

1.3.2.1 PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S2

SYNAPAUSE VAGINAL CREAM 1 mg/g

Estriol

Contains sugar: Glycerol (sugar alcohol)

Read all of this leaflet carefully because it contains important information for you.

SYNAPAUSE VAGINAL CREAM is available without a doctor's prescription, for you to treat a mild illness. Nevertheless, you still need to use SYNAPAUSE VAGINAL CREAM carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Do not share SYNAPAUSE VAGINAL CREAM with any other person.
- Ask your healthcare provider or pharmacist if you need more information or advice.
- You must see a doctor if your symptoms worsen or do not improve.

What is in this leaflet:

1. What SYNAPAUSE VAGINAL CREAM is and what it is used for
2. What you need to know before you use SYNAPAUSE VAGINAL CREAM
3. How to use SYNAPAUSE VAGINAL CREAM
4. Possible side effects

5. How to store SYNAPAUSE VAGINAL CREAM
6. Contents of the pack and other information

1. What SYNAPAUSE VAGINAL CREAM is and what it is used for

SYNAPAUSE VAGINAL CREAM belongs to a group of medicines called hormone replacements.

SYNAPAUSE VAGINAL CREAM is used for hormone replacement therapy (HRT) to restore the mucosal layer of the vaginal wall as well as when you are having vaginal surgery.

2. What you need to know before you use SYNAPAUSE VAGINAL CREAM

Do not use SYNAPAUSE VAGINAL CREAM:

- if you are hypersensitive (allergic) to estriol or any of the other ingredients of SYNAPAUSE VAGINAL CREAM (listed in section 6).
- if you are pregnant or you think you may be pregnant.
- if you are breastfeeding your baby.
- if you have a tumour (e.g. a breast tumour (lump in the breast, bloody discharge from the nipple, changes in the shape or texture of the nipple or breast) or a tumour in your womb (abnormal vaginal bleeding, pain in the lower abdomen)).
- if you have a known, past or suspected breast cancer including a family history of breast cancer.
- if you have a history of non-cancerous breast diseases.

- if you recently had unexpected vaginal bleeding.
- if your menstrual periods started early (before the age of 12 years).
- if you have had abnormal growth of the lining of your womb (endometrial hyperplasia with symptoms such as heavy and long menstrual bleeding).
- if you have or have had a blood circulation disorder such as blood clots in the veins of the legs or the lungs.
- if you have or have had a blood clotting disorder (thrombophilic disorder, such as protein C, protein S or anti-thrombin deficiency).
- if you have or have had a disease caused by blood clots in the arteries, such as angina or a heart attack.
- if you have or have had liver disease (with symptoms such as yellow eyes and skin (jaundice), nausea, abdominal pain and swelling, swelling of the legs) where the function of the liver has not returned to normal.
- if you have porphyria (inherited disorder of blood pigment metabolism).
- if you suffer from known inherited genetic mutations (genes that protect you from getting certain cancers).
- if you have previously received radiation therapy on your chest or breast.
- if you were previously exposed to a medicine called diethylstilbestrol, medicines previously used to supplement a woman's natural estrogen production.

Warnings and precautions

Talk to your doctor or pharmacist before using SYNAPAUSE VAGINAL CREAM:

- Before you start using SYNAPAUSE VAGINAL CREAM, your doctor should enquire about your own and your family's medical history. Your doctor may decide to examine your breasts and/or your abdomen and may do an internal examination. You will also have to have periodic check-ups, especially examinations of the breasts. Your doctor will tell you how often these tests should be performed.
- Once you have started using SYNAPAUSE VAGINAL CREAM, you should see your doctor for regular check-ups (at least once every year). At these check-ups, your doctor may discuss with you the benefits and risks of continuing to apply SYNAPAUSE VAGINAL CREAM.
- Ensure that you go for regular breast screening and cervical smear tests and regularly check your breasts for any changes such as dimpling of the skin, changes in the nipple, or any lumps you can see or feel. Report any changes to your doctor or nurse (see Breast cancer below).
- Check with your doctor or pharmacist before using SYNAPAUSE VAGINAL CREAM if you are using a 'barrier' method of contraception, this includes condoms or diaphragms. This is because SYNAPAUSE VAGINAL CREAM can damage the rubber and stop them from working properly. Talk to your doctor about using another type of contraception while you are using this medicine.
 - Inform your doctor if you have or have had any of the following conditions,

or if any of these conditions deteriorated during pregnancy or with previous use of hormones:

