PATIENT ALERT CARD

SyreniRing 0.120mg/0.015mg per 24 hours

VAGINAL DELIVERY SYSTEM

etonogestrel/ethinylestradiol

WHAT I NEED TO KNOW ON COMBINED HORMONAL CONTRACEPTIVES (CHCs)

Combined Hormonal Contraceptives (commonly named "pill") 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

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. By reporting side effects you can help provide more information on the safety of this medicine.

MARKETING AUTHORISATION HOLDER

Crescent Pharma Ltd., Key House, Sarum Hill, Basingstoke, RG21 8SR, UK.
PL 20416/0567

Further information is available in the patient information leaflet.

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.

What is in this leaflet

1. What SyreniRing is and what is it used for

2. What you need to know before you use SyreniRing
2.1 When you should not use SyreniRing
2.2 Warnings and precautions
    Blood clots
    Cancer
2.3 Children and adolescents
2.4 Other medicines and SyreniRing
    Laboratory tests
2.5 Pregnancy and breast-feeding
2.6 Driving and using machines

3. How to use SyreniRing
3.1 How to insert and remove SyreniRing
3.2 Three weeks in, one week out
3.3 When to start with the first ring
3.4 What to do if…
    Your ring is accidentally expelled from the vagina
    Your ring has temporarily been out of the vagina
    Your ring breaks
    You have inserted more than one ring
    You have forgotten to insert a new ring after the ring-free interval
    You have forgotten to remove the ring
    You have missed a menstrual period
    You have unexpected bleeding
    You want to change the first day of your menstrual period
    You want to delay your menstrual period
3.5 When you want to stop using SyreniRing

4. Possible side effects

5. How to store SyreniRing

6. Contents of the pack and other Information
    What SyreniRing contains
    What SyreniRing looks like and contents of the pack
    Manufacturer and Product Licence Holder

1. What SyreniRing is and what it is used for

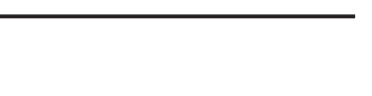
SyreniRing is a contraceptive vaginal ring used to prevent pregnancy. Each ring contains a small amount of two female sex hormones – etonogestrel and ethinylestradiol. The ring slowly releases these hormones into the blood circulation. Because of the low amount of hormones that is released, SyreniRing 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 non-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 organs;
- 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 antibodies;
- 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 (or have ever had) 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:
  - severe diabetes with blood vessel damage
  - 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 ask 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?
• swelling of one leg or along a vein in the leg or foot, especially when accompanied by: • pain or tenderness in the leg which may be felt only when standing or walking; • increased warmth in the affected leg; • change in colour of the skin on the leg e.g. turning pale, red or blue.	Deep vein thrombosis
• sudden unexplained breathlessness or rapid breathing; • sudden cough without an obvious cause, which may bring up blood; • sharp chest pain, which may increase with deep breathing; • severe light headedness or dizziness; • rapid or irregular heartbeat; • severe pain in your stomach; 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').	Pulmonary embolism
Symptoms most commonly occur in one eye: • immediate loss of vision or • painless blurring of vision which can progress to loss of vision.	Retinal vein thrombosis (blood clot in the eye)
• chest pain, discomfort, pressure, heaviness; • sensation of squeezing or fullness in the chest, arm or below the breastbone; • fullness, indigestion or choking feeling; • upper body discomfort radiating to the back, jaw throat, arm and stomach; • sweating, nausea, vomiting or dizziness; • extreme weakness, anxiety, or shortness of breath; • rapid or irregular heartbeats.	Heart attack
• sudden weakness or numbness of the face, arm or leg, especially on one side of the body; • sudden confusion, trouble speaking or understanding; • sudden trouble seeing in one or both eyes; • sudden trouble walking, dizziness, loss of balance or coordination; • sudden, severe or prolonged headache with no known cause; • loss of consciousness or fainting, with or without seizure. 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.	Stroke
• swelling and slight blue discolouration of an extremity; • severe pain in your stomach (acute abdomen).	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 norelgestromin, or 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).

