

PATIENT ALERT CARD  
**SyreniRing 0.120mg/0.015mg per 24 hours**

**VAGINAL DELIVERY SYSTEM**

etonogestrel/ethinylestradiol

**WHAT IS NEED TO KNOW ON COMBINED HORMONAL CONTRACEPTIVES (CHCs)**

Combined Hormonal Contraceptives (commonly named "pills") are not intended to treat any disease; its use is intended to prevent undesired pregnancies.

Contraceptive pills are one of the most reliable reversible methods of contraception if used correctly.

All combined hormonal contraceptives, including the one prescribed to you, increase the risk of the formation of a blood clot. The overall risk of developing a blood clot using combined hormonal contraceptive is low, however, blood clots can be serious and in very rare cases, even fatal. It is especially important that you recognise when you have a higher risk of a blood clot and what signs and symptoms you should look for, and what actions you need to take.

**WHEN IS THE RISK OF DEVELOPING A BLOOD CLOT GREATEST?**

- In the first year of use of a combined hormonal contraceptive, including if you are restarting after a 4 week or more break.
- Being overweight or obese.
- Being older than 35 years.
- If you smoke.

- When one of your relatives had a blood clot below the age of 50 years. Blood clots include Deep Vein Thrombosis (DVT), Lung / Pulmonary embolism (PE), heart attack or stroke.
- If you have given birth in the previous 6 weeks.
- If you smoke and are older than 35 year-old, you are strongly advised to quit smoking or use a non-hormonal contraceptive.

**WHEN TO SEEK IMMEDIATE MEDICAL ADVICE**

You should see your doctor immediately if you notice any of the following symptoms, since you could be suffering from a deep vein thrombosis, a pulmonary embolism, a heart attack or a cerebrovascular attack (stroke).

**Symptoms of Deep Vein Thrombosis:**

- Severe pain or swelling in either of your legs or feet that may be accompanied by pain on pressure, heat or change in the skin colour, such as turning pale, red or blue.

**Symptoms of Pulmonary Embolism:**

- Sudden cough without an obvious cause, which may produce bloody or blood-streaked sputum
- Severe pain in the chest, which may increase with deep breathing
- Sudden unexplained breathlessness, difficulty in breathing or rapid breathing that may occur whether you are active or at rest

**Symptoms of a Heart Attack:**

- Sudden chest pain or discomfort
- Upper body discomfort, pressure or heaviness radiating to one or both arms, the back, shoulders, neck, jaw, or upper part of the stomach (above the belly button).
- Feeling of fullness, indigestion or choking
- Cold sweat, nausea, vomiting or dizziness

**Symptoms of a Cerebrovascular Attack (stroke):**

- Sudden weakness or numbness of the face, arm or leg, especially on one side of the body
- Sudden confusion
- Trouble in speaking or understanding
- Sudden blurred or loss of vision in one or both eyes
- Severe or persistent headache/ migraine
- Loss of consciousness or fainting

**PACKAGE LEAFLET: INFORMATION FOR THE USER**

**SyreniRing 0.120mg/0.015mg per 24 hours**

**VAGINAL DELIVERY SYSTEM**

etonogestrel/ethinylestradiol

**Important things to know about combined hormonal contraceptives (CHCs):**

- They are one of the most reliable reversible methods of contraception if used correctly.
- They slightly increase the risk of having a blood clot in the veins and arteries, especially in the first year or when restarting a combined hormonal contraceptive following a break of 4 or more weeks.
- Please be alert and see your doctor if you think you may have symptoms of a blood clot (see section 2 "Blood clots").

**Read all of this leaflet carefully before you start using SyreniRing because it contains important information for you.**

- 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 only. Do not pass it on to others. It may harm them.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

Your medicine is available as the above name but will be referred to as SyreniRing throughout this leaflet.

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**Manufacturer and Product Licence Holder**

**1. What SyreniRing is and what it is used for**

SyreniRing is a contraceptive vaginal ring used to prevent pregnancy. Each ring contains a small amount of two female sex hormones - etonogestrel and ethinylestradiol. The ring slowly releases these hormones into the blood circulation. Because of the low amount of hormones that are released, SyreniRing is considered a low-dose hormonal contraceptive. Since SyreniRing releases two different types of hormones it is a so-called combined hormonal contraceptive.

