

Cyclo-Progynova® 2 mg

Estradiol valerate and norgestrel

MEDA

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 any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- In this leaflet, Cyclo-Progynova 2 mg will be called Cyclo-Progynova.

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1. What Cyclo-Progynova is for

Cyclo-Progynova belongs to a group of medicines called hormone replacement therapy (HRT). Cyclo-Progynova contains two hormones called estradiol (an oestrogen) and norgestrel (a progestogen). These act in different ways in your body. During the menopause (sometimes called “the change of life”) a woman’s body slowly produces less oestrogen. This may cause hot flushes, night sweats, mood swings and dryness in the vagina. Over a long time it may also cause a thinning of the bones, which may be more likely to then break (osteoporosis). Cyclo-Progynova works by replacing the oestrogen you lose during the menopause and therefore improves the unpleasant symptoms you may get. Oestrogen can also make the lining of your womb grow more than usual, which may lead to cancer developing there. The other hormone in Cyclo-Progynova called a progestogen reduces the chance of getting cancer of the womb.

1.1 Cyclo-Progynova is used for:

- Treating symptoms of the menopause. This includes hot flushes, night sweats, mood swings and dryness in the vagina
- Preventing thinning of the bones (osteoporosis) in women who are not allowed to take other types of medicines to prevent this from happening

There are some small risks with taking HRT and you should discuss this with your doctor before you start taking Cyclo-Progynova (also see Section 2).

2. Before you take Cyclo-Progynova

2.1 Do not take Cyclo-Progynova if you have, or have ever had:

- An allergic reaction to estradiol or norgestrel
- An allergic reaction to any of the other ingredients of Cyclo-Progynova (listed in section 6)
- Breast or womb cancer
- Bleeding from your vagina and the cause is not known
- Endometrial hyperplasia that is not being treated (an overgrowth of the lining of the womb)
- Blood clots in a vein in your leg (deep vein thrombosis or DVT) or in your lungs (pulmonary embolus) or any other problems with blood clots forming.
- if you have a high risk of venous or arterial thrombosis (blood clot)
- Angina, a stroke or other heart disease
- Liver problems
- Kidney problems
- Porphyria (a rare blood disorder).

If any of the above applies to you, do not take Cyclo-Progynova and talk to your doctor or pharmacist.

2.2 Check with your doctor before taking Cyclo-Progynova if you have, or have ever had any of the following:

- Uterine fibroids (lumps of fibrous and muscular tissue in your womb)
- Endometriosis (where tissue from the womb is found outside the womb)
- Endometrial hyperplasia (overgrowth of the lining of the womb)
- Risk factors for cancer, such as history of the disease in your family
- Risk factors for blood clotting problems
- Risk factors for angina, a stroke or heart disease
- You have elevated levels of triglycerides (special type of blood lipids)
- chloasma (patches of discoloration on the skin)
- High blood pressure
- Diabetes
- Gallstones
- Adenoma of the anterior lobe of the pituitary gland (pituitary adenoma)
- Migraine or severe headache
- Systemic lupus erythematosus, (SLE or lupus for short)
- Epilepsy
- Asthma
- Otosclerosis (hearing loss due to a problem with the bones in the ear).
- A condition known as hereditary angioedema (see section 4).
- Chorea minor
- Premature menopause

2.3 Safety of HRT

As well as benefits, HRT has some risks which you may wish to discuss with your doctor when you are deciding whether to start HRT, or whether to carry on taking it.

Effects on your heart or circulation

2.4 Heart disease

HRT is not recommended for women who have or have recently had heart disease. 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 oestrogen 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.

2.5 Stroke

Recent research suggests that HRT slightly increases the risk of having a stroke. Other things that can increase the risk of stroke include:

- Getting older
- High blood pressure
- Smoking
- Drinking too much alcohol
- An irregular heartbeat.

If you are worried about any of these things, or if you have had a stroke in the past, talk to your doctor to see if you should take HRT.

Compare:

- 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**.

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.

2.6 Blood clots

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.

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
- You have had a blood clot before
- Any of your close family have had blood clots
- You have had one or more miscarriages
- You have any blood clotting problem that needs treatment with a medicine such as warfarin
- You’re off your feet for a long time because of major surgery, injury or illness
- You have a rare condition called SLE (see Section 2).