	Risk of developing a blood clot in a year
Women who are **not using** a combined hormonal pill/patch/ring and are not pregnant	About 2 out of 10,000 women
Women using a combined hormonal contraceptive pill containing **levonorgestrel, norethisterone or norgestimate**	About 5-7 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/m2);
- 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 need to have 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 gave birth less than a few weeks ago.

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

Air travel (> 4 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 the above conditions change while you are 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?

Like a blood clot in a vein, a clot in an artery can cause 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:

- with increasing age (beyond about 35 years);
- **if you smoke.** When using a combined hormonal contraceptive like SyreniRing you are advised to stop smoking. If you are unable to stop smoking and are older than 35 your doctor may advise you to use a different type of contraceptive;
- if you are overweight;
- if you have high blood pressure;
- if a member 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 get migraines, especially migraines 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:

- Epilepsy (e.g. primidone, phenytoin, barbiturates, carbamazepine, oxcarbamazepine, topiramate, felbamate);
- Tuberculosis (e.g. rifampicin);
- HIV infections (e.g. ritonavir, nelfinavir, nevirapine, efavirenz);
- Hepatitis C virus infection (e.g. boceprevir, telaprevir);
- Other infectious diseases (e.g. griseofulvin).
- High blood pressure in the blood vessels of the lungs (bosentan);
- Depressive moods (the herbal remedy St. John's wort).

If you are taking medicines or herbal products that might make SyreniRing less effective, a barrier contraceptive method should also be used (for example, a male condom). Since the effect of another medicine on SyreniRing may last up to 28 days after stopping the medicine, it is necessary to use the additional barrier contraceptive method for that long. Note: Do not use SyreniRing with a diaphragm, cervical cap, or female condom.

SyreniRing may influence the effect of other medicines, e.g.

- medicines containing ciclosporin,
- the anti-epileptic lamotrigine (this could lead to an increased frequency of seizures).

Do not use SyreniRing if you have Hepatitis C and are taking the medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir or glecaprevir / pibrentasvir or sofosbuvir/velpatasvir/voxilaprevir as this may cause increases in liver function blood test results (increase in ALT liver enzyme).

Your doctor will prescribe another type of contraceptive prior to start of the treatment with these medicinal products.

SyreniRing can be restarted approximately 2 weeks after completion of this treatment. See section 2.1 'When you should not use SyreniRing'.

Ask your doctor or pharmacist for advice before taking any medicine.

You can use tampons while using SyreniRing. Insert SyreniRing before inserting a tampon.

You should be careful when removing a tampon to be sure that the ring is not accidentally pulled out. If the ring does come out, simply rinse the ring in cool to lukewarm water and immediately reinsert it.

Ring breakage has occurred when also using a vaginal product such as a lubricant or treatment for infection (see section 3.4 '*What to do if…Your ring breaks*'). Using spermicides or vaginal yeast products will not reduce the contraceptive efficacy of SyreniRing.

Laboratory tests

If you are having any blood or urinary test, tell your health care professional that you are using SyreniRing as it may affect the results of some tests.

2.5 Pregnancy and breast-feeding

SyreniRing must not be used by women who are pregnant, or who think they may be pregnant. If you get pregnant while using SyreniRing you should remove the ring and contact your doctor.

If you want to stop SyreniRing because you want to get pregnant, see section 3.5 '*When you want to stop using SyreniRing*'.

SyreniRing is not usually recommended for use during breast-feeding. If you wish to use SyreniRing while breast-feeding, please seek the advice of your doctor.

2.6 Driving and using machines

SyreniRing is unlikely to affect your ability to drive or use machines.

3. How to use SyreniRing

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

You can insert and remove SyreniRing yourself. Your doctor will tell you when to start using SyreniRing for the first time. The vaginal ring must be put in on the correct day in your monthly cycle (see section 3.3 '*When to start with the first ring*') and left in place for 3 weeks in a row. Regularly check that SyreniRing is in your vagina (for example, before and after intercourse) to ensure that you are protected from pregnancy. After the third week, you take SyreniRing out and have a one week break. You will usually have your monthly period during this ring-free interval.

While using SyreniRing, you should not use certain female barrier contraceptive methods, such as a vaginal diaphragm, cervical cap, or female condom. These contraceptive barrier methods should not be used as your back-up method of birth control because SyreniRing may interfere with the correct placement and position of a diaphragm, cervical cap, or female condom. You can however use a male condom as an extra barrier contraceptive method.