SyreniRing works just like a combined contraceptive pill (the Pill) but instead of taking a pill every day, the ring is used for 3 weeks in a row. SyreniRing releases two female sex hormones that prevent the release of an egg cell from the ovaries. If no egg cell is released you cannot become pregnant.

**2. What you need to know before you use SyreniRing**

**General notes**

Before you start using SyreniRing you should read the information on blood clots in section 2. It is particularly important to read the symptoms of a blood clot - see section 2 "Blood clots".

In this leaflet, several situations are described where you should stop using SyreniRing, or where SyreniRing may be less reliable. In such situations you should not have intercourse or you should take extra hormonal contraceptive precautions - such as using a condom or another barrier method. Do not use rhythm or temperature methods. These methods can be unreliable because SyreniRing alters the monthly changes of the body temperature and of the cervical mucus.

**SyreniRing, like other hormonal contraceptives, does not protect against HIV infection (AIDS) or any other sexually transmitted disease.**

**2.1 When you should not use SyreniRing**

You should not use SyreniRing if you have any of the conditions listed below. If you do have any of the conditions listed below, you must tell your doctor. Your doctor will discuss with you what other form of birth control would be more appropriate. If you:

- have (or have ever had) a blood clot in a blood vessel of your legs (deep vein thrombosis, DVT), your lungs (pulmonary embolus, PE) or other blood vessel

- know you have a disorder affecting your blood clotting - for instance, protein C deficiency, protein S deficiency, antithrombin III deficiency, Factor V Leiden or antiphospholipid syndrome

- need an operation or if you are off your feet for a long time (see section "Blood clots")

- have ever had a heart attack, or a stroke;

- have ever had any severe angina pectoris (a condition that causes severe chest pain and may be a first sign of a heart attack) or transient ischaemic attack (TIA - temporary stroke symptoms);

- have any of the following diseases that may increase your risk of a clot in the arteries: - very high blood pressure

- a very high level of fat in the blood (cholesterol or triglycerides)

- a condition known as hyperhomocysteinaemia

- have (or have ever had) a type of migraine called "migraine with aura";

- have (had) inflammation of the pancreas (pancreatitis) associated with high levels of fat in your blood;

- have (had) severe liver disease and your liver is not yet working normally;

- have (had) a benign or malignant tumour in the liver;

- have (had), or if you may have, cancer of the breast or the genital organs;

- have any unexplained vaginal bleeding;

- are allergic to ethinylestradiol or etonogestrel, or any of the other ingredients of this medicine (listed in section 6).

- If any of these conditions appear for the first time while using SyreniRing, remove the ring immediately and contact your doctor. In the meantime, use non-hormonal contraceptive measures.

- Do not use SyreniRing if you have hepatitis C and are taking the medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir or glecaprevir / pibrentasvir (see also section 2.4 "Other medicines and SyreniRing").

**2.2 Warnings and precautions**

**When should you contact your doctor?**

**Seek urgent medical attention**

If you notice possible signs of a blood clot that may mean you are suffering from a blood clot in the leg (i.e. deep vein thrombosis), a blood clot in the lung (i.e. pulmonary embolism), a heart attack or a stroke (see "Blood clots" section below).

For a description of the symptoms of these serious side effects please go to "How to recognize a blood clot".

**Tell your doctor if any of the following conditions apply to you.**

- If the condition develops, or gets worse while you are using SyreniRing, you should also tell your doctor if you:

- have a close relative that has or has ever had breast cancer;

- have epilepsy (see section 2.4 "Other Medicines and SyreniRing");

- have liver disease (for instance jaundice) or gallbladder disease (for instance gallstones);

- have Crohn's disease or ulcerative colitis (chronic inflammatory bowel disease);

- have systemic lupus erythematosus (SLE - a disease affecting your natural defense system);

- have haemolytic uraemic syndrome (HUS - a disorder of blood clotting causing failure of the kidneys);

- have sickle cell anaemia (an inherited disease of the red blood cells);

- have elevated levels of fat in the blood (hypertriglyceridaemia) or a positive family history for this condition. Hypertriglyceridaemia has been associated with an increased risk of developing pancreatitis (inflammation of the pancreas);