- Uterine fibroids (non-cancerous growths in the uterus with symptoms such as heavy menstrual bleeding, prolonged periods and pelvic pain).
- Endometriosis (disorder in which tissue that normally lines the uterus grows outside the uterus with symptoms such as pain and menstrual irregularities).
- Clots in the blood vessels (thrombosis, deep vein thrombosis, lung embolism) or an increased risk of developing this.
- If anyone in your family has ever had an estrogen-dependent cancer (such as a close relative who has had breast cancer).
- High blood pressure.
- Liver disorders (symptoms such as yellow eyes and skin (jaundice), nausea, abdominal pain and swelling, and swelling of the legs).
- Diabetes (group of diseases that result in too much sugar in the blood (high blood glucose) with symptoms such as excessive thirst or urination, fatigue, weight loss or blurred vision).
- Gallstones (hardened deposit within the fluid in the gallbladder, a small organ under the liver with symptoms such as pain in the back or upper right abdomen).
- Migraine or (severe) headache.
- Systemic lupus erythematosus (inflammatory disease caused when the immune system attacks its own tissues with symptoms such as fatigue, joint pain, rash and fever).

- Thickening of the womb layer.
 - Epilepsy (recurrent fits).
 - Asthma.
 - Otosclerosis (inherited deafness).
 - High levels of fats called 'triglycerides' in your blood.
(hypertriglyceridaemia).
 - Severe pruritus (very itchy skin).
 - Cholestatic jaundice (a condition where bile flow from the liver is reduced causing yellowing of the skin and eyes).
 - Herpes gestation (a rare, autoimmune blistering disease that occurs during pregnancy).
 - Exogenous estrogens such as SYNAPAUSE VAGINAL CREAM may cause or worsen the symptoms of hereditary or acquired angioedema (a condition where parts of your body, usually the face (especially lips and eyelids), tongue, or throat, swell up due to fluid build-up under the skin)
- Tell your doctor if you have hepatitis C and you are taking the combination medicine regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir. Taking the combination of these medicines with some estrogen-containing products may cause increases in liver function blood test results (increase in ALT liver enzyme); the risk of this happening with SYNAPAUSE VAGINAL CREAM is currently unknown.
 - Tell your doctor if you notice any change in your condition while using SYNAPAUSE VAGINAL CREAM.

- Reasons for immediately stopping SYNAPAUSE VAGINAL CREAM:
 - Jaundice (your skin goes yellow) or a decrease in liver function.
 - A sudden increase in blood pressure.
 - If you get migraine or severe headaches, for the first time.
 - Pregnancy.

SYNAPAUSE VAGINAL CREAM and psychiatric disorders

Some women using hormonal medicines including SYNAPAUSE VAGINAL CREAM 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.

Effects on your risk of developing cancer

Endometrial cancer (cancer of the lining of the womb)

The risk of endometrial hyperplasia (abnormal growth of the lining of your womb with symptoms such as heavy and long menstrual bleeding) and endometrial cancer (cancer of the lining of the womb) is increased when using HRT such as SYNAPAUSE VAGINAL CREAM.

To prevent endometrial stimulation the maximum dose should not be exceeded, nor should the maximum dose be used for longer than several weeks. In case of long-term treatment your doctor may want to examine your uterus (womb) or alternatively prescribe the use of a progestogen.

Tell your doctor if breakthrough bleeding or spotting appears at any time on

therapy, the reason should be investigated. Caution is advised when using this therapy if you have undergone hysterectomy because of endometriosis, especially if you are known to have residual endometriosis.

Breast cancer

Women who have breast cancer, or have had breast cancer in the past, should not use SYNAPAUSE VAGINAL CREAM. Use of SYNAPAUSE VAGINAL CREAM increases the risk of breast cancer.

Taking estrogen or estrogen-progestogen combined HRT increases the risk of breast cancer. The risk increases with the duration of HRT use and returns to normal within about 5 years after stopping HRT. Women using combined HRT have a slightly greater risk of developing breast cancer than women using estrogen-only HRT.

It is not known whether SYNAPAUSE VAGINAL CREAM is associated with the same higher risk of breast cancer as other HRT. Nevertheless, if you are concerned about the risk of breast cancer, discuss the risk compared to the benefits of treatment with your doctor.

Be sure to regularly check your breasts for any changes such as dimpling of the skin, changes in the nipple, or any lumps you can see or feel. If you notice any changes make an appointment to see your doctor straight away.