3.1 How to insert and remove SyreniRing

1. Before inserting the ring, check it is not out of date (see section 5 'How to store SyreniRing').
2. Wash your hands before inserting or removing the ring.
3. Choose the position for inserting that is most comfortable to you, like standing with one leg up, squatting, or lying down.
4. Remove SyreniRing from its sachet. Store the sachet for later use.
5. Hold the ring between your thumb and index finger, press the opposite sides together and insert the ring into the vagina (see Figures 1– 4). When SyreniRing is in place you should not feel anything. If you feel uncomfortable, gently push SyreniRing a bit further into the vagina. The exact position of the ring inside the vagina is not important.
6. After 3 weeks you remove SyreniRing from the vagina. You can do this by hooking your index finger under the front rim of the ring or by grasping the rim and pulling it out (see Figure 5). If you locate the ring in your vagina, but are unable to remove it, you should contact your doctor.
7. Dispose of the used ring with the normal household waste, preferably inside the sachet. Do not flush SyreniRing down the toilet.

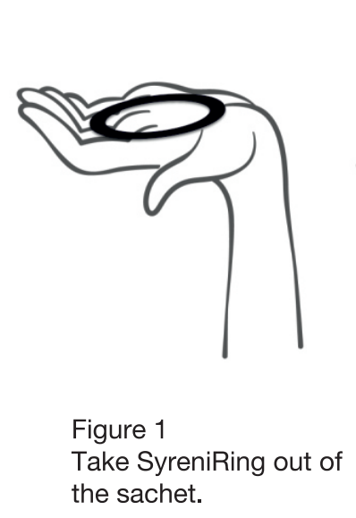


Figure 1
Take SyreniRing out of the sachet.

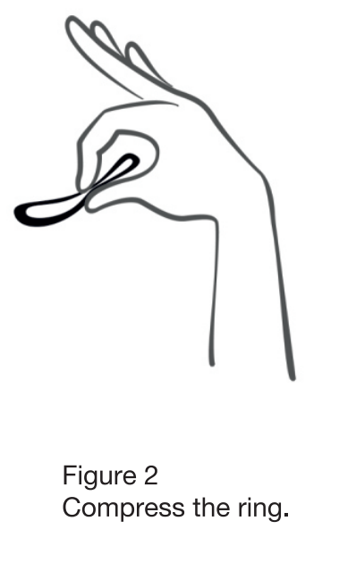


Figure 2
Compress the ring.

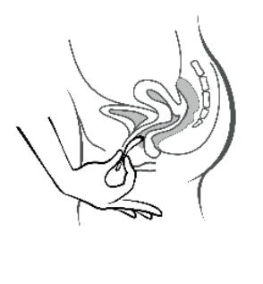


Figure 4A

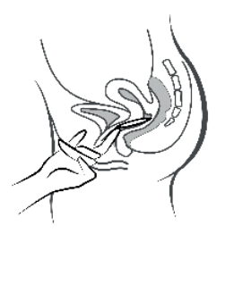


Figure 4B

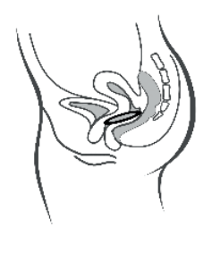


Figure 4C

Insert the ring into the vagina with one hand (Figure 4A), if necessary, the labia may be spread with the other. Push the ring into the vagina until the ring feels comfortable (Figure 4B). Leave the ring in place for 3 weeks (Figure 4C).

