1. WHAT IS PROGYLUTON AND WHEN IS IT USED?

Progyluton belongs to a type of treatment called hormone replacement therapy. It contains two female sex hormones known as estradiol (an estrogen) and norgestrel (a progestogen). The active ingredient estradiol is equivalent to the natural hormone and possesses the same properties, whereas norgestrel has an effect similar to that of the natural corpus luteum hormone progesterone.

In the fertile years of a woman estrogens and progestogens are produced by the ovaries. They regulate the monthly cycle and the normal course of a pregnancy. In the menopause (change of life), which is a natural process and occurs in every woman, the ovaries cease producing these hormones, usually between the ages of 45 and 55, but also in younger women whose ovaries have been surgically removed or inactivated by irradiation.

In many women the discontinuation of estrogen production in the menopause leads to typical complaints. In particular these include hot flashes, tendency to have outbreaks of sweating, sleep disturbances, depressive moods, nervous irritability, headache, dizziness, as well as regression of the mucous membranes in the area of urinary and sex organs. These disturbances can be alleviated or removed by replacing the hormone that is no longer produced in the body. The composition and effect of Progyluton is tuned in such a way that when taken regularly a cyclical pattern ensues that corresponds to the normal cycle.

Depressive moods are only favorably influenced by Progyluton when they occur in conjunction with hot flashes.

Other applications are missing or missed periods resulting from hormonal disturbances, and too frequent, too rare or irregular menstruation.

The active ingredient estradiol induces the growth of the mucous lining of the womb (endometrium), just like the estrogens did that used to be produced by the ovaries before the menopause. This inducement of uterine mucous membrane growth can sometimes lead to irregular bleeding and in some cases to an undesired proliferation of the endometrium called endometrial hyperplasia. Owing to the progestogen contained in Progyluton the risk of endometrial hyperplasia is reduced in practice by the periodic bleeding during which the endometrium is regularly shed, thus protecting the womb. For this reason Progyluton is only employed in women with an intact womb.

Progyluton is used during the change of life (perimenopause).

Progyluton may only be used on prescription and under constant supervision by a doctor.

2. WHAT NEEDS TO BE TAKEN INTO ACCOUNT HERE?

Physical exercise and natural nutrition are wise measures to be taken in the menopause, as they can enhance the effect of Progyluton.

Progyluton is not a contraceptive (cf. “When is caution needed when taking Progyluton?”).

Hormone replacement therapy may be associated with a higher risk of contracting certain diseases such as breast cancer, cardiovascular diseases (heart attack, stroke, venous thrombosis and pulmonary embolisms - development of blood clots in vessels). With prolonged hormone replacement therapy using another preparation very rare cases of a loss of memory power and mental performance were observed in elderly women. Your doctor will weigh up the risks of hormone therapy compared with the expected benefits and will discuss this with you.

3. WHEN MUST PROGYLUTON NOT BE USED?

Progyluton must not be used if you:

• are pregnant or breastfeeding,
• have unexplained vaginal bleeding,
• are suffering from breast cancer, or if there is a suspicion that you may have breast cancer,
• uterine fibroids (tumors of the womb),
• suspected endometriosis (occurrence of uterine mucous membrane outside the womb {accompanied} with pain and bleeding,
• diseases of the liver or gall bladder,
• diabetes (sugar),
• severely enhanced triglyceride levels (a kind of fat) in the blood,
• if jaundice occurred in a past pregnancy or when hormones were taken,
• high blood pressure,
• chloasma (brown spots in the face); in this case you should avoid sunlight and ultraviolet radiation,
• epilepsy,
• pain or benign changes in the breast,
• asthma,
• migraine,
• porphyria (an hereditary metabolic disease),
• congenital hearing disturbance (otosclerosis),
• systemic lupus erythematosus (autoimmune disease involving vascular inflammation and other characteristic symptoms),
• St. Vitus dance (chorea minor).

4. WHEN IS CAUTION ADVISED WHEN TAKING PROGYLUTON?
Before starting to take Progyluton you will be given a thorough general and gynecological checkup, and he or she will advise you to examine your breasts on your own and will show you how to do it.

As a precautionary measure checkups should be conducted approximately every six months when Progyluton is taken for long periods.

During treatment with Progyluton pregnancy must not occur (see “May Progyluton be taken during pregnancy or lactation?”). If needed, nonhormonal methods of contraception (with the exception of the calendar method according to Knaus-Ogino and the temperature method) must be used. If during treatment withdrawal bleeding fails to occur at regular intervals of approx. 28 days, pregnancy must be considered a possibility despite the contraceptive measures. Treatment must then be discontinued pending clarification by the doctor. If bleeding repeatedly occurs during the three weeks during which Progyluton is taken, the doctor must be seen, but until then taking must not be stopped.