If any of these things apply to you, talk to your doctor to see if you should take HRT. Your doctor will discuss with you the benefits and risks of Cyclo-Progynova. She/he will check, e.g. whether you have a higher risk of getting a thrombosis due to a combination of risk factors or perhaps one very strong risk factor. In the case of a combination of factors the risk may be higher than simply adding two individual risks. If the risk is too high, your doctor will not prescribe HRT treatment.

Compare:

- 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.

You must 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

2.7 Surgery (Surgical operations)

If you’re 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.

Effects on your risk of developing cancer

2.8 Breast cancer

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

Taking HRT slightly increases the risk of breast cancer; so does having a later menopause, alcohol intake and adiposity. The risk for a post-menopausal woman taking oestrogen-only HRT for 5 years is about the same as for a woman of the same age who is still having periods over that time and not taking HRT. The risk for a woman who is taking oestrogen plus progestogen HRT is higher than for oestrogen-only HRT (but oestrogen plus progestogen HRT is beneficial for the endometrium, see ‘Endometrial cancer’ below).

For all kinds of HRT, the extra risk of breast cancer goes up the longer you take it, but returns to normal within about 5 years after stopping HRT.

Your risk of breast cancer is also higher if you:

- Have a close relative (mother, sister or grandmother) who has had breast cancer
- are seriously overweight.

Compare:

- Looking at women aged 50 who are **not taking HRT** — on average, **32 in 1000** will be diagnosed with breast cancer by the time they reach the age of 65.
- For women who start taking **oestrogen-only HRT** at age 50 and take it for **5 years**, the figure will be **33 and 34 in 1000 (i.e. an extra 1-2 cases)**.
- If they take oestrogen-only HRT for **10 years**, the figure will be **37 in 1000 (i.e. an extra 5 cases)**.
- For women who start taking **oestrogen plus progestogen HRT** at age 50 and take it for **5 years**, the figure will be **38 in 1000 (i.e. an extra 6 cases)**.
- If they take oestrogen plus progestogen HRT for **10 years**, the figure will be **51 in 1000 (i.e. an extra 19 cases)**.

If you notice any changes in your breast, such as:

- dimpling of the skin
- changes in the nipple
- any lumps you can see or feel

Make an appointment to see your doctor as soon as possible.

Additionally, you are advised to join mammography screening programs when offered to you. For mammogram screening, it is important that you inform the nurse/healthcare professional who is actually taking the x-ray that you use HRT, as this medication may increase the density of your breasts which may affect the outcome of the mammogram. Where the density of the breast is increased, mammography may not detect all lumps.

2.9 Endometrial cancer (cancer of the lining of the womb)

Taking oestrogen-only HRT for a long time can increase the risk of cancer of the lining of the womb (the endometrium). Taking a progestogen as well as the oestrogen helps to lower the extra risk.

If you still have your womb, your doctor will usually prescribe a progestogen as well as oestrogen. These may be prescribed separately, or as a combined HRT product.

If you have had your womb removed (a hysterectomy), your doctor will discuss with you whether you can safely take oestrogen without a progestogen.

If you've had your womb removed because of endometriosis, any endometrium left in your body may be at risk. So your doctor may prescribe HRT that includes a progestogen as well as an oestrogen.

Your product, **Cyclo-Progynova** contains a progestogen.

Compare

- Looking at women who still have a uterus and who are **not taking HRT** – on average **5 in 1000** will be diagnosed with endometrial cancer between the ages of 50 and 65.
- For women who **take oestrogen-only HRT**, the number will be **2 to 12 times higher**, depending on the dose and how long you take it.
- The addition of a progestogen to oestrogen-only HRT substantially reduces the risk of endometrial cancer.

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

If the bleeding or spotting:

- carries on for more than the first few months
- starts after you've been on HRT for a while
- carries on even after you've stopped taking HRT.

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

2.10 Ovarian cancer

Ovarian cancer is rare – much rarer than breast cancer. It can be difficult to diagnose, because there are often no obvious signs of the disease. The use of oestrogen-only or combined oestrogen-progestagen HRT 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 to 54 who are not taking HRT, about 2 women in 2000 will be diagnosed with ovarian cancer over a 5-year period. For women who have been taking HRT for 5 years, there will be about 3 cases per 2000 users (i.e. about 1 extra case).