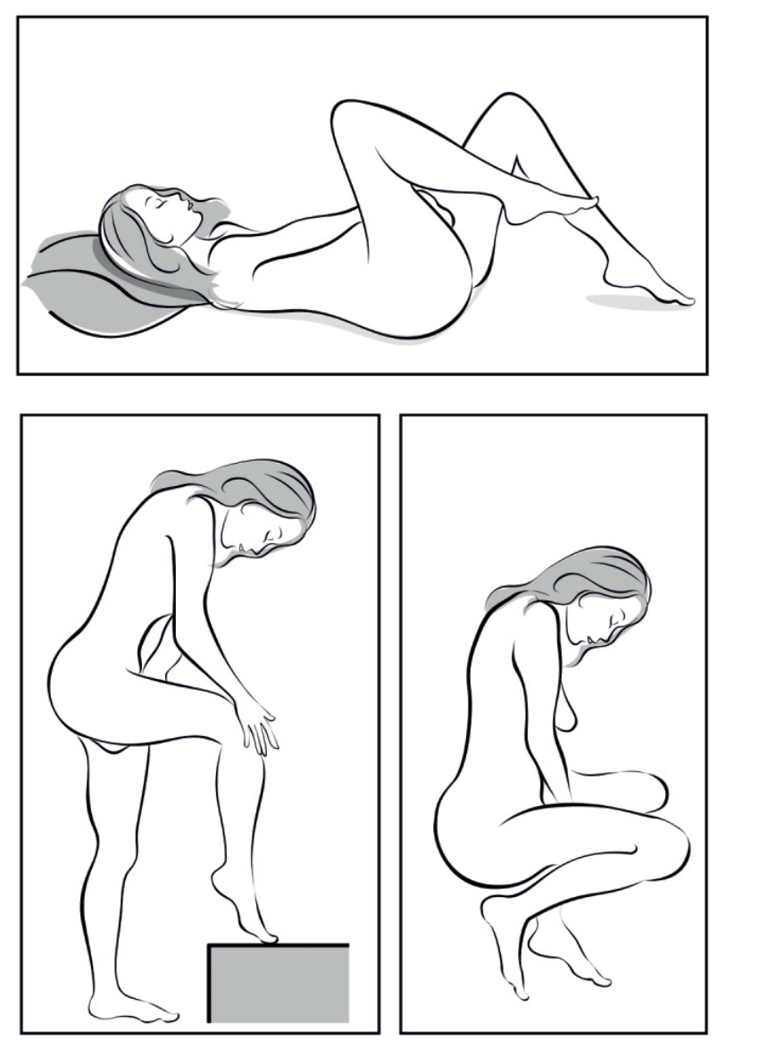


Figure 3
Choose a comfortable position to insert the ring.

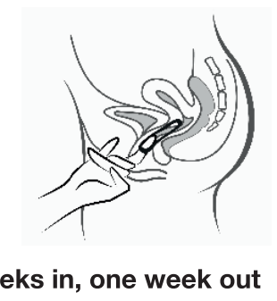


Figure 5:
SyreniRing can be removed by hooking the index finger under the ring or by grasping the ring between the index and middle finger and pulling it out.

3.2 Three weeks in, one week out

1. Starting with the day you put it in, the vaginal ring must be left in place **without interruption** for 3 weeks.
2. After 3 weeks you remove the ring on the same day of the week and at approximately the same time as it was put in. For example, if you put SyreniRing in on a Wednesday at about 22.00 h, you should remove the ring 3 weeks later, on Wednesday, at about 22.00 h.
3. After you have removed the ring, you do not use a ring for 1 week. During this week a vaginal bleed should occur. Usually this starts 2–3 days after removal of SyreniRing.
4. Start a new ring exactly after the 1 week interval (again on the same day of the week and approximately the same time), even if you have not stopped bleeding.

If the new ring is inserted more than 3 hours too late, the protection from pregnancy may be reduced. Follow the instructions in section 3.4 '*What to do if you have forgotten to insert a new ring after the ring-free interval*'.

If you use SyreniRing as described above, your vaginal bleed will take place every month on roughly the same days.

3.3 When to start with the first ring

- *You have not used a hormonal contraceptive during the last month*

  Insert the first SyreniRing on the first day of your natural cycle (i.e. the first day of your menstrual period). SyreniRing starts working straight away. You don't need to take any other contraceptive precautions.

