**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986**
The medicine is dispensed with a doctor's prescription only.

# Femoston 1/10 mg

## Film-coated tablets

**The active ingredients and their quantities:**
Each film-coated tablet containing estradiol only:
Estradiol 1 mg
Each film-coated tablet containing a combination of estradiol and dydrogesterone:
Estradiol 1 mg
Dydrogesterone 10 mg
For a list of inactive and allergenic ingredients in the medicine – please see section 6 ("Further Information").

**Read the leaflet carefully in its entirety before using the medicine.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

### 1. WHAT IS THE MEDICINE INTENDED FOR?

Femoston 1/10 mg is a Hormone Replacement Therapy (HRT). It contains two types of female hormones, an estrogen called estradiol and a progestogen called dydrogesterone. Femoston 1/10 mg is suitable for postmenopausal women with at least 6 months since their last natural period.

Femoston 1/10 mg is intended for:
- **Relief of symptoms occurring after menopause**
  During menopause, the amount of estrogen produced by a woman's body decreases. This can cause symptoms such as a feeling of warmth in the face, neck and chest ("hot flashes"). Femoston 1/10 mg alleviates these symptoms after cessation of menstruation. You will only be prescribed Femoston 1/10 mg if your symptoms hinder your daily life routine.
- **Prevention of osteoporosis**
  Some postmenopausal women may develop bone depletion (osteoporosis). You should discuss all available treatments with your doctor. If you are at an increased risk of fractures due to osteoporosis, and other medicines are not suitable for you, you can use Femoston 1/10 mg to prevent osteoporosis.

The treatment with Femoston 1/10 mg is intended for women with a normal uterus.
Experience in treating women over the age of 65 is limited.

**Therapeutic group:** Sex hormones, progestogens and estrogens, for continuous therapy.

### 2. BEFORE USING THE MEDICINE

**Medical history and routine examinations**
The use of hormone replacement therapy carries risks, which need to be considered when deciding whether to start or continue treatment. The experience in treating women with premature menopause (due to ovarian failure or surgery) is limited. The risk of using hormone replacement therapy in women with premature menopause may be different.
Please talk to your doctor before you begin or resume hormone replacement therapy, your doctor will ask you about your medical history and that of your family's. Your doctor may decide to perform a physical examination. This examination may include a breast examination and/or an internal examination, if necessary.
Once you have started treatment with Femoston 1/10 mg you should see your doctor for periodic check-ups (at least once a year). During these check-ups, discuss with the doctor the benefits and risks of continuing to use Femoston 1/10 mg.
Go for routine breast screening, as recommended by the doctor.

**☒ Do not use the medicine:**
If one or more of the following conditions applies to you. If you are not sure about any of the points appearing below, talk to your doctor before using Femoston 1/10 mg.
**Do not use Femoston 1/10 mg if:**
- You have, or have had **breast cancer**, or if there is a suspicion that you have breast cancer
- You have **cancer which is sensitive to estrogens**, such as cancer of the uterine lining (endometrium), or if you are suspected of having such a cancer
- You have **any unexplained vaginal bleeding**
- You have **excessive thickening of the uterine lining** (endometrial hyperplasia) that is not being treated
- 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)
- You have a **blood clotting disorder** (such as deficiency in protein C, protein S, or antithrombin deficiency)
- You have or have recently had a disease caused by blood clots in the arteries, such as a **heart attack, stroke or angina**
- You have or have had a **liver disease** and your liver function test results have not returned to normal values
- You have a rare inherited blood problem called "porphyria"
- You are **sensitive (allergic)** to estradiol, dydrogesterone or to any of the other ingredients contained in the medicine. For a list of the inactive ingredients, see section 6 "Further Information"

If any of the above-listed conditions appear for the first time while taking Femoston 1/10 mg, stop taking the medicine and consult the doctor immediately.

