrogen-only HRT. Looking at women in their 50s who are not taking HRT — on average, 32 in 1000 will be diagnosed with breast cancer. For 1000 women in their 50s, 2 to 6 extra cases may occur if they are taking HRT for 5 years, and 5 to 19 extra cases may occur if HRT is used for 10 years. Be sure to 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.

Ovarian cancer

Ovarian cancer (cancer of the ovaries) is very rare, but it is serious. It can be difficult to diagnose, because there are often no obvious signs of the disease.

Some studies have indicated that taking estrogen-only HRT for more than 5 years may increase the risk of ovarian cancer. It is not yet known whether other kinds of HRT increase the risk in the same way.

Effects on your heart or circulation

Heart disease

HRT is not recommended for women who have heart disease, or have had heart disease recently. If you have ever had heart disease, talk to your doctor to see if you should be taking HRT.

HRT will not help to prevent heart disease.

Studies with one type of HRT (containing conjugated estrogen plus the progestogen MPA) have shown that women may be slightly more likely to get heart disease during the first year of taking the medication. For other types of HRT, the risk is likely to be similar, although this is not yet certain.

If you get:

- a pain in your chest that spreads to your arm or neck

See a doctor as soon as possible and do not take any more HRT until your doctor says you can. This pain could be a sign of heart disease.

Stroke

Recent research with one type of HRT (containing conjugated estrogen plus the progestogen MPA) has shown a slight increase in the risk of having a stroke.

Looking at women in their 50s who are not taking HRT — 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 HRT, the figure would be 4 in 1000.

Looking at women in their 60s who are not taking HRT — 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 HRT, the figure would be 15 in 1000.

It is not yet known whether other kinds of HRT increase the risk in the same way.

If you get:

- unexplained migraine-type headaches, with or without disturbed vision

See a doctor as soon as possible and do not take any more HRT until your doctor says you can. These headaches may be an early warning sign of a stroke.

Blood clots

Estrogen and estrogen-progestogen combined HRT may increase the risk of blood clots in the veins (also called deep vein thrombosis, or DVT), especially during the first year of taking it. It is unknown if Livial increases the risk in the same way.

These blood clots are not always serious, but if one travels to the lungs, it can cause chest pain, breathlessness, collapse or even death. This condition is called pulmonary embolism, or PE. DVT and PE are examples of a condition called venous thromboembolism, or VTE.

You are more likely to get a blood clot

- if you are seriously overweight
 - if you have had a blood clot before
 - if any of your close family have had blood clots
 - if you have had one or more miscarriages
 - if you have any blood clotting problem that needs treatment with a medicine such as warfarin
 - if you are off your feet for a long time because of major surgery, injury or illness
 - if you have a rare condition called systemic lupus erythematosus
- If any of these things apply to you, talk to your doctor to see if you should take HRT.

Looking at women in their 50s who are not taking HRT — on average, over a 5-year period, 3 in 1000 would be expected to get a blood clot. For women in their 50s who are taking HRT, the figure would be 7 in 1000.

Looking at women in their 60s who are not taking HRT — on average, over a 5-year period, 8 in 1000 would be expected to get a blood clot. For women in their 60s who are taking HRT, the figure would be 17 in 1000.

If you get:

- painful swelling in your leg;
- sudden chest pain;
- difficulty breathing;

See a doctor as soon as possible and do not take any more HRT until your doctor says you can. These may be signs of a blood clot.

If you are going to have surgery, 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.

Taking Livial with food and drink.

You can eat and drink normally while you're taking Livial.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine. If you are pregnant or breast-feeding or think you may be pregnant, do not take Livial.

Driving and using machines

As far as is known, Livial has no effect on alertness and concentration.

Important information about some of the ingredients of Livial

Livial tablets contain lactose. If you react badly to lactose or milk, talk to your doctor or pharmacist.

Using other medicines

Other medicines may influence the effects of Livial, or Livial may affect other medicines. Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicine, especially:

- Medicines for blood clotting problems, such as warfarin, as your doctor may need to adjust the dose of these medicines

Remember to mention medicines you bought over the counter, without a prescription.