  You can also start SyreniRing between day 2 and day 5 of your cycle, but if you have sexual intercourse during the first 7 days of SyreniRing use make sure that you also use an additional contraceptive method (such as a condom). You only have to follow this advice when you use SyreniRing for the first time.
- *You have used a combined Pill during the last month*

  Start using SyreniRing at the latest the day following the tablet-free period of your present Pill. If your Pill pack also contains inactive tablets, start SyreniRing at the latest on the day after the last inactive tablet. If you are not sure which tablet this is, ask your doctor or pharmacist. Never extend the hormone-free interval of your current Pill pack beyond its recommended length. If you have used the Pill consistently and correctly and if you are sure that you are not pregnant, you can also stop taking the Pill on any day of your current Pill pack and start using SyreniRing immediately.
- *You have used a transdermal patch during the last month*

  Start using SyreniRing at the latest the day following your usual patch-free break. Never extend the patch-free break beyond its recommended length.

  If you have used the patch consistently and correctly and if you are sure that you are not pregnant, you can also stop using the patch on any day and start using SyreniRing immediately.
- *You have used a minipill (progestagen-only pill) during the last month*

  You can stop taking the minipill any day and start SyreniRing the next day, at the same time you would normally have taken your pill. But make sure you also use an additional contraceptive method (such as a condom) for the first 7 days of ring use.
- *You have used an injectable or implant or a progestagen-releasing intrauterine device (IUD) during the last month*

  Start using SyreniRing when your next injection is due or on the day that your implant or your progestagen-releasing IUD is removed. But make sure you also use an additional contraceptive method (such as a condom) for the first 7 days of ring use.
- *After having a baby*

  If you have just had a baby, your doctor may tell you to wait until after your first normal period before you start using SyreniRing. Sometimes it is possible to start sooner. Your doctor will advise you. If you are breast-feeding and want to use SyreniRing, you should discuss this first with your doctor.
- *After a miscarriage or an abortion*

  Your doctor will advise you.

3.4 What to do if….

Your ring is accidentally expelled from the vagina

SyreniRing may accidentally be expelled from the vagina – for example, if it has not been inserted properly, while removing a tampon, during sexual intercourse, during constipation, or if you have a prolapse of the womb. Therefore, you should regularly check whether the ring is still in your vagina (for example, before and after intercourse)

Your ring has temporarily been out of the vagina

SyreniRing might still protect you from getting pregnant, but this depends on how long it has been out of your vagina.

- If the ring has been out of the vagina for **less than 3 hours**, it will still protect you from pregnancy. You should rinse the ring with cold to lukewarm water (do not use hot water) and put the ring back in as soon as possible but only if the ring has been out of the vagina for less than 3 hours.
- **More than 3 hours during the 1st and 2nd week**, it may not protect you from pregnancy. You should rinse the ring with cold to lukewarm water (do not use hot water) and put the ring back in the vagina as soon as you remember, and leave the ring in place without interruption for at least 7 days. Use a male condom if you have sexual intercourse during these 7 days. If you are in your 1st week, and you had sexual intercourse during the past 7 days, there is a possibility you may be pregnant. In that case contact your doctor.
- **More than 3 hours in the 3rd week,** it may not protect you from pregnancy. You should discard that ring and choose between one of the following two options:
  1 - Insert a new ring immediately
  This will start the next three-week use period. You may not have your period, but breakthrough bleeding and spotting may occur.
  2 - Do not insert the ring again. Have your period first and insert a new ring no later than 7 days from the time the previous ring was removed or fell out.
  You should only choose this option if you have used SyreniRing continuously during the previous 7 days.
- *If* SyreniRing was out of the vagina for an unknown amount of time, you may not be protected from pregnancy. Perform a pregnancy test and consult your doctor prior to inserting a new ring.

Your ring breaks

SyreniRing may break. Vaginal injury associated with ring breakage has been reported. If you notice that your SyreniRing has broken, discard it and start with a new ring as soon as possible. Use extra contraceptive precautions (e.g. a male condom) during the next 7 days. If you had sexual intercourse before you noticed the ring breakage, please contact your doctor.

You have inserted more than one ring

There have been no reports of serious harmful effects due to an overdose of the hormones in SyreniRing. If you have accidentally inserted more than one ring, you may feel sick (nausea) or have vomiting or vaginal bleeding. Remove excess rings and contact your doctor if these symptoms persist.

You have forgotten to insert a new ring after the ring-free interval

If your **ring-free interval** was **longer than 7 days**, put a new ring as soon as you remember. Use extra contraceptive precautions (such as a male condom) if you have sexual intercourse during the next 7 days. **If you had sexual intercourse in the ring-free interval, there is a possibility you may be pregnant.** In that case contact your doctor immediately. The longer the ring-free interval, the higher the risk that you have become pregnant.