All women on SYNAPAUSE VAGINAL CREAM should receive yearly breast examinations by a healthcare provider and perform monthly breast self-examinations. Mammography evaluations should be done based on patient age, risk factors, and prior mammogram results.

Ovarian cancer (cancer of the ovaries)

Ovarian cancer (cancer of the ovaries) is very rare.

Long-term (at least 5 to 10 years) use of estrogen-only HRT, such as SYNAPAUSE VAGINAL CREAM, is thought to carry a slight risk of ovarian cancer.

Effects on your heart or circulation

Coronary artery disease (CAD)

Women taking estrogen-progestogen HRT, are slightly more likely to get heart disease during the first year of taking the medication than those not taking any HRT. As the baseline absolute risk of heart disease is strongly dependent on age, the number of extra cases of heart disease due to estrogen-progestogen use is very low in healthy women close to menopause but will rise with more advanced age.

For other types of HRT, the risk is likely to be similar, although this is not yet certain.

Stroke

Combined estrogen-progestogen and estrogen-only HRT increase the risk of stroke up to 1,5-fold.

If you have symptoms that might indicate that you have a stroke (such as unexplained migraine-type headaches, with or without disturbed vision), see a doctor as soon as possible. Stop using SYNAPAUSE VAGINAL CREAM until your doctor says you can continue with your treatment.

Blood clots

HRT increases the risk of blood clots in the veins (also called deep vein thrombosis or DVT) 1,3 to 3-fold, especially during the first year of taking it. It is unknown if SYNAPAUSE VAGINAL CREAM increases the risk in the same way. These blood clots may travel to the lungs and 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 older,
- if you are pregnant or have recently had a baby,
- if you use estrogens such as SYNAPAUSE VAGINAL CREAM,
- if you are seriously overweight,
- if you have had a blood clot before in the leg, lung or another organ,
- if any of your close family have had blood clots,
- if you have any blood clotting problem that needs treatment with a medicine such as warfarin,

- if you are off your feet for a long time because of major surgery, injury or illness,
- if you have a rare condition called systemic lupus erythematosus (inflammatory disease caused when the immune system attacks its own tissues with symptoms such as fatigue, joint pain, rash and fever),
- if you have cancer.

If any of these apply to you, talk to your doctor.

If you have symptoms that might indicate that you have developed blood clots (such as painful swelling in your leg, sudden chest pain and/or difficulty breathing), see a doctor as soon as possible. Stop using SYNAPAUSE VAGINAL CREAM until your doctor says you can continue with your treatment.

If you are going to have surgery, make sure your doctor knows about it. You may need to stop using SYNAPAUSE VAGINAL CREAM 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 using SYNAPAUSE VAGINAL CREAM again.

Other effects

HRT will not prevent memory loss. The risk of memory loss may be somewhat higher in women who start using HRT after the age of 65.

In case of vaginal infections, these should be treated before therapy with SYNAPAUSE VAGINAL CREAM is started.

Important information about some of the ingredients of SYNAPAUSE VAGINAL CREAM

SYNAPAUSE VAGINAL CREAM contains cetyl alcohol and stearyl alcohol. This may cause local skin reactions (e.g. contact dermatitis).

Children

There is no experience with SYNAPAUSE VAGINAL CREAM in children younger than 15 years.

Other medicines and SYNAPAUSE VAGINAL CREAM

Always tell your healthcare provider if you are taking any other medicines (this includes complementary or traditional medicines).

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

- Oral contraceptives: medicines used for birth control.
- Insulins: medicines used to treat high blood glucose.
- Anticonvulsants: medicines used to treat epilepsy such as hydantoins, phenobarbital, phenytoin, barbiturates or carbamazepine.
- Corticosteroid hormones: medicines used to treat conditions such as arthritis, lupus or allergies.
- Oral anticoagulants: medicines used to stop blood clots such as warfarin.
- Lamotrigine: medicine used to treat epilepsy.
- Medicines for hepatitis C virus (HCV) (such as combination regimen ombiasvir/paritaprevir/ritonavir with or without dasabuvir as well as a regimen

with glecaprevir/pibrentasvir) may cause increases in liver function blood test results (increase in ALT liver enzyme) in women using CHCs containing ethinylestradiol. Estriol contains estriol instead of ethinylestradiol. It is not known whether an increase in ALT liver enzyme can occur when using Estriol with this HCV combination regimen. Your doctor will advise you.

