

**The name of your medication is:****Progynova 28**

Dear Patient,

Please read this leaflet carefully before you start using Progynova 28. This leaflet will provide information about the benefits and risks of using Progynova 28. It will also advise you about how to take Progynova 28 properly and when to tell your doctor about health-related conditions. If you have any questions or need more advice, ask your doctor, professional health care provider or pharmacist. This product has been prescribed for you personally and you should not pass it on to others.

**What does Progynova 28 contain? (Composition)**

Each blister pack of Progynova 28 contains 28 tablets, each containing 1.0 mg estradiol valerate or 2.0 mg estradiol valerate as active substance.

Progynova 28 also contains the following other ingredients: lactose monohydrate; maize starch; polyvidone 25 000; talc; magnesium stearate; sucrose; polyvidone 700 000; macrogol 6 000; calcium carbonate; glycerol 85 %; titanium dioxide; ferric oxide pigment, yellow; indigo carmine lake; montanglycol wax.

**What is Progynova 28? (Pharmaceutical form and pharmaco-therapeutic group)**

Progynova 28 is a sugar-coated tablet for hormone replacement therapy (HRT).

**What pack sizes of Progynova 28 are available?**

<fill in the approved pack size>

**How does Progynova 28 work? (Properties of preparation)**

Progynova 28 contains estradiol valerate, a prodrug of the natural human estradiol. During the climacteric ('the change of life') the estradiol production of the ovaries declines. Although the change of life is natural, it often causes distressing symptoms, which are connected with the gradual loss of the hormones produced by the ovaries. In addition the loss of these hormones may, in some women, lead to thinning of the bones in later life (postmenopausal osteoporosis).

Progynova 28 replaces the hormone estradiol that the body no longer makes. The estradiol prevents or relieves troublesome symptoms (climacteric complaints) such as hot flushes, sweats, sleep disturbances, nervousness, irritability, dizziness, headaches as well as involuntary loss of urine, vaginal dryness and burning.

If you still have a womb (you have not had a hysterectomy) your doctor will prescribe another hormone progestogen to take with Progynova 28.

Some women are more likely than others to develop osteoporosis in later life depending on their medical history and lifestyle. If it is appropriate, you may be prescribed Progynova 28 to prevent osteoporosis. Your doctor will be able to advise you further.

**Why take Progynova 28? (Indications)**

Progynova 28 provides hormone replacement therapy (HRT) for the treatment of climacteric complaints after the cessation of monthly bleeding or after removal of the ovaries (ovariectomy). In addition, it is employed for preventing the bone disease in later life, so-called postmenopausal osteoporosis.

**When should Progynova 28 not be taken? (Contra-indications)**

You must not take Progynova 28 if you have any of the conditions listed below. If any of these apply to you, tell your doctor who will be able to advise you further.

- If you are pregnant or breastfeeding.
- If you have unspecified vaginal bleeding.
- If you have or if there is a suspicion of cancer of the breast.
- If you have or if there is a suspicion of other malignancies influenced by sex hormones.
- If you have or have had liver tumors (benign or malignant).
- If you have severe liver disease.
- If you recently had a heart attack and/or stroke.
- If you have or have had a thrombosis (the formation of a blood clot) in the blood vessels of the legs (deep venous thrombosis) or the lungs (pulmonary embolism).
- If you have severely elevated blood levels of triglycerides (special type of blood lipids).
- If you are allergic to any of the ingredients of Progynova 28 (*see composition*).

If any of these conditions appear for the first time while using Progynova 28, stop taking it at once and consult your doctor.

**What needs to be taken into consideration before using Progynova 28?**

Your doctor will carry out gynecological, breast, blood pressure and other examinations as appropriate. If you are known to have any liver disease, your doctor will arrange for your liver function to be checked regularly.

If there is a suspicion of an adenoma of the anterior lobe of the pituitary gland, this should be ruled out by your doctor before starting treatment.

If you still have the ability to become pregnant Progynova 28 is unlikely to alter it. If you are taking contraceptive precautions other than oral (or other hormonal) contraceptives when you start Progynova 28, continue to do so until your doctor tells you that you no longer require contraceptive protection. If you have been taking an oral (or other hormonal) contraceptive, you must change to an alternative (non-hormonal) form of contraception before starting Progynova 28. On the other hand, if your doctor has already advised you that you need no longer use any contraceptive, you need not do so while taking Progynova 28.

## **What precautions have to be taken? (Precautions and warnings for use)**

### **Before you start to take Progynova 28**

Your doctor will discuss with you the benefits and risks of Progynova 28.

Two large clinical trials with conjugated equine estrogens (CEE) and medroxyprogesterone acetate (MPA), hormones used for hormone replacement therapy (HRT), suggest that the risk of getting a heart attack (myocardial infarction) may be slightly increased in the first year of use. This risk was not observed in a large clinical trial with CEE alone. In two large clinical trials with these hormones, the risk of stroke was 30 – 40% increased.