- need an operation, or you are off your feet for a long time (see in section 2 "Blood clots");

- have just given birth you are at an increased risk of blood clots. You should seek your doctor how soon after delivery you can start using SyreniRing;

- have an inflammation in the veins under the skin (superficial thrombophlebitis);

- have varicose veins;

- have a condition that occurred for the first time or worsened during pregnancy or previous use of sex hormones (e.g. hearing loss, porphyria [a disease of the blood], herpes gestationis [skin rash with vesicles during pregnancy], Sydenham's chorea [a disease of the nerves in which sudden movements of the body occur]).

- have (or have ever had) chloasma (yellowish-brown pigment patches, so called "pregnancy patches", particularly on the face). If so, avoid too much exposure to the sun or ultraviolet light.

- have a medical condition that makes it difficult to use SyreniRing - for example, if you are constipated, have a prolapse of the uterine cervix or have pain during intercourse;

- have an urgent, frequent, burning, and/or painful urination, and cannot locate the ring in the vagina. These symptoms may indicate accidental placement of SyreniRing into the urinary bladder;

- experience symptoms of angioedema such as swollen face, tongue and/or throat and/or difficulty swallowing or hives potentially with difficulty breathing contact a doctor immediately. Products containing estrogens may cause or worsen the symptoms of hereditary and acquired angioedema.

**BLOOD CLOTS**

Using a combined hormonal contraceptive such as SyreniRing increases your risk of developing a blood clot compared with not using one. In rare cases a blood clot can block blood vessels and cause serious problems.

**Blood clots can develop:**

- in veins (referred to as a "venous thrombosis", "venous thromboembolism" or VTE)

- in the arteries (referred to as an "arterial thrombosis", "arterial thromboembolism" or ATE).

Recovery from blood clots is not always complete. Rarely, there may be serious lasting effects or, very rarely, they may be fatal.

**It is important to remember that the overall risk of a harmful blood clot due to SyreniRing is small.**

**HOW TO RECOGNISE A BLOOD CLOT**

Seek urgent medical attention if you notice any of the following signs or symptoms.

Are you experiencing any of these signs?	What are you possibly suffering from?
<ul style="list-style-type: none"><li>• swelling of one leg or along a vein in the leg or foot, especially when accompanied by:</li><li>• pain or tenderness in the leg which may be felt only when standing or walking;</li><li>• increased warmth in the affected leg;</li><li>• change in colour of the skin on the leg e.g. turning pale, red or blue.</li></ul>	Deep vein thrombosis
<ul style="list-style-type: none"><li>• sudden unexplained breathlessness or rapid breathing;</li><li>• sudden cough without an obvious cause, which may bring up blood;</li><li>• sharp chest pain, which may increase with deep breathing;</li><li>• severe light headaches or dizziness;</li><li>• rapid or irregular heartbeats;</li><li>• severe pain in your stomach;</li><li>• If you are unsure, talk to a doctor, as some of these symptoms such as coughing or being short of breath may be mistaken for a milder condition such as a respiratory tract infection (e.g. a "common cold").</li></ul>	Pulmonary embolism
<ul style="list-style-type: none"><li>• Sudden weakness or numbness of the face, arm or leg, especially on one side of the body</li><li>• Sudden confusion</li><li>• Trouble in speaking or understanding</li><li>• Sudden blurred or loss of vision in one or both eyes</li><li>• Severe or persistent headache/ migraine</li><li>• Loss of consciousness or fainting</li></ul>	Arterial vein thrombosis (blood clot in the eye)

Symptoms most commonly occur in one eye:

- immediate loss of vision or
- painless blurring of vision which can progress to loss of vision.

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**YOU SHOULD PARTICULARLY WATCH OUT FOR SYMPTOMS OF BLOOD CLOTS IF:**

- Recently had surgery or an operation, requiring staying in bed for a long time
- Have been bedridden for a longer period (i.e. due to injury or illness)
- Have been on a long journey (e.g. flights over 4 hours)

**REMEMBER TO TELL YOUR DOCTOR, NURSE OR SURGEON ABOUT USING A CHC, IF YOU:**

- Need surgery or an operation, requiring staying in bed for a long time
- Other medicine is prescribed to you

If you suspect that the intake of combined hormonal contraceptive is connected to a side effect, you should report it to your doctor or pharmacist. You can also report side effects directly to the MHRA via the Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard). By reporting side effects you can help provide more information on the safety of this medicine.