- Succinylcholine: medicine used for muscle relaxation during anaesthesia.
- Medicines for sleeplessness such as barbiturates.
- Medicines for fungal or bacterial infections such as griseofulvin, rifamycins, troleandomycin or rifabutin.
- Medicines for viral infections such as nevirapine, efavirenz, ritonavir or nelfinavir.
- St John's wort: herbal medicine used to treat depression.
- Bosentan: medicine used to treat high blood pressure in the blood vessels of the lungs.
- Beta-adrenergic blockers: medicines used to treat abnormal heart rhythms such as acebutolol and betoxolol.
- Theophyllines: medicines used to treat respiratory diseases such as asthma.
- Hepatitis C medications such as the combination medicine regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir.

Pregnancy, breastfeeding and fertility

You should not use SYNAPAUSE VAGINAL CREAM if you are pregnant or breastfeeding your baby.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before using this medicine.

Driving and using machines

SYNAPAUSE VAGINAL CREAM is not expected to influence your ability to drive. However, you should not drive, use machinery or perform any tasks that require concentration until you are certain that SYNAPAUSE VAGINAL CREAM does not adversely affect your ability to do so safely (see section 4).

3. How to use SYNAPAUSE VAGINAL CREAM

Do not share medicine prescribed for you with any other person.

Always use SYNAPAUSE VAGINAL CREAM exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

For vaginal complaints the usual dosage is 1 application daily during the first 2 to 3 weeks; later, the dose is gradually decreased based on relief of symptoms to, for instance, 1 application twice a week.

When you are having vaginal surgery, the usual dose is 1 application per day in the 2 weeks before surgery; 1 application twice a week in the 2 weeks after surgery.

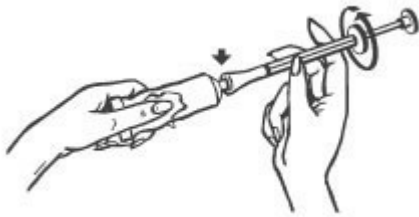
Use the applicator to apply the cream in the vagina.

It is good idea to do this before retiring at night.

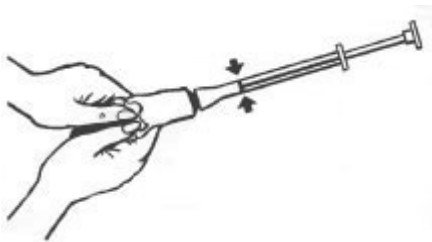
One application (applicator filled to the ring mark) contains 0,5 g of SYNAPAUSE VAGINAL CREAM, which has 0,5 mg estriol in it.

Instructions:

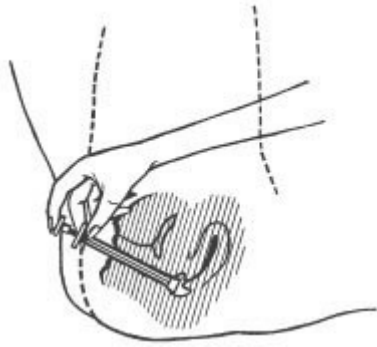
1. Remove cap from the tube, invert it, and use the sharp point to open the tube.
2. Screw the end of the applicator onto the tube. Make sure the plunger is fully inserted into the barrel.



3. Squeeze tube slowly to fill the applicator with the cream until the plunger stops (at the red ring, see arrows in picture below).



4. Unscrew applicator from tube and put cap back on tube.
5. To apply the cream, lie down, insert the end of the applicator deep into the vagina.
6. Slowly push plunger all the way in until the applicator is empty.



7. After use, pull plunger out of barrel beyond the point of resistance and wash both in warm, soapy water. Do not use detergents. Rinse well afterwards. **DO NOT PUT THE APPLICATOR IN HOT OR BOILING WATER.**
8. The applicator can be re-assembled by fully inserting the plunger into the barrel beyond the point where resistance is felt.

Discard the applicator once the tube is empty.

If you have the impression that the effect of SYNAPAUSE VAGINAL CREAM is too strong or too weak, tell your doctor or pharmacist.

If you use more SYNAPAUSE VAGINAL CREAM than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you have swallowed some cream, you should consult a doctor. Symptoms that may arise are nausea, vomiting, breast tenderness or pain in the breasts, headache, excessive production of cervical mucus, in females, vaginal bleeding may occur after a few days.

If you forget to use SYNAPAUSE VAGINAL CREAM

Do not use a double dose to make up for forgotten individual doses.