Prior to the start of treatment your doctor will discuss the benefits and risks of treatment with Progyluton.

It is important that you should inform your doctor if you are suffering or have at any time suffered any of the following disorders. In these cases it may be necessary to have checkups at closer intervals:

• uterine fibroids (tumors of the womb),
• suspected endometriosis (occurrence of uterine mucous membrane outside the womb {accompanied} with pain and bleeding,
• diseases of the liver or gall bladder,
• diabetes (sugar),
• severely enhanced triglyceride levels (a kind of fat) in the blood,
• if jaundice occurred in a past pregnancy or when hormones were taken,
• high blood pressure,
• chloasma (brown spots in the face); in this case you should avoid sunlight and ultraviolet radiation,
• epilepsy,
• pain or benign changes in the breast,
• asthma,
• migraine,
• porphyria (an hereditary metabolic disease),
• congenital hearing disturbance (otosclerosis),
• systemic lupus erythematosus (autoimmune disease involving vascular inflammation and other characteristic symptoms),
• St. Vitus dance (chorea minor).
• Coronary heart disease and stroke
Two major clinical trials with conjugated estrogens from horses and medroxyprogesterone acetate (a progestogen), which are both used in hormone replacement therapy seem to indicate that the risk of suffering a heart attack may be slightly higher in the first year of administration. This risk was not observed when conjugated estrogens were used on their own. In two major trials involving these hormones the risk of suffering a stroke was 30 to 40 per cent higher, both when estrogens were used alone and when the combined preparation was used.

Although there are no such data for Progyluton it should not be employed to prevent heart conditions and/or stroke.

• Enhanced risk of developing a thrombosis (blood clot)
Scientific investigations would indicate that the use of preparations with active ingredients like those that Progyluton contain are associated with a slightly higher risk of developing blood clots (thrombosis, embolism) (see “What side effects can Progyluton have?”).
The generally recognized risk factors of thrombosis include a personal or family history (occurrence of bloodclotting disturbances in a close relative at a relatively young age may point to a family disposition), high blood pressure (hypertension), bloodclotting or metabolic disturbances, advancing age, severe overweight and smoking.

If you become bedbound owing to a serious illness or an accident or are to undergo surgery your doctor will decide whether you should temporarily stop taking Progyluton because the thrombosis risk may be higher in these cases.

• Cancer of the mucous lining of the womb
If estrogens are taken by themselves for prolonged periods the risk of developing cancer of the uterine lining (endometrial cancer) will rise. The progestogen in Progyluton counteracts this risk.

If irregular or serious bleeding occurs during Progyluton treatment you should inform your doctor.

• Breast cancer
In certain studies breast cancer was diagnosed somewhat more frequently in women who received hormone replacement therapy (HRT) for several years. This risk increases with the duration of treatment. With products that contain only estrogen this increase in risk might be neutral. If women discontinue HRT, the additional risk disappears within a few years. A similar increase in breast cancer diagnosis is observed with regular alcohol consumption or obesity (excessive fatness). HRT enhances opacity in mammographic images. In certain cases this can make it more difficult to diagnose breast cancer from mammography. For this reason your doctor may decide to employ other methods for breast cancer checkups.

If breast cancer has occurred in your family's past (e.g. in your mother or mother's sisters), there might be an enhanced risk of this disease occurring in you, too. Since the influence of hormone replacement therapy on this risk is not conclusive, you should inform your doctor about this.

• Liver tumor
In rare cases after the use of hormonal active ingredients such as those that are contained in Progyluton, benign liver tumors, and even more rarely malignant liver tumors have been observed, which in isolated cases led to life-threatening hemorrhages in the abdominal cavity.

For this reason the doctor is to be informed if unusual pain occurs in the upper abdomen and does not disappear soon of its own accord.

• Dementia
Studies have suggested that if you are 65 or older when starting hormone replacement therapy the risk of memory loss (dementia) may be enhanced.

**Reasons for immediate discontinuation of treatment are:**

Headache that occurs like migraine for the first time or that is particularly severe and at close intervals, sudden impairment of perception (e.g. visual or hearing impairments), disturbed sensations, initial signs of vein inflammation with blood clotting (thrombosis) or of diseases resulting from blood clots (embolism) (e.g. unusual pain or swelling in the legs), stabbing pain connected with breathing or coughing without apparent cause, fainting), painful and crushed feeling in the chest. In all these cases there may be an increased risk of thrombosis occurring.

Other reasons for discontinuation are:

- Occurrence of jaundice, occurrence of liver inflammation (hepatitis) or other liver complaints, itching over the whole body, increase in frequency of epileptic fits, major rise in blood pressure, the first occurrence or reoccurrence of severe depression, pregnancy.