**Special warnings regarding use of the medicine**
**❗ Before treatment with Femoston 1/10 mg, tell the doctor if** you have ever suffered from any of the following effects, as they may reoccur or become worse during treatment with Femoston 1/10 mg. In such a case, you should be examined by your doctor more frequently:
- Uterine fibroids.
- Growth of uterine lining outside the uterus (endometriosis) or a history of excessive growth of the uterine lining (endometrial hyperplasia).
- A brain tumor that may be affected by the levels of progestogens (meningioma).
- Increased risk of developing blood clots [for further information, see later on in the leaflet in "Blood clots in a vein (thrombosis)"].
- Increased risk of getting an estrogen-sensitive cancer (such as a mother, sister or grandmother who has had breast cancer).
- Hypertension.
- A liver disorder such as a benign liver tumor.
- Diabetes.
- Gallstones.
- Migraine or severe headaches.
- An immune system disease that affects many organs of the body [systemic lupus erythematosus, SLE (lupus)].
- Epilepsy.
- Asthma.
- A disease affecting the eardrum and hearing (otosclerosis).
- High blood lipid levels (triglycerides).
- Fluid retention due to heart or kidney problems.

The preparation is intended for treatment of symptoms and not to prevent them.
If you have been treated with the preparation Femoston 1/10 mg for 3 months and have not noticed an improvement in the symptoms, you should return to the doctor.

**Stop taking Femoston 1/10 mg and see a doctor immediately** if you notice any of the following conditions while taking hormone replacement therapy:
- Any of the conditions mentioned in the section "Do not use Femoston 1/10 mg if:"
- Yellowing of the skin or the whites of the eyes (jaundice). These may be signs of a liver disease.
- A large increase in blood pressure (symptoms may be: headache, tiredness, dizziness).
- Migraine-like headaches which occur for the first time.
- If you become pregnant.
- If you notice signs of blood clots, such as: painful swelling and redness of the legs, sudden chest pain, difficulty in breathing. For further information, see "Blood clots in a vein (thrombosis)" discussed further on in the leaflet.

**Note:** Femoston 1/10 mg is not a contraceptive. If less than 12 months have passed since your last menstrual period or if you are under the age of 50, you may still need to use additional contraceptive methods to prevent pregnancy. Consult your doctor about this.

**Hormone replacement therapy and cancer**
**Excessive thickening of the uterine lining (endometrial hyperplasia) and endometrial cancer:**
Taking estrogen-only hormone replacement therapy will increase the risk of excessive thickening of the uterine lining and endometrial cancer. The progestogen in Femoston 1/10 mg protects you from this extra risk.

**Abnormal vaginal bleeding**
While taking Femoston 1/10 mg, bleeding will occur once a month (called withdrawal bleeding). However, if you have abnormal bleeding or drops of blood (spotting) besides the monthly bleeding, which:
- Lasts beyond the first 6 months
- Begins after you have been taking Femoston 1/10 mg for more than 6 months
- Continues after you stop taking Femoston 1/10 mg

**Contact your doctor as soon as possible.**

**Breast cancer**
Evidence indicates that taking estrogen-progestogen combined, and possibly also estrogen-only hormone replacement therapy increases the risk of breast cancer. The increased risk depends on the duration of time that you take hormone replacement therapy. The additional risk can be assessed after several years of treatment with the preparation. The risk returns to normal in the population within about 5 years after stopping treatment.
*Comparison*
Women aged 50-79 who are not taking hormone replacement therapy, on average, 9-17 out of 1000 women will be diagnosed with breast cancer over a 5-year period.
For women aged 50-79 who are taking estrogen-progestogen hormone replacement therapy over a period of 5 years, there will be an average of 13-23 women out of 1000 with breast cancer (meaning, an additional 4 to 6 cases).
**Check your breasts regularly. See your doctor if you notice any changes such as:**
- dimpling of the skin
- changes in the nipple
- lumps you can see or feel

In addition, it is recommended that you join mammography screening programs when they are offered to you. When undergoing a mammogram, it is important that you inform the nurse or the medical staff member who is performing the screening that you are using hormone replacement therapy. This is because the treatment may increase the density of your breasts which may affect the results of the test. When breast density is increased, not all lumps may be detected in a mammogram.

**Ovarian cancer**
Ovarian cancer is rarer than breast cancer. The use of estrogen-only or combined estrogen-progestogen hormone replacement therapy has been associated with a slightly increased risk of ovarian cancer. The risk of ovarian cancer varies with age. For example, in women aged 50-54 who are not taking hormone replacement therapy, about 2 women in 2000 will be diagnosed with ovarian cancer over a 5-year period. In women who take hormone replacement therapy for 5 years, there will be about 3 cases out of 2000 women taking it (meaning, about 1 additional case).