4. Possible side effects

SYNAPAUSE VAGINAL CREAM can have side effects.

Not all side effects reported for SYNAPAUSE VAGINAL CREAM are included in this leaflet. Should your general health worsen or if you experience any untoward effects while using SYNAPAUSE VAGINAL CREAM, please consult your healthcare provider for advice.

If any of the following happens, stop taking SYNAPAUSE VAGINAL CREAM and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching.

These are all very serious side effects. If you have them, you may have had a serious reaction to SYNAPAUSE VAGINAL CREAM. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- benign and malignant hormone-dependent tumours such as endometrial cancer, breast cancer or ovarian cancer,
- dementia (memory loss, decreased thinking skills),
- stroke (trouble walking, speaking and understanding, as well as paralysis or

numbness of the face, arm or leg),

- angioedema (a condition where deep layers of the skin swell up due to fluid buildup),
- coronary artery disease (chest pain, shortness of breath),
- venous thromboembolism i.e. deep leg or pelvic vein blood clots which may pass to your lungs,
- palpitations (rapid irregular action of the heart; irregular heartbeat),
- cystitis (traces of blood in the urine, dark, cloudy, or strong-smelling urine, pain just above the pubic bone, in the lower back, or in the abdomen, burning sensation when urinating, urinating frequently or feeling the need to urinate frequently).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Side effects with unknown frequency:

- Application site irritation,
- enlargement, tension, tenderness, discomfort and pain of the breast,
- gall bladder disease (upper abdominal pain after eating, nausea, bloating, indigestion),
- skin disorders, such as brownish pigmentation of the skin (chloasma), various skin diseases with blisters and nodules or bleeding into the skin (erythema multiforme, erythema nodosum, vascular purpura),
- depression (apathy, general discontent, guilt, hopelessness, loss of interest or pleasure in activities, mood swings, or sadness),

- headache,
- nausea (feeling sick),
- vomiting (being sick),
- pain in the lower abdomen,
- fluid retention (swelling of affected body parts, stiff joints, unexplained weight fluctuations),
- pain in the leg,
- increased frequency of micturition (increased frequency of urination),
- breakthrough bleeding/spotting, vaginal/cervical discharge, pre-menstrual tension, endometrial hyperplasia (abnormal growth of the lining of your womb with symptoms such as heavy and long menstrual bleeding),
- flu-like symptoms such as fever, chills, muscle aches, cough, congestion, runny nose, headaches and fatigue.

Using SYNAPAUSE VAGINAL CREAM for several years increases the risk of breast cancer.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the **Med** Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

By reporting side effects, you can help provide more information on the safety of
SYNAPAUSE VAGINAL CREAM.

5. How to store SYNAPAUSE VAGINAL CREAM

Store all medicines out of reach of children.

Store in a cool place at or below 25 °C. Do not freeze.

Keep in original packaging until required for use.

Do not store in a bathroom.

Do not use after the expiry date stated on the label.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What SYNAPAUSE VAGINAL CREAM contains

The active substance per gram of SYNAPAUSE VAGINAL CREAM is 1 mg estriol.

The other ingredients are cetyl alcohol, cetyl palmitate, chlorhexidine dihydrochloride, glycerol, lactic acid, octyldodecanol, polysorbate 60, purified water, sodium hydroxide (for pH adjustment), sorbitan stearate and stearyl alcohol.

Preservative: Chlorhexidine dihydrochloride 0,01 % *m/m*

What SYNAPAUSE VAGINAL CREAM looks like and contents of the pack

SYNAPAUSE VAGINAL CREAM is a white to almost white, smooth, homogeneous, creamy mass.

SYNAPAUSE VAGINAL CREAM is filled in collapsible aluminium tubes containing 15 g of cream. The tubes are provided with a HDPE screw cap. The delivery device consists of a colourless styrene acrylonitrile syringe applicator with a white polyethylene cap and a white polyethylene plunger rod. Each tube is packed, together with an applicator in a carton.

**Holder of the Certificate of Registration**

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

Hotline: 0800 122 912 (South Africa)

This leaflet was last revised in

12 March 2026

Registration number

V/18.6/201

Access to the corresponding Professional Information**SAHPRA Repository of Professional Information and Patient Information****Leaflets:**

<https://www.sahpra.org.za/pi-pil-repository/>

Aspen Pharmacare:

E-mail: Medinfo@aspenpharma.com

Tel: 0800 118 088