PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Name, form and strength of the preparation

Depo-Provera® 150 mg/ml

Suspension for injection

Medroxyprogesterone acetate 150 mg/ml

A list of allergenic and inactive ingredients in the preparation is in section 6.

Read this 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 to treat you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar to yours.

WHAT MUST I KNOW ABOUT THE MEDICINE?

- The contraceptive effectiveness of the Depo-Provera® preparation is conditional upon your perseverance in receiving an injection of the preparation once every three months.
- Depo-Provera® is administered as a single injection of 150 mg into the muscle of the upper arm or buttock. At the end of three months, make sure to return to your doctor for the next injection.
- If more than three months have elapsed between injections, or more than 6 weeks after giving birth, you must be checked by your doctor before resuming use of Depo-Provera® injections.

For information regarding side effects, please see section 4.

1. WHAT IS THE MEDICINE INTENDED FOR?

- Depo-Provera® is a contraceptive agent, which is used when the prevention of pregnancy is medically indicated and no other means can be used for this purpose.

Therapeutic group:

- A derivative of progesterone - Depo-Provera® contains the active ingredient medroxyprogesterone acetate, which is chemically similar to the natural hormone - progesterone.

  Progesterone is produced by the ovaries during the second half of the menstrual cycle. Depo-Provera® prevents follicular maturation in the ovaries, and as a result, passage of the oocyte from the ovary to the uterus is prevented, and therefore, fertilization is not possible and pregnancy is prevented.

  Depo-Provera® is given as an intramuscular injection **once every three (3) months** (12 weeks).

2. BEFORE USING THE MEDICINE

☒ Do not use this medicine if:

- × you are sensitive (allergic) to the active ingredient or to any of the other ingredients in the medicine.
- × you are pregnant or suspect you are pregnant.
- × you are suffering from vaginal bleeding without any known reason.
- × you have or suspect you have breast cancer.
- × you have or suspect you have cancer of the genital organs.
- × you had a stroke.
- × you are suffering, or have suffered in the past, from thromboembolic diseases such as: blood clots.
- × you suffer from liver diseases.
- × you suffer from metabolic bone disease.
- × you are suffering, or have suffered in the past, from a disease of the blood vessels that affects the blood vessels of the brain.

Special warnings regarding use of the medicine

! If you are sensitive to any food or medicine, inform the doctor before taking this medicine.

! Before beginning use of Depo-Provera® injections, you must have a complete gynecological examination (including breasts) and pregnancy should be ruled out. In order to rule out pregnancy, women who are starting to use Depo-Provera® for the first time, must receive the injection within the first 5 days of the menstrual cycle or within 5 days from giving birth if you are not breastfeeding, or in the sixth week after giving birth if you are breastfeeding.

A gynecological examination should be repeated every year.

! If you have any signs of pregnancy, contact your doctor immediately.

! Please inform your doctor of any family history of breast cancer, if you suffer or have suffered in the past, from fibrocystic breast disease, lumps in the breast, bleeding from the nipples, kidney diseases, irregular menstrual cycle or very little bleeding, high blood pressure, headaches and migraines, asthma, epilepsy, diabetes or a family history of diabetes, a history of depression, liver function disturbances, obesity, smoking, history of heart diseases or high cholesterol levels, including a family history, sharp pain or swelling of the thigh (this may indicate a blood clot in this area), blood clotting disturbances or stroke, vision problems, such as partial or full loss of vision or double vision.

! Use of other contraceptive methods should be considered in women at risk for osteoporosis, for example:

- Chronic alcohol use and/or smoking.
- Chronic use of medicines that can reduce bone density (e.g., anticonvulsants or corticosteroids).
- Low BMI or eating disorders, e.g., anorexia nervosa or bulimia.
- Metabolic bone disease.
- Family history of osteoporosis.

  Please inform the doctor if you are taking additional medicines, including non-prescription medicines.

! Certain blood tests may be affected by hormones such as those in Depo-Provera®. Therefore, if you are sent for laboratory tests, tell your doctor that you are using Depo-Provera® for contraception.

! During the course of treatment, it is recommended to ensure adequate calcium and vitamin D intake, treatment intended to prevent osteoporosis, a rare side effect of the medicine.

! A bone density test may be necessary in cases of long-term use of this medicine.

! Use of this medicine does not protect against the contagion of sexually transmitted diseases (e.g., AIDS).

! What should you do if you wish to conceive while still under the continuing influence of the preparation?