**Although such data are not available for Progynova 28, it should not be used to prevent heart disease and/or stroke.**

If HRT is used in the presence of any of the conditions listed below you will need to be kept under close observation. Your doctor can explain this to you. Therefore, if any of these apply to you, tell your doctor before starting to use Progynova 28.

#### You have an increased risk of thrombosis (the formation of a blood clot) in your veins.

The risk increases with age and may also be higher:

- if you or anyone in your immediate family has ever had a thrombosis in the blood vessels of the legs or lungs;
- if you are overweight;
- if you have varicose veins.

If you are already using Progynova 28, tell your doctor well in advance of any expected hospitalization or surgery. This is because the risk of having deep venous thrombosis may be temporarily increased as a result of an operation, serious injuries or immobilization.

- You have fibroids of the womb;
- you have or have had endometriosis (the presence of tissue of the lining of the womb in places in the body where it is not normally found);
- you have liver or gallbladder disease;
- you have had jaundice during pregnancy or previous use of sex steroids;
- you suffer from diabetes;
- you have elevated levels of triglycerides (a special type of blood lipids);
- you have high blood pressure;
- you have or have had chloasma (yellow brown patches on the skin); if so, avoid too much exposure to the sun or ultraviolet radiation.
- you suffer from epilepsy;
- you have lumpy or painful breasts (benign breast disease);
- you suffer from asthma;

- you suffer from migraine;
- you have the inherited disease called porphyria;
- you suffer from inherited deafness (otosclerosis);
- you have systemic lupus erythematosus (SLE; a chronic inflammatory disease);
- you have or have had chorea minor (illness with unusual movements);
- you suffer from episodes of swelling in body parts such as hands, feet, face, airway passages that are caused by a defect in the gene that controls a blood protein called C1-inhibitor (hereditary angioedema).  
The hormone estradiol valerate in Progynova 28 may induce or exacerbate symptoms of hereditary angioedema.
- you are 65 years or older when HRT is initiated. The reason is that there is limited evidence from clinical studies that hormonal treatment may increase the risk of significant loss of intellectual abilities such as memory capacity (dementia).

### **HRT and cancer**

- Endometrial cancer

The risk of cancer of the lining of the womb (endometrial cancer) increases when estrogens are used alone for prolonged periods. If you are taking Progynova 28 and have not had a hysterectomy you will need additional progestogen hormone treatment. Your doctor will advise you about this. The appropriate addition of a progestogen eliminates this increase in risk.

Please inform your doctor if you frequently have bleeding irregularities or persistent bleeding during the treatment with Progynova 28.

- Breast cancer

In some studies breast cancer has been diagnosed slightly more often in women taking Hormone Replacement Therapy (HRT) for several years. The risk increases with duration of treatment. It may be lower or possibly neutral with estrogen-only products. If women stop taking HRT this increased risk disappears within a few years.

Similar increases in breast cancer diagnosis are observed with e.g., delay of natural menopause, alcohol intake or adiposity.

HRT increases the density of mammographic images. This may complicate the mammographic detection of breast cancer in some cases. Therefore your doctor may choose to use other breast cancer screening techniques as well.

- Ovarian cancer

In one study, ovarian cancer was reported to occur slightly more often in women who had been on estrogen therapy for longer than 10 years. A survey of 15 other studies did not find an increased risk for women on estrogen therapy. Currently the influence of this replacement therapy on ovarian cancer is not clear.

- Liver tumor

During or after the use of hormones such as those that are contained in Progynova 28, benign liver tumors have rarely occurred, and malignant liver tumors even more rarely. In isolated cases, bleeding from such tumors into the abdominal cavity has endangered life. Although such events are extremely improbable you should inform your doctor about any unusual feelings in your upper abdomen that do not disappear within a short time.

### **Reasons for stopping Progynova 28 immediately**

You should stop treatment at once and consult your doctor if you have any of the following conditions:

- Your very first attack of migraine (typically a throbbing headache and nausea preceded by visual disturbances);
- worsening of preexisting migraine, any unusually frequent or unusually severe headaches;
- sudden disturbances of vision or hearing;
- inflamed veins (phlebitis).

If you get a blood clot while you are taking Progynova 28 or there is a suspicion thereof you should stop taking it immediately and contact your doctor. Warning signs to look out for are:

- coughing blood;
- unusual pains or swelling of your arms or legs;
- sudden shortness of breath;
- fainting.

Progynova 28 must also be stopped at once if you become pregnant or if you develop jaundice.

### **What should be observed when you participate in road traffic or when you operate machines?**

No observed effects

### **What to do if you are taking any other medications? (Interactions)**

Oral contraceptives should not be used. Consult your doctor for contraceptive advice, if required.

Some medicinal products may stop hormone replacement therapy (HRT) from working properly. These include medicinal products used for the treatment of epilepsy (e.g. hydantoins, barbiturates, primidone, carbamazepine) and tuberculosis (e.g. rifampicin); and antibiotics (e.g. penicillins and tetracyclines) for some other infectious diseases. Always tell the doctor who prescribes HRT which medicinal products you are already using. Also tell any other doctor or dentist who prescribes another medicinal product (or the dispensing pharmacist) that you use Progynova 28.