**Interactions with other medicinal products**

No oral contraceptives (the “Pill” to prevent pregnancy) must be taken at the same time. If contraception is needed please consult your doctor.

When taken with other drugs there is the possibility of mutual impairment of effect. Such drugs include certain agents for epilepsy, tuberculosis, infectious diseases, inflammatory conditions and asthma; likewise agents to dilute blood, agents against excessive blood sugar, against hyperacidity in the stomach, against sleeplessness and anxiety states and depression as well as plant-based preparations containing St.-John’s-wort (Hypericum).
Each pack contains one (or three) sheets with 7 self-adhesive strips labelled with the days of the week. To prepare the pack choose the strip where the day of the week on which you want to start to take the tablets appears on the left hand side. Stick this strip on the tablet pack by the mark “day of the week”. So that the 1st day appears above the tablet marked ‘1’. For example: If the tablets are to be started on a Wednesday, the strip starting with ‘Wed’ should be stuck to the pack. Each tablet is now marked with the appropriate day of the week and it is always possible to quickly check whether the daily tablet has been taken. The remaining strips are not required.

Tablet-taking always starts with the well marked “Start” and continues in the direction of the arrows until all the 21 coated tablets have been taken. Swallow the coated tablets whole with some liquid. After the 21 days of treatment take a break of seven days, during which menstruation-like withdrawal bleeding occurs - roughly two to four days after the last coated tablet was taken. Unless prescribed otherwise by the doctor start a new pack after the seven-day break on the same day the previous one was started.

The time of day the tablet-taking occurs is immaterial, but one should always stick to the time initially selected, e.g. after breakfast or after the evening meal. If you forget to take the coated tablet at the usual time of day, take it as soon as you noticed that you forgot it, and take the next tablet at the usual time of day. If more than 24 hours have elapsed you should leave the missed tablet in the blister pack. Continue taking the remaining coated tablets at the customary time of day.

If several tablets are missed there may be irregular bleeding.

What should one do if one took too many Progyluton tablets?
There have been no reports of overdosage. However, it is possible for nausea, vomiting and irregular bleeding to occur. No special treatment is needed, but you should see your doctor.

Your doctor will determine - according to your needs - how long you should take Progyluton.
8. WHAT ELSE MUST BE BORNE IN MIND?
Drugs must be stored carefully and out of the reach of children.
The medicinal product may only be used up to the “EXP” date shown on the container.
Store below 30°C
Your doctor or pharmacist can give you further information. These persons have the more detailed professional datasheet at their disposal.

9. WHAT DOES PROGYLUTON CONTAIN?
Active ingredients:
11 white coated tablets, each containing 2 mg estradiol valerate, and 10 light brown tablets containing 2 mg estradiol valerate and 0.5 mg norgestimate as well as excipients.

10. WHERE DO YOU OBTAIN PROGYLUTON?
What packs are available?
You can only obtain Progyluton in pharmacies on medical prescription.
There are calendar packs containing 1 x 21 coated tablets and 3 x 21 coated tablets.

11. MANUFACTURER
Schering GmbH and Co. Produktions KG
D - 99427 - Weimar, Germany
a subsidiary of:
Bayer Schering Pharma AG
D - 13342 - Berlin, Germany

Do not change the prescribed dosage on your own. If you think that the drug is too weak or strong in its effect, talk to your doctor or pharmacist.

7. WHAT SIDE EFFECTS CAN PROGYLUTON HAVE?
The most serious side effects that can occur in association with a hormone replacement therapy are described in the section above entitled “When is caution advised when taking Progyluton?”. Please read that section for further information.
Other side effects reported by women on hormone replacement therapy which can be neither corroborated nor ruled out in connection with Progyluton are:

**Common:**
Weight gain or loss, headache, lower abdominal pain, nausea, skin rashes, itching skin, uterine or vaginal bleeding including spotting (bleeding irregularities normally disappear during treatment).

**Uncommon:**
Hypersensitivity reactions, depressive moods, dizziness, visual impairment, palpitation, gastrointestinal problems, serious skin conditions, urticaria (hives), breast pain, breast tension, edema (fluid retention in the tissues).

**Rare:**
Anxiety states, decrease or increase in libido, migraine, complaints in connection with the wearing of contact lenses, flatulence, vomiting, hirsutism (unnaturally increased facial and body hair), acne, muscle cramps, painful menstrual bleeding, increased vaginal secretion, premenstrual syndrome, breast engorgement, fatigue.
If you suffer from hereditary angioedema (episodic swelling of parts of the body like the hands, feet, face or respiratory tract) the taking of estrogens may trigger or exacerbate those symptoms.
Many of these complaints may be temporary, but they usually regress of the own accord or disappear when you continue tablet-taking.
If irregular bleeding persists you must inform your doctor.
Inform your doctor or pharmacist if you notice side effects which have not been described here.