Depo-Provera® is a long-acting contraceptive. Therefore, in order to return to fertility, you must wait some time until the effect of the last injection has passed. With cessation of using Depo-Provera®, the regular and normal menstrual cycle will resume. Studies carried out in the U.S.A. showed that the average time it took to conceive was about 10 months from the time of the last injection (93% conceived within 18 months of receiving the last injection), regardless of the duration of treatment with this preparation.

! If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, inform the doctor or pharmacist.

! Pregnancy and breastfeeding:

Before the first injection as well as before any injection that is given late (a lapse of more than 12 weeks and 5 days between injections), your doctor will check if you are pregnant. Do not use Depo-Provera® if you are pregnant. Medicines containing hormones may affect the developing fetus. If you think you have become pregnant while using Depo-Provera®, refer to the doctor immediately.

Depo-Provera® is not recommended for use in the first weeks after delivery in women who are breastfeeding. Your doctor will recommend that you wait at least 6 weeks after delivery before starting to use Depo-Provera®. No harmful effects were observed among infants exposed to Depo-Provera® in the breast milk.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions! Check with the doctor or pharmacist if you are uncertain.

The dosage and treatment regimen will be determined by the doctor only.

Depo-Provera® is given by injection by a doctor or nurse.

Depo-Provera® is administered as an intramuscular injection once every three (3) months (12 weeks).

Do not exceed the recommended dose!

If you took an overdose, or if a child accidentally swallowed the medicine, immediately proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take this medicine: If you forgot to get the injection or you were late in getting the injection, there is a chance you will become pregnant. Consult the doctor regarding when you can get the next Depo-Provera® injection and which contraceptive methods to use in the meantime.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of this medicine may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Refer do a doctor immediately in the event of:

Osteoporosis (see "Special warnings regarding use of the medicine"), leg cramps, heavy vaginal bleeding, development of blood clots, vaginitis, vaginal discharge or irritation, swelling/tenderness/sensitivity or pain in breasts, sharp chest pain, coughing of blood.

Allergic reaction that may be manifested by breathing difficulties, low blood pressure, convulsions, edema, sudden and severe headache, fainting, vision disturbances, swelling, swelling or numbness of the hands or legs.

Hot flushes, backache, depression, insomnia, acne, pelvic pains, excessive hair loss, rash, arthralgia, persistent pain, pus or bleeding at the injection site, high fever, hirsutism, reduced glucose tolerance, secretion of milk from the breasts, development of jaundice, changes in liver function.

There is a low risk of anaphylactic reactions (severe allergic reactions which may require urgent medical attention or hospitalization). Possible signs include: swelling of the face, lips, tongue or throat, difficulty breathing or swallowing, rash, shock or collapse.

Deep vein thrombosis is a condition in which a blood clot forms in one of the deep veins, usually in the leg. Possible symptoms include: swelling of the leg, pain and tenderness in the leg, a change in the color of the skin, such as redness and skin that feels hot.

Women who use Depo-Provera® tend to have lower bone density than women of the same age who have never used the medicine. The effect of Depo-Provera® on bone density is higher in the first 2-3 years of use. Afterwards, bone density stabilizes and there appears to be some recovery when treatment is stopped. It is still unknown whether Depo-Provera® increases the risk of osteoporosis (weak bones) and fractures at later ages.

Side effects that are common (frequency of up to 1:10)

Crampy abdominal pains or abdominal discomfort, flatulence, nausea, changes in appetite, headaches, dizziness, disruption of normal menstrual cycle, irregular or unexpected bleeding, changes in the intensity of menstrual bleeding, amenorrhea (absence of menstrual bleeding), swelling, hair loss, rash, weakness or tiredness, injection site reactions, nervousness, insomnia, inability to reach orgasm, emotional disturbances, bleeding between periods, reduced libido.

Side effects that are uncommon (frequency of up to 1:100)

Hypertension, varicose veins, inflammation in a vein, pulmonary embolism (a blood clot in the lungs which causes chest pain and breathlessness), allergic reactions (such as swelling of the face), abnormal blood test results for liver function, feeling of dizziness, changes in body weight, convulsions, muscle cramps, pain in hands and legs, sleepiness, migraine, vaginal dryness, menstrual pains, changes in breast size, painful intercourse, ovarian cyst, premenstrual syndrome, infections of the urinary tract or reproductive organs, an increase in the thickness of the lining of the womb, dark patches on the skin, anxiety, difficulty breathing, fluid retention, urticaria, local itching.

Side effects occurring rarely (frequency of up to 1:1,000)

Tachycardia, breast lumps and bleeding from the nipple, thirst, hoarseness, rectal bleeding, paralysis, breast cancer, anemia.