2.11 Dementia

HRT will not prevent memory loss. In one study of women who started using combined HRT after the age of 65, a small increase in the risk of dementia was observed.

2.12 Liver tumor

During or after the use of hormones such as those that are contained in Cyclo-Progynova, 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.

2.13 Tell your doctor if you are taking any of the following medicines:

- Anticonvulsants such as phenobarbital or phenytoin (to treat epilepsy)
- Antibiotics such as rifampicin or rifabutin (to treat infections)
- Herbal medicines containing the herb St. John's Wort
- Insulin or other medicines to treat diabetes
- Protease inhibitors (to treat HIV)
- Transcriptase inhibitors such as nevirapine or efavirenz (to treat HIV)
- Any other medicine, including medicines obtained without a prescription.

2.14 Contraception

This medicine will not act as a contraceptive. Ask your doctor for advice if you are already using a contraceptive. This medicine may interfere with it.

2.15 Pregnancy and breast-feeding

Do not take Cyclo-Progynova if you are pregnant or breast-feeding.

If you become pregnant whilst taking this medicine, you must immediately stop taking this medicine and ask your doctor for advice.

2.16 Driving and using machines

Whilst taking Cyclo-Progynova you may feel dizzy. If this happens, do not drive or operate machinery.

2.17 Warning about sugar intolerance

This medicine contains sugar. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Cyclo-Progynova

Always take Cyclo-Progynova exactly as your doctor has told you.

Important:
Your doctor will choose the dose that is right for you. Your dose will be shown clearly on the label that your pharmacist puts on your medicine. If it does not, or you are not sure, ask your doctor or pharmacist.

3.1 When to start taking your medicine for the first time

Depending on your situation you should start to take this medicine at the following times of the month:

- If you are having regular periods, start taking the medicine on the fifth day of your period.
- If you are not having regular periods, you can start at any time.
- If you are changing from another HRT medicine that gives you a period complete the treatment course of the other medicine. Then on the next day start to take this medicine.
- If you are changing from another HRT medicine that does not give you a period, you can start at any time.

3.2 How to use the medicine

- Your pack contains 1 foil memo-strip and 7 blue stickers showing days of the week. Each blue sticker starts with a different day of the week.
- Peel off a strip that starts with your starting day. Stick this sticker along the top of the foil memostrip where it states 'fix the blue sticker here' so that the first day is above the pill marked 'start'.
- You can now see on which days you have to take each tablet. Take one tablet each day, following the direction of the arrows, until you have finished all 21 tablets.
- Swallow the tablets whole with water. Do not chew the tablets.
- Take the tablets at the same time every day.
- After day 21 you will have a 7 day tablet free break. During this week, bleeding similar to a period may occur. This is normal.
- Start the next strip immediately after the 7 day break. You will start your new strip of tablets on the same day of each month. Take the tablets even if your bleeding has not finished.

If you are not sure how to use the sticker and the memo-pack then please ask your pharmacist for advice.

3.3 Medical check-ups

Once you are taking this medicine:

- Regularly check your breasts for any changes. If you notice dimpling of the skin, changes in the nipple, or any lumps you must see your doctor as soon as possible.
- Go for regular breast screening
- Go for regular cervical smear tests
- See your doctor for regular check-ups (at least once a year). At these check-ups, your doctor will discuss with you the benefits and risks of continuing to take HRT.

3.4 What bleeding pattern to expect with Cyclo-Progynova

As with normal periods, the amount of blood loss will vary from woman to woman.

Your bleeding pattern may change when you are taking this medicine. You may have:

- Bleeding in the first three weeks of starting the tablets. If so, ask your doctor for advice.
- Heavier bleeding. You may notice this more if your periods have become short or lighter before you started treatment. This is normal.
- Bleeding in the break where you take no tablets. This is normal.

If after several months you are still getting spotting or breakthrough bleeding, or you are worried about your bleeding you must see your doctor.

3.5 If you take more Cyclo-Progynova than you should

If you accidentally take too much of your medicine, immediately tell your doctor or go to the nearest hospital casualty department.