You have forgotten to remove the ring

- If your ring has been left in place for between 3 and **4 weeks**, it will still protect you from pregnancy. Have your regular ring-free interval of one week and subsequently insert a new ring.
- If your ring has been left in place for **more than 4 weeks** there is a possibility of becoming pregnant. Contact your doctor before you start with a new ring.

You have missed a menstrual period

- **You have followed the instructions for SyreniRing**

  If you have missed a menstrual period but you followed the instructions for SyreniRing, and have not used other medicines, it is very unlikely that you are pregnant. Continue to use SyreniRing as usual. If you miss your menstrual period twice in a row, however, you may be pregnant. Tell your doctor immediately. Do not start the next SyreniRing until your doctor has checked you are not pregnant.
- **If you have not followed the instructions for SyreniRing**

  If you have missed a menstrual period and you did not follow the instructions, and you do not have your expected period in the first normal ring-free interval, you may be pregnant. Contact your doctor before you start with a new SyreniRing.

You have unexpected bleeding

While using SyreniRing, some women have unexpected vaginal bleeding between menstrual periods. You may need to use sanitary protection. In any case, leave the ring in the vagina and continue to use the ring as normal. If the irregular bleeding continues, becomes heavy or starts again, tell your doctor.

You want to change the first day of your menstrual period.

If you follow the instructions for SyreniRing, your menstrual period (withdrawal bleed) will begin in the ring-free interval. If you want to change the day it starts, you can make the ring-free interval shorter (but never longer!).

For example, if your period usually begins on a Friday, you can change this to a Tuesday (3 days earlier) from next month onwards. Simply insert your next ring 3 days earlier than usual.

If you make your ring-free interval very short (for example, 3 days or less), you may not have your usual bleeding. You may have spotting (drops or flecks of blood) or breakthrough bleeding while using the next ring.

If you are not sure how to proceed, contact your doctor for advice.

You want to delay your menstrual period

Although it is not the recommended regimen, delay of your menstrual period (withdrawal bleed) is possible by inserting a new ring immediately after removing the current ring, with no ring-free interval between rings.

You can leave the new ring inserted for up to a maximum of 3 weeks. You may experience spotting (drops or flecks of blood) or breakthrough bleeding while using this new ring. When you want your period to begin, just remove the ring. Have your regular ring free interval of one week and subsequently insert a new ring.

You can ask your doctor for advice before deciding to delay your menstrual period.

3.5 When you want to stop using SyreniRing

You can stop using SyreniRing any time you want.

If you do not want to become pregnant, ask your doctor about other methods of birth control.

If you stop using SyreniRing because you want to get pregnant, you should wait until you have had a natural period before trying to conceive. This helps you calculate when the baby will be due.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. If you get any side effect, particularly if severe or persistent, or have any change to your health that you think may be due to SyreniRing, please talk to your doctor.

An increased risk of blood clots in your veins (venous thromboembolism (VTE)) or blood clots in your arteries (arterial thromboembolism (ATE)) is present for all women taking combined hormonal contraceptives. For more detailed information on the different risks from taking combined hormonal contraceptives, please see section 2, "What you need to know before you use SyreniRing".

Contact a doctor immediately if you experience any of the following symptoms of angioedema: swollen face, tongue and/or throat and/or difficulty swallowing or hives potentially with difficulty breathing (see also section "Warnings and precautions").

Users of ring containing Etonogestrel / Ethinylestradiol have reported the following side effects.