Side effects of unknown frequency:

Disturbed liver function, decreased bone density, swelling of ankles and wrists, vaginal cysts, cessation of milk supply in breastfeeding women, feeling pregnant, delay in becoming pregnant after discontinuing use of the medicine, scaling of skin, scleroderma (a rare autoimmune disease that affects the skin and other parts of the body), weakness in the face muscles, blood disorders, stretch marks, thromboembolic changes.

Possible effect on menstrual cycle:

Depo-Provera® will usually affect the nature of a woman's menstrual cycle. After the first injection, it is likely that your menstrual cycle will be irregular, usually prolonged, or you will have spotting. This effect can continue in some women and is considered normal. One third of women will not have any bleeding at all after the first injection. After 4 injections, most women will not have monthly bleeding at all.

If you experience very heavy or prolonged bleeding, consult with the doctor.

After stopping Depo-Provera®, your periods will return to normal within a few months.

Possible effect on the bones:

Depo-Provera® works by lowering levels of estrogen and other hormones. However, low estrogen levels may lead to reduced bone density. This effect is at its peak in the first 2-3 years of Depo-Provera® use. Afterwards, the level of bone density stabilizes and it appears that there is a certain increase in bone density upon discontinuing use of the medicine. It is still unknown whether the use of Depo-Provera® increases the risk of osteoporosis and fractures later in life. The following are risk factors for developing osteoporosis. Consult the doctor if they apply to you, as in such a case use of another contraceptive method should be considered: chronic alcohol or tobacco use, chronic use of medicines that reduce bone density, e.g., for treatment of epilepsy or steroids, low BMI or eating disorders (anorexia or bulimia), previous fracture that was not caused by a fall, a family tendency for osteoporosis, a metabolic bone disease.

Adolescents (up to 18 years of age): The bones of adolescent girls grow rapidly and get stronger. The stronger the bones are when adulthood is reached, the greater the protection against osteoporosis in later stages in life. Use of Depo-Provera® may lead to reduced bone density during this important period. Bone strength begins to rise again when treatment with Depo-Provera® is stopped, but it is not known whether eventually the bone density reaches the same levels as it would have if Depo-Provera® had never been used. Before using Depo-Provera®, adolescents should discuss with the doctor whether another contraceptive method would be more suitable for them.

! During the course of treatment, it is recommended to ensure adequate calcium and vitamin D intake, treatment intended to prevent osteoporosis, and to perform physical activity meant to prevent osteoporosis.

Possible risk of cancer:

Studies of women who used different types of contraceptive methods found that in women who used Depo-Provera® no increase was observed in the overall risk of developing cancer of the ovary, womb, cervix or liver.

Possible risk of breast cancer:

Breast cancer is rare among women under 40 years of age, whether or not they use hormonal contraceptives. Depo-Provera® slightly increases the risk of breast cancer compared with women who have never used it. However, any excess risk is small in relation to the overall risk of breast cancer, particularly in young women.

In older women, the risk of developing breast cancer is higher and therefore, the increase in the number of cases due to Depo-Provera® is greater in older women than in younger women.

For example:

In a 15-year-old adolescent girl who uses Depo-Provera® for 5 years, the increase in the risk of developing breast cancer by the age of 30 is negligible.

A 25-year-old woman who uses Depo-Provera® for 5 years increases her risk of developing breast cancer by the age of 40 from 44 cases per 10,000 women (who did not use Depo-Provera®) to up to 47 cases per 10,000 women.

A 35-year-old woman who uses Depo-Provera® for 5 years increases her risk of developing breast cancer by the age of 50 from 160 cases per 10,000 women (who did not use Depo-Provera®) to 170 cases per 10,000 women.

- If a side effect occurs, if one of the side effects worsens, or if you are suffering from a side effect not mentioned in the leaflet, consult with the doctor.

5. HOW SHOULD THE MEDICINE BE STORED?

Store the preparation at room temperature, below 25°C.

Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach of children and/or infants 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. The expiry date refers to the last day of that month.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Polysorbate 80, Methyl paraben, Propyl paraben, Macrogol 3000, Sodium chloride, Sodium hydroxide, Hydrochloric acid, Water for injection.

What the medicine looks like and the contents of the package:

Depo-Provera® 150 mg/ml: a pre-filled 1 ml syringe that contains a white, sterile suspension.

Registration holder: Pfizer PFE Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

Manufacturer: Pfizer Manufacturing Belgium NV/SA, Puurs, Belgium.

This leaflet was checked and approved by the Ministry of Health in February 2015.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Depo-Provera® 150 mg/ml: 069.69.24309.00