3. How you take Livial

Livial is for oral use. Take one tablet each day. Swallow it with some

water or other drink. Take the tablet at the same time each day. The strips with Livial are marked with the days of the week. Start by taking the tablet marked with that day. For example, if it is a Monday, take a tablet marked Monday on the upper row of the strip. Follow the days of the week until the strip is empty. Start the next strip the next day. Do not leave a break between strips or packs.

Livial should not be taken until twelve months after your last natural menstrual bleed. If Livial is taken sooner than this, the chance of irregular vaginal bleeding may be increased.

If you have the impression that the effect of Livial is too strong or too weak, talk to your doctor immediately.

If you take more Livial than you should:

If you may have taken more Livial than you should, talk to a doctor or pharmacist immediately.

If anybody takes too many tablets, there is no need for great concern. However, you should talk to your doctor straight away. Signs of an overdose may include feeling sick, being sick or vaginal bleeding.

If you forgot to take Livial:

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.

Do not take a double dose to make up for forgotten individual doses.

4. Possible side effects

Like all medicines, Livial may have side effects. Most of these side effects are mild.

Common side effects observed in clinical studies (occurring in 1–10% of the women using Livial) 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 0.1–1% of the women using Livial) was amnesia.

Other side effects observed with Livial in market use were:

- Dizziness, headache, migraine, depression
- Rash or itching
- Visual disturbances
- Gastro-intestinal upset
- Fluid retention
- Joint pain, muscle pain
- Changes in liver function

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

Tell your doctor if vaginal bleeding or spotting occurs, or if any of the above mentioned side effects become troublesome or continue.

Other side effects, which may occur with estrogen-progestogen combined HRT are:

- benign and malignant hormone-dependent tumors
- blood clots in the veins
- heart attack and stroke
- gall bladder disease
- skin problems such as rashes, discoloration or red patches on the skin
- dementia (decline in mental function marked by memory loss)

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

5. Storing Livial

Keep Livial out of reach and sight of children.

Keep your Livial tablets in the original package and in the outer carton at 2–25 °C. Check if there are special storage conditions given on the box.

Do not use Livial after the expiry date stated on the carton

6. More about Livial

The most important natural sex hormones in women are estrogen and progesterone. These hormones are necessary for normal sexual development and functioning of women and play an important role in the control of the menstrual cycle. Estrogens also play an important role in bone formation. Bone is built up during youth and peak bone mass is reached between age 20–30. After this age, bone mass diminishes, first slowly, but later in life bone loss is accelerated, especially after the menopause. The menopause is the period (usually around the age of 50) when the ovaries gradually stop producing estrogens. If the ovaries are removed surgically (ovariectomy) before the menopause, the decrease in hormone production occurs very abruptly.

The decrease in hormone production often leads to the well-known climacteric symptoms, such as hot flushes and night sweats. The shortage of sex hormones may also cause the lining of the vagina to become thin and dry. As a result sexual intercourse may be painful and vaginal infections may occur more frequently. These physical problems are in some women accompanied by mood changes, nervousness, depression, irritability and loss of sexual desire.

A problem that often goes unnoticed, is the accelerated loss of bone in the years around and after the menopause. Gradually, the bones become brittle and may easily break (osteoporosis), especially in your spine, hip and wrists. Osteoporosis may also cause back pain, loss of height and a curved back.

Livial contains tibolone, a substance that has favorable effects on different tissues in the body, such as brain, vagina and bone. This results in the relief of climacteric symptoms such as hot flushes and night sweats, a beneficial effect on the lining of the vagina and a favorable effect on mood and sexual desire. Livial can also stop the process of bone loss that occurs after the menopause in your spine, hip and wrists. Unlike some hormone replacement therapies, Livial does not stimulate the lining of the womb. Treatment with Livial therefore does not lead to monthly vaginal bleeding.

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This leaflet was revised on June 2005

This is a medicament

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament. The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers & Union of Arab Pharmacists