3.6 If you forget to take Cyclo-Progynova

- If your tablet is less than 12 hours late, take the tablet as soon as possible, then take your next tablet at the normal time.
- If your tablet is more than 12 hours late, leave the forgotten tablet in the pack, and take your next tablet at the normal time.
- You may get some vaginal bleeding (breakthrough bleeding) if you have missed a tablet. This is normal.

If you have any further questions about the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines Cyclo-Progynova can cause side effects, although not everybody gets them.

If you have any of the following symptoms:

- Chest pain that spreads to your arm or neck
- Sudden numbness or confusion
- Difficulty breathing
- Severe rash that might blister
- Sudden pain and swelling in your leg
- You notice yellowing of your skin or eyes
- Severe or prolonged headache, possibly with disturbed vision for the first time.

Seek immediate medical help and stop taking Cyclo-Progynova.

If you get any of the following symptoms:

- If you notice any changes in your breast such as a lump, dimpling in the skin or the nipple changing
- If bleeding or spotting carries on for more than the first few months, or starts after you have been taking the tablets for a while
- If bleeding or spotting carries on even after you've stopped taking HRT.

See your doctor as soon as possible.

Important: All the symptoms in the boxes above are signs that you may be developing a serious problem. If you ignore these symptoms they may become worse.

Other possible side effects

The following symptoms, which may or may not have been caused by hormone replacement therapy, and which in some cases were probably symptoms of the climacteric, have been reported in users of different oral hormone replacement therapy preparations:

Common undesirable effects (between 1 and 10 in every 100 users may be affected)

- weight loss or gain
- Headache
- stomach pain, nausea
- rash, itching
- vaginal bleeding including Spotting (bleeding irregularities usually subside during continued treatment)

Uncommon undesirable effects (between 1 and 10 persons in every 1,000 users may be affected)

- allergies (hypersensitivity reaction)
 - depressed mood
 - dizziness
 - visual disturbances
 - palpitations(irregular, rapid beating or pulsation of the heart)
 - dyspepsia (indigestion)
 - erythema nodosum (reddish painful nodules),
 - urticaria (hives)
 - breast pain, breast tenderness
 - edema(swelling due to excessive fluid retention)
- Rare undesirable effects** (between 1 and 10 in every 10,000 users may be affected)
- anxiety, libido decreased or libido increased (an increase or a decreased interest in sex)
 - migraine
 - contact lens intolerance
 - bloating, vomiting
 - hirsutism (excessive hair growth), acne
 - muscle cramps
 - dysmenorrhea (painful period), vaginal discharge, Pre-menstrual-like syndrome, swollen breast
 - 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 Cyclo-Progynova may induce or exacerbate symptoms of hereditary angioedema.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cyclo-Progynova

Keep out of the reach and sight of children. Do not use Cyclo-Progynova after the expiry date on the carton. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Return any medicine you no longer need to your pharmacist.

6. Further information

6.1 What Cyclo-Progynova contains

- There are two active substances in this medicine. The white tablets contain 2mg of estradiol valerate. The pale-brown tablets contain 2 mg of estradiol valerate and 0.5 mg of norgestrel.
- The other ingredients are lactose, maize starch, povidone, talc, magnesium stearate (E572), sucrose, calcium carbonate (E170), polyethylene glycol 6000.

The white tablets also contain titanium dioxide (E171), yellow ferric oxide (E172) and red brown ferric oxide (E172)

The pale-brown tablets also contain glycerin and montan glycol wax.

6.2 What Cyclo-Progynova looks like

Cyclo-Progynova is made up of white and pale brown tablets.

Each carton contains 1 or 3 memo-packs. Each memo-pack contains 21 tablets, which include 11 white tablets and 10 pale brown tablets.

Not all pack sizes may be marketed.

6.3 Marketing Authorisation Holder

Meda Pharmaceuticals Ltd, Skyway House, Parsonage Road, Takeley, Bishop's Stortford, CM22 6PU.

6.4 Manufacturer

Bayer Weimar GmbH und Co KG, Weimar, Dobreinerstrasse 20D-99427, Germany and Bayer Pharma AG, Berlin, Germany
This leaflet was last updated on April 2016.

If this leaflet is difficult to see or read or you would like it in a different format, please contact Meda Pharmaceuticals Ltd, Skyway House, Parsonage Road, Takeley, Bishop's Stortford, CM22 6PU.