Common: may affect up to 1 in 10 women

- *abdominal pain, feeling sick (nausea)*
- *yeast infection of the vagina (such as 'thrush'); discomfort in the vagina due to the ring; genital itching; secretion from the vagina*
- *headache or migraine; depressive moods; lower sex drive*
- *breast pain; pelvic pain; painful menstrual periods*
- *acne*
- *weight gain*
- *the ring falling out*

Uncommon: may affect up to 1 in 100 women

- disturbed vision; dizziness
- swollen abdomen; vomiting, diarrhoea or constipation
- feeling tired, unwell or irritable; mood changes; mood swings
- extra fluid in the body (oedema)
- bladder or urinary tract infection
- difficulty or pain when passing urine; strong desire or need to pass urine; passing urine more often
- problems during intercourse, including pain, bleeding or partner feeling the ring
- increased blood pressure
- increased appetite
- back pain; muscle spasms; pain in legs or arms
- less sensitive skin
- sore or larger breasts; fibrocystic breast disease (cysts in the breasts which may become swollen or painful)
- inflammation of the cervix; cervical polyps (growths in the cervix); rolling outward of the margin of the cervix (ectropion)
- changes to menstrual periods (e.g. periods can be heavy, long, irregular or stop altogether); pelvic discomfort; premenstrual syndrome; spasm of the uterus
- vaginal infection (fungal and bacterial); burning feeling, smell, pain, discomfort or dryness in the vagina or vulva
- hair loss, eczema, itching, rash or hot flushes.
- hives

Rare: may affect up to 1 in 1,000 women

- harmful blood clots in a vein or artery, for example:
  - in a leg or foot (i.e. DVT)
  - in a lung (i.e. PE)
  - heart attack
  - stroke
  - mini-stroke or temporary stroke-like symptoms, known as a transient ischaemic attack (TIA)
  - blood clots in the liver, stomach/intestine, kidneys or eye. The chance of having a blood clot may be higher if you have any other conditions that increase this risk. (See section 2 for more information on the conditions that increase risk for blood clots and the symptoms of a blood clot.)
- breast discharge

Not known (cannot be estimated from the available data)

- chloasma (yellowish-brown pigmentation patches on the skin, particularly of the face)
- penis discomfort of the partner (such as irritation, rash, itching)
- inability to remove ring without medical assistance (e.g., because of adherence to vaginal wall)
- vaginal injury associated with ring breakage

Breast cancer and liver tumours have been reported in users of combined hormonal contraceptives. For more information, see section 2.2 *Warnings and precautions, Cancer*.

SyreniRing may break. For more information, see section 3.4 What to do if…Your ring breaks.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. 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 or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store SyreniRing

Keep this medicine out of the sight and reach of children.

If you discover that a child has been exposed to the hormones from SyreniRing, ask your doctor for advice.

This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from light.

SyreniRing should be inserted at least one month prior to the expiry date, which is stated on the carton and sachet after EXP. The expiry date refers to the last day of that month.

Do not use SyreniRing if you notice a colour change in the ring or any visible signs of deterioration.

This medicinal product may pose a risk to the environment. After removal, SyreniRing should be placed in the sachet and properly closed. The closed sachet should be disposed with the normal household waste or it should be taken back to the pharmacy for its proper destruction according to local requirements.

Do not flush SyreniRing down the toilet. As with other medicines, do not throw away any unused or outdated rings via wastewater or household waste. Ask your pharmacist how to throw away any unused rings no longer required. These measures will help protect the environment.

6. Contents of the pack and other information

What SyreniRing contains

- The active substances are: etonogestrel and ethinylestradiol.
  SyreniRing contains 8.25 mg etonogestrel and 2.60 mg ethinylestradiol. The ring releases etonogestrel and ethinylestradiol at an average amount of 0.120 mg/0.015 mg, respectively per 24 hours, over a period of 3 weeks.
- The other ingredients are: ethylene vinyl acetate copolymer 28% vinyl acetate and polyurethane (a type of plastic that will not dissolve in the body).

What SyreniRing looks like and contents of the pack

Vaginal delivery system.

SyreniRing is flexible, transparent, and colourless to almost colourless ring, with an outer diameter of 54mm and a cross-sectional diameter of 4mm.

Each ring is packed in an aluminum sachet. The sachet is packed in a cardboard box together with this package leaflet and stickers for your calendar to help you to remember when to insert and remove the ring.

Each box contains:
1 ring
3 rings
6 rings
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Crescent Pharma Ltd., Key House,
Sarum Hill, Basingstoke, RG21 8SR, UK.

Manufacturer
Laboratorios León Farma, S.A.
Calle La Vallina s/n,
Polígono Industrial Navatejera,
Villaquilambre, León 24193
Spain

This leaflet was last revised in January 2025.