**MARKETING AUTHORISATION HOLDER**

Crescent Pharma Limited, 3 & 4 Quindhampton Business Units, Pohampton Lane, Overton, RG25 5ED, UK. PL 20416/0567

Further information is available in the patient information leaflet.

Are you experiencing any of these signs?	What are you possibly suffering from?
<ul style="list-style-type: none"><li>• chest pain, discomfort, pressure, heaviness;</li><li>• sensation of queasiness or fullness in the chest, arm or below the breastbone;</li><li>• fullness, indigestion or choking feeling;</li><li>• upper body discomfort radiating to the back, jaw, throat, arm and stomach;</li><li>• sweating, nausea, vomiting or dizziness;</li><li>• extreme weakness, anxiety, or shortness of breath;</li><li>• rapid or irregular heartbeats.</li></ul>	Heart attack
<ul style="list-style-type: none"><li>• sudden weakness or numbness of the face, arm or leg, especially on one side of the body;</li><li>• sudden, severe or prolonged headache with no known cause;</li><li>• sudden trouble seeing in one or both eyes;</li><li>• sudden trouble walking, dizziness, loss of balance or coordination;</li><li>• sudden, severe or prolonged headache with no known cause;</li><li>• loss of consciousness or fainting, with or without seizure.</li></ul> <p>Sometimes the symptoms of stroke can be brief with an almost immediate and full recovery, but you should still seek urgent medical attention, as you may be at risk of another stroke.</p>	Stroke
<ul style="list-style-type: none"><li>• swelling and slight blue discolouration of an extremity;</li><li>• severe pain in your stomach (acute abdomen).</li></ul>	Blood clots blocking other blood vessels

**BLOOD CLOTS IN A VEIN**

**What can happen if a blood clot forms in a vein?**

- The use of combined hormonal contraceptives has been connected with an increase in the risk of blood clots in the vein (venous thrombosis). However, these side effects are rare. Most frequently, they occur in the first year of use of a combined hormonal contraceptive.
- If a blood clot forms in a vein in the leg or foot it can cause a deep vein thrombosis (DVT).
- If a blood clot travels from the leg and lodges in the lung it can cause a pulmonary embolism.
- Very rarely a clot may form in a vein in another organ such as the eye (retinal vein thrombosis).

**When is the risk of developing a blood clot in a vein highest?**

The risk of developing a blood clot in a vein is highest during the first year of taking a combined hormonal contraceptive for the first time. The risk may also be higher if you restart taking a combined hormonal contraceptive (the same product or a different product) after a break of 4 weeks or more.

After the first year, the risk gets smaller but is always slightly higher than if you were not using a combined hormonal contraceptive.

When you stop using SyreniRing your risk of a blood clot returns to normal within a few weeks.

**What is the risk of developing a blood clot?**

The risk depends on your natural risk of VTE and the type of combined hormonal contraceptive you are taking.

The overall risk of a blood clot in the leg or lung (DVT or PE) with SyreniRing is small.

- Out of 10,000 women who are not using any combined hormonal contraceptive and are not pregnant, about 2 will develop a blood clot in a year.
- Out of 10,000 women who are using a combined hormonal contraceptive that contains levonorgestrel, norethisterone, or norgestimate, about 5-7 will develop a blood clot in a year.
- Out of 10,000 women who are using a combined hormonal contraceptive that contains norgestrel/etonogestrel, such as SyreniRing, between about 6 and 12 women will develop a blood clot in a year.

The risk of having a blood clot will vary according to your personal medical history (see "Factors that increase your risk of a blood clot" below).