**Effect of hormone replacement therapy on heart and blood circulation**
**Blood clots in a vein (thrombosis)**
The risk **of blood clots in the veins** is about 1.3 to 3 times higher in women taking hormone replacement therapy than in women who do not take this treatment, especially during the first year of use. Blood clots can be severe, and if a blood clot reaches the lungs, it can cause chest pain, shortness of breath, fainting and even death.
The likelihood of developing a blood clot in the veins increases as you get older, as well as if any of the following applies to you. Inform your doctor if one or more of the following conditions apply to you:
- You are unable to walk for a long time due to major surgery, injury or illness (see also section 3 "If you need to undergo surgery")
- You are severely overweight (BMI>30 kg/m$^2$)
- You have a blood clotting problem that requires long-term treatment with a medicine used to prevent blood clots
- If one of your close relatives has suffered a blood clot in the leg, lung or any other organ
- You have systemic lupus erythematosus (lupus)
- You have cancer

For signs of a blood clot, see section 2 "Stop taking Femoston 1/10 mg and see a doctor immediately".
*Comparison*
Looking at women in their 50s who do not take hormone replacement therapy, on average 4-7 out of 1000 women are expected to develop blood clots in the veins over a 5-year period. In women in their 50s who are taking estrogen-progestogen hormone replacement therapy over a 5-year period, there will be 9-12 cases out of 1000 (meaning, 5 additional cases).

**Heart diseases (heart attack)**
There is no evidence that hormone replacement therapy will prevent a heart attack. Women over the age of 60 who take estrogen-progestogen hormone replacement therapy are slightly more likely to develop heart disease than women who do not take hormone replacement therapy.

**Stroke**
The risk of stroke is 1.5 times higher in women taking hormone replacement therapy than those not taking this therapy. The number of additional cases of stroke following use of the therapy increases with age.
*Comparison*
When looking at women in their 50s who do not take hormone replacement therapy, an average of 8 out of 1000 women are expected to experience stroke in a 5-year period. In women in their 50s who take hormone replacement therapy over a 5-year period, 11 cases out of 1000 are expected (meaning, 3 additional cases).

**Additional conditions**
Hormone replacement therapy will not prevent memory loss. There is some evidence of a higher risk of memory loss in women who begin hormone replacement therapy after the age of 65. Consult with your doctor.

Tell the doctor if you are suffering from or have suffered in the past from any of the following medical conditions, since he will need to monitor you more frequently:
- **Heart diseases**
- **Kidney problems**
- **Higher than normal levels of certain blood lipids (hypertriglyceridemia**)

**❗ Children**
Femoston 1/10 mg is not intended for use in children.

**❗ Laboratory tests**
If you need to have laboratory tests performed, tell your doctor or the laboratory staff that you are taking Femoston 1/10 mg, since this medicine could affect the results of some tests.

**❗ If you are taking, or have recently taken, other medicines, including non-prescription medicines, herbal medicines or other natural products, and nutritional supplements, tell the doctor or pharmacist.**
Some medicines may interfere with the effect of Femoston 1/10 mg. This might lead to abnormal bleeding. This applies to the following medicines:
- Medicines for epilepsy (such as phenobarbital, phenytoin, and carbamazepine)
- Medicines for tuberculosis (such as rifampicin, and rifabutin)
- Medicines for HIV infections (AIDS) (such as ritonavir, nelfinavir, nevirapine, efavirenz)
- Herbal medicines containing the herb St. John's wort (Hypericum perforatum)

**❗ Use of the medicine and food**
Femoston 1/10 mg can be taken with or without food.

**❗ Pregnancy and breastfeeding**
Femoston 1/10 mg is intended for postmenopausal women only. If you become pregnant, stop taking Femoston 1/10 mg and contact the doctor. Femoston 1/10 mg is not intended for use during breastfeeding.

**❗ Driving and operating machinery**
The effect of Femoston 1/10 mg on driving or operating machinery has not been studied. No effect is expected.

**❗ Important information about some of the ingredients of the medicine**
Femoston 1/10 mg contains lactose. If you have been told by the doctor that you have an intolerance to any sugars, consult the doctor before taking the medicine.

### 3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. You should check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation. The dosage and treatment regimen will be determined by the doctor only.

**When to start taking Femoston 1/10 mg**
Do not start taking Femoston 1/10 mg until at least 6 months have passed since your last natural menstrual period.

You can start taking Femoston 1/10 mg on any day that suits you if:
- You are not currently taking any preparation for hormone replacement therapy.
- You are switching from a preparation of hormone replacement therapy that is "continuous combined": meaning, you take a tablet every day or use a patch that contains both an estrogen and a progestogen together.

Start taking Femoston 1/10 mg the day after you finish the 28-day cycle if:
- You are switching from another hormone replacement therapy preparation that is "cyclic" or "continuous". Meaning, you take a tablet or use a patch that contains estrogen for the first part of the cycle, and then take a tablet or use a patch that contains both an estrogen and a progestogen together, for up to a period of 14 days.

**How to take the medicine**
- Swallow the tablet with water.
- You can take the tablet with or without food. There is no information regarding crushing/halving/chewing.
- Try to take the tablet at the same time every day. This is to ensure that there is a fixed amount of the medicine in your body. This will also help you remember to take the tablets.
- Take one tablet every day without a break between packs. The blisters are marked with the days of the week. This will make it easier for you to remember when to take the tablets.
- Your doctor aims to give you the lowest dose, for the shortest amount of time, to treat your symptoms. Talk to your doctor if you think the dose is too high or not high enough.
- If you are taking Femoston 1/10 mg to prevent osteoporosis, the doctor will adjust the dose according to your bone density.
- Take one white tablet every day for the first 14 days, followed by one grey tablet every day for the next 14 days. This is as shown on the 28-day pack.

**If you are about to undergo surgery,** tell the surgeon that you are taking Femoston 1/10 mg. You may need to stop taking Femoston 1/10 mg about 4-6 weeks before the operation to reduce the risk of blood clots [see section 2 "Blood clots in a vein (thrombosis)"]. Ask the doctor when you can resume taking Femoston 1/10 mg.

**Do not exceed the recommended dose**

**If you have accidentally taken a higher dosage** than necessary, or if you or someone else took too many Femoston 1/10 mg tablets, it is unlikely that they will be harmed. You may experience nausea, vomiting, chest sensitivity, dizziness, abdominal pain, drowsiness/tiredness, and withdrawal bleeding. No treatment is necessary, but if you are concerned, contact the doctor for advice.

**If you forgot to take the medicine,** take the missed tablet as soon as you remember. If more than 12 hours have passed since taking the last tablet, take the next dose without taking the forgotten dose. Do not take a double dose. Bleeding or spotting may occur if a dose is forgotten.
Adhere to the treatment regimen as recommended by the doctor. Do not stop treatment with the medicine without consulting the doctor. If you have further questions about the use of this medicine, ask the doctor or pharmacist.

**Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take medicine. Wear glasses if you need them.**
**If you have further questions regarding the use of the medicine, consult the doctor or pharmacist.**

### 4. SIDE EFFECTS

As with any medicine, the use of Femoston 1/10 mg may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.
The following diseases are reported more often in women taking hormone replacement therapy, compared to women not taking this therapy:
- Breast cancer
- Abnormal thickening or cancer of the uterine lining (endometrial hyperplasia or endometrial cancer)
- Ovarian cancer
- Blood clots in the veins of the legs or lungs (venous thromboembolism)
- Heart disease
- Stroke
- Probable memory loss if treatment begins after age 65

For further information about these side effects, see section 2 "Before using the medicine"

Very common side effects (effects that may affect more than 1 in 10 users):
- Headache
- Abdominal pain
- Back pain
- Pain or tenderness in the breasts

Common side effects (effects that may affect up to 1 in 10 users):
- Vaginal thrush (a vaginal infection due to a fungus called Candida albicans)
- Depression, irritability
- Migraine. If you have a migraine-like headache for the first time, stop taking Femoston 1/10 mg and see a doctor immediately
- Dizziness
- Nausea, vomiting, bloating (abdominal swelling) including flatulence
- Allergic skin reactions [including rash, severe itching or hives (urticaria)]
- Menstrual irregularities such as irregular bleeding, spotting, painful periods, heavier bleeding or reduced bleeding
- Pelvic pain
- Vaginal discharge
- Generally feeling unwell, weakness or tiredness
- Swelling of the ankles, feet or fingers (peripheral edema)
- Weight gain

Uncommon side effects (effects that may affect up to 1 in 100 users):
- Cystitis-like symptoms
- Growing uterine masses (fibroids)
- Hypersensitivity reactions such as shortness of breath (allergic asthma)
- Change in sex drive
- Blood clots in the legs or lungs (venous thromboembolism or pulmonary embolism)
- Hypertension
- Circulatory problems (peripheral vascular disease)
- Enlarged and prominent veins (varicose veins)
- Indigestion
- Liver disorders, which may include yellowing of the skin (jaundice), weakness, generally feeling unwell and abdominal pain. If you notice yellowing of the skin or the whites of your eyes, stop taking Femoston 1/10 mg and contact the doctor immediately
- Gallbladder disease
- Swelling of the breasts
- Premenstrual syndrome
- Weight loss

Rare side effects (effects that may affect up to 1 in 1000 users): (*"Rare" frequency is attributed to side effects from post-marketing reports not observed in clinical trials)
- Illness resulting from the destruction of red blood cells (hemolytic anemia)*
- Meningioma (a brain tumor)*
- Change in the surface of the eye (deepening of corneal curvature)*, not being able to wear contact lenses (contact lens intolerance)*
- Heart attack
- Stroke*
- Swelling of the skin around the face and neck area. This may cause breathing difficulties (angioedema)
- Red or brown colored patches on the skin
- Painful red skin nodules (erythema nodosum)*, discoloration of the skin, especially of the face or neck known as "pregnancy patches" (chloasma or melasma)*, leg cramps*

The following side effects have been observed in other types of hormone replacement therapies:
- Benign or malignant tumors which may be affected by estrogen levels, such as endometrial cancer, ovarian cancer (see section 2 for further information)
- Increase in the size of tumors that may be affected by progestogen levels (such as meningioma)
- Immune system disease affecting many organs in the body (systemic lupus erythematosus)
- Probable dementia
- Exacerbation of seizures (epilepsy)
- Uncontrollable muscle spasms (chorea)
- Blood clots in the arteries (arterial thromboembolism)
- Inflammation of the pancreas (pancreatitis) in women with pre-existing high levels of certain blood lipids (hypertriglyceridemia)
- Rash with target-shaped red areas or sores (erythema multiforme)
- Urinary incontinence
- Painful/lumpy breasts (fibrocystic breasts)
- Cervical erosion
- Exacerbation of a rare blood pigment disorder (porphyria)
- High levels of certain blood lipids (hypertriglyceridemia)
- Increased total thyroid hormones

**If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, you should consult with the doctor.**

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://forms.gov.il/globaldata/getsequence/getsequence/aspx?formType=AdversEffectMedic@moh.gov.il

### 5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.
Do not use the medicine after the expiry date (exp. date) that appears on the package/label. The expiry date refers to the last day of that month.
Storage conditions: Store in the original package, below 30°C.

### 6. FURTHER INFORMATION

In addition to the active ingredient(s), the medicine also contains:
- Each film-coated white tablet containing only estradiol contains:
  Lactose Monohydrate, Maize Starch, Hypromellose, Colloidal Anhydrous Silica and Magnesium Stearate.
  The tablet film-coating contains:
  Hypromellose, Titanium Dioxide (E171) and Macrogol 400.
- Each film-coated grey tablet containing an estradiol and dydrogesterone combination contains:
  Lactose Monohydrate, Maize Starch, Hypromellose, Colloidal Anhydrous Silica and Magnesium Stearate.
  The tablet film-coating contains:
  Polyvinyl Alcohol, Titanium Dioxide (E171), Macrogol 3350, Talc and Iron Oxide Black (E172).
- Each film-coated tablet containing estradiol alone contains 119.1 mg lactose monohydrate.
- Each film-coated tablet containing an estradiol and dydrogesterone combination contains 110.2 mg lactose monohydrate.

What the medicine looks like and the contents of the package
<u>Appearance</u>:
Film-coated tablet containing only estradiol:
Round, biconvex tablet, film-coated with a white coating, on one side of which is imprinted the number '379'.
Film-coated tablet containing an estradiol and dydrogesterone combination:
Round, biconvex tablet, film-coated with a gray coating, on one side of which is imprinted the number '379'.
<u>Packaging</u>:
Each carton package contains: 28, 84 (3 x 28) or 280 (10 x 28) film-coated tablets packaged in a blister pack.
Not all packages are marketed.

**License holder and address:** Abbott Medical Laboratories Ltd., Kiryat Atidim, Building 4, P.O.B. 58099, Tel Aviv 61580.
**Manufacturer's name and address:** Abbott Healthcare Products B.V, Weesp, the Netherlands
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