If you are diabetic your doctor may alter the dose of the diabetes medication.

If you are in doubt about any medicinal products you are taking, ask your doctor.

Excess intake of alcohol during use of hormone replacement therapy has an influence on the treatment. Your doctor will advise you.

The use of HRT may affect the results of certain laboratory tests. Always tell your doctor or the laboratory staff that you are using a hormone replacement therapy.

### **How should Progynova 28 be taken? (Dosage and administration)**

Each pack covers 28 days of treatment. You have to take one tablet daily.

If you still have your monthly bleeding you should start Progynova 28 tablets within the first 5 days of menstruation.

- In any other case your doctor may advise you to start immediately.
- If you still have a womb (you have not had a hysterectomy) your doctor will prescribe another hormone (progestogen). He will advise you how to take this.

It does not matter at what time of the day you take your tablet, but once you have selected a particular time, you should keep to it every day. The tablet should be swallowed whole with some liquid.

When you have finished each pack start the next pack on the following day. Never leave a break between packs. Tablet taking should be continuous.

Please observe these instructions for use, otherwise you will not fully benefit from Progynova 28!

### **What should you do if you miss a dose?**

If you are less than 24 hours late, take it as soon as possible, and take the next one at your normal time.

If you discontinue tablet taking for several days, irregular bleeding may occur.

### **What if a dose is taken or used greater than prescribed? (Overdose)**

There have been no reports of ill-effects from overdose. Overdosage may cause nausea and vomiting and irregular bleeding. No specific treatment is necessary but you should consult your doctor if you are concerned.

### **Does Progynova 28 cause any undesirable effects?**

Like all medicines, Progynova 28 can have undesirable effects.

- **Serious undesirable effects**

Serious undesirable effects associated with the use of hormone replacement therapy, as well as related symptoms, are described under **What precautions have to be taken?** (Precautions and warnings for use), especially in the sub-sections: **Before you start to use Progynova 28, HRT and cancer** and **Reasons for stopping Progynova 28 immediately**.

*Please read these sub-sections carefully and consult your doctor immediately where appropriate.*

The following undesirable effects have been reported in users of hormone replacement therapy preparations:

- **Common undesirable effects** (between 1 and 9 persons out of every 100 may experience this effect)

Metabolism and nutrition disorders

Weight increase or Weight decrease.

Nervous system disorders

Headache.

Gastrointestinal disorders

Abdominal pain, Nausea.

Skin and subcutaneous tissue disorders

Rash, Pruritus.

Reproductive system and breast disorders

Uterine/Vaginal bleeding including Spotting.

- **Uncommon undesirable effects** (between 1 and 9 persons out of every 1,000 may experience this effect)

Immune system disorders

Hypersensitivity reaction.

Psychiatric disorders

Depressed mood.

Nervous system disorders

Dizziness.

Eye disorders

Visual disturbances.

Cardiac disorders

Palpitations.

Gastrointestinal disorders

Dyspepsia.

Skin and subcutaneous tissue disorders

Erythema nodosum, Urticaria.

Reproductive system and breast disorders

Breast pain, Breast tenderness.

General disorders and administration site conditions

Edema.

- **Rare undesirable effects** (between 1 and 9 persons out of every 10,000 may experience this effect)

Psychiatric disorders

Anxiety, Libido decreased or Libido increased.

Nervous system disorders

Migraine.

Eye disorders

Contact lens intolerance.

Gastrointestinal disorders

Bloating, Vomiting.

Skin and subcutaneous tissue disorders

Hirsutism, Acne.

Musculoskeletal and connective tissue disorders

Muscle cramps.

Reproductive system and breast disorders

Dysmenorrhea, Vaginal discharge, Pre-menstrual-like syndrome, Breast enlargement.

General disorders and administration site conditions

Fatigue.

In women with episodes of swelling in body parts such as hands, feet, face, airway passages that are caused by a defect in the gene that controls a blood protein called C1-inhibitor (hereditary angioedema) the hormone estradiol valerate in Progynova 28 may induce or exacerbate symptoms of hereditary angioedema (see under '**What precautions have to be taken?**' (Precautions and warnings for use) '**Before you start to take Progynova 28**').

If you notice any unwanted effects not mentioned in this leaflet or if you are unsure about the effect of this product, please inform your doctor or pharmacist.

**How should Progynova 28 be stored?**

Please note the expiry date on the pack. Do not use after this date.

Keep out of the reach and sight of children.

**The marketing authorization holder**

The following company is responsible for marketing Progynova 28

<fill in the name and address of the local affiliate company>

**The manufacturer**

Progynova 28 is produced by:

<fill in the name and address of the approved manufacturing company>

**Date on which this text was last revised in line with GLC decision**

17.03.2006

**IF YOU HAVE ANY FURTHER QUESTIONS PLEASE CONSULT YOUR DOCTOR OR PHARMACIST.**