Women who are not using a combined hormonal pill/patching and are not pregnant	Risk of developing a blood clot in a year
Women using a combined hormonal contraceptive pill containing <b>levonorgestrel, norethisterone or norgestimate</b>	About 2 out of 10,000 women
Women using SyreniRing	About 6-12 out of 10,000 women

**Factors that increase your risk of a blood clot in a vein**

The risk of a blood clot with SyreniRing is small but some conditions will increase the risk. Your risk is higher:

- if you are very overweight (body mass index or BMI over 30 kg/m<sup>2</sup>).
- if one of your immediate family has had a blood clot in the leg, lung or other organ at a young age (e.g. below the age of about 50). In this case you could have a hereditary blood clotting disorder;
- if you have ever had an operation, or if you are off your feet for a long time because of an injury or illness, or you have your leg in a cast. The use of SyreniRing may need to be stopped several weeks before surgery or while you are less mobile. If you need to stop using SyreniRing ask your doctor when you can start using it again;
- as you get older (particularly above about 35 years);
- if you have given birth less than a few weeks ago.

The risk of developing a blood clot increases the more conditions you have.

At least 4-6 hours may temporarily increase your risk of a blood clot, particularly if you have some of the other factors listed.

It is important to tell your doctor if any of these conditions apply to you, even if you are unsure. Your doctor may decide that SyreniRing needs to be stopped.

If any of these conditions appear for the first time while using SyreniRing, for example a close family member experiences a thrombosis for no known reason, or you gain a lot of weight, tell your doctor.

**BLOOD CLOTS IN AN ARTERY**

**What can happen if a blood clot forms in an artery?**

Some women who take a combined hormonal contraceptive can have serious problems. For example, it can cause a heart attack or a stroke.

**Factors that increase your risk of a blood clot in an artery**

It is important to note that the risk of a heart attack or stroke from using SyreniRing is very small but can increase:

- if you are overweight;
- if you have high blood pressure;
- if one of your immediate family has had a heart attack or stroke at a young age (less than about 50). In this case you could also have a higher risk of having a heart attack or stroke;
- if you, or someone in your immediate family, have a high level of fat in the blood (cholesterol or triglycerides);
- if you have angina pectoris, especially migraine with aura;
- if you have a problem with your heart (valve disorder, disturbance of the rhythm called atrial fibrillation)
- if you have diabetes.

If you have more than one of these conditions or if any of them are particularly severe, the risk of developing a blood clot may be increased even more.

If any of the above conditions change while you are using SyreniRing, for example, you start smoking, a close family member experiences a thrombosis for no known reason, or you gain a lot of weight, tell your doctor.

**Cancer**

The information given below was obtained in studies with combined oral contraceptives and it may also apply to SyreniRing. Information about vaginal administration of contraceptive hormones (as in SyreniRing) is not available.

Breast cancer has been found slightly more often in women using combined pills, but it is not known whether this is caused by the treatment. For example, it may be that tumours are found more in women on combined pills because they are examined by the doctor more often.

The increased occurrence of breast cancer becomes gradually less after stopping the combined pill.

It is important to regularly check your breasts and you should contact your doctor if you feel any lump. You should also tell your doctor if a close relative has, or ever had breast cancer (see section 2.2 "Warnings and precautions").

In rare cases, benign liver tumours, and in even fewer cases malignant liver tumours have been reported in pill users. Contact your doctor if you have unusual severe abdominal pain.

For users of the combined Pill it has been reported that cancer of the endometrium (the lining of the womb) and cancer of the ovaries occur less frequently. This may also be the case for SyreniRing but this has not been confirmed.

**Psychiatric disorders**

Some women using hormonal contraceptives including SyreniRing have reported depression or depressed mood. Depression can be serious and may sometimes lead to suicidal thoughts. If you experience mood changes and depressive symptoms contact your doctor for further medical advice as soon as possible.

**2.3 Children and adolescents**

The safety and efficacy of SyreniRing in adolescents under the age of 18 have not been studied.

**2.4 Other medicines and SyreniRing**

Always tell your doctor which medicines or herbal products you are already using. Also tell any other doctor or dentist (or pharmacist) who prescribes another medicine (or the dispensing pharmacist) that you use SyreniRing. They can tell you if you need to take additional contraceptive precautions (for example, male condoms) and, if so, for how long or, whether the use of another medicine you need must be changed.

**Some medicines:**

- can have an influence on the blood levels of SyreniRing,
- can make it **less effective in preventing pregnancy**,
- can cause unexpected bleeding.

These include medicines used for the treatment of: