

1.3.2 PATIENT INFORMATION LEAFLET

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 pharmacist if you need more information or advice.
- You must see a doctor if your symptoms worsen or do not improve.

SCHEDULING STATUS **S2**

PROPRIETARY NAME AND DOSAGE FORM

SYNAPAUSE VAGINAL CREAM

WHAT SYNAPAUSE VAGINAL CREAM CONTAINS

Each gram of SYNAPAUSE VAGINAL CREAM contains:

Active ingredient: Estriol 1 mg.

Inactive ingredients: Cetyl alcohol, cetyl palmitate, chlorhexidine dihydrochloride, glycerol, lactic acid, octyldodecanol, polysorbate 60, sodium hydroxide, sorbitan stearate, stearyl alcohol

Preservative: Chlorhexidine hydrochloride 0,01 % m/m

Contains sugar: Glycerol (sugar alcohol)

Contains alcohol: Glycerol, cetyl alcohol, stearyl alcohol

WHAT SYNAPAUSE VAGINAL CREAM IS USED FOR

SYNAPAUSE VAGINAL CREAM is used to restore the mucosal layer of the vaginal wall.

BEFORE YOU APPLY SYNAPAUSE VAGINAL CREAM

SYNAPAUSE VAGINAL CREAM **may NOT be suitable** for you if the answer is YES to any of the following questions:

- Are you pregnant or do you think you may be pregnant?
- Are you breastfeeding your baby?
- Do you have a tumour (e.g. a breast tumour or a tumour in your womb)?
- Have you recently had unexpected vaginal bleeding?
- Have you ever had an allergic reaction to one of the ingredients of SYNAPAUSE VAGINAL CREAM?
- Have you had abnormal growth of the lining of your womb (endometrial hyperplasia)?
- Have you or have you had a blood circulation disorder such as blood clots (in the veins of the legs or the lungs)?
- Have you had a blood clotting disorder (thrombophilic disorder, such as protein C, protein S or anti-thrombin deficiency)?
- Have you or have you had a disease caused by blood clots in the arteries, such as angina pectoris, stroke or a heart attack?
- Have you or have you had liver disease where the function of the liver has not returned to normal?
- Do you have porphyria?

Take special care with 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 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.

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
- Endometriosis
- 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 oestrogen-dependent cancer (such as a close relative who has had breast cancer)
- High blood pressure
- Heart disease
- Liver disorders
- Kidney disorders
- Diabetes
- Gallstones
- Migraine or (severe) headache
- Systemic lupus erythematosus
- Thickening of the womb layer
- Epilepsy
- Asthma
- Otosclerosis (inherited deafness).

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 and breastfeeding.

Effects on your risk of developing cancer

Endometrial cancer (cancer of the lining of the womb)

Every woman is at risk of getting endometrial cancer (cancer of the lining of the womb), when using hormone replacement therapy, 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.

Breakthrough bleeding or spotting may occur during the first few months of using SYNAPAUSE VAGINAL CREAM.

If the bleeding or spotting:

- carries on for more than the first few months
- starts after you have been on hormone replacement therapy for a while
- carries on even after you have stopped using SYNAPAUSE VAGINAL CREAM

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

become thicker.

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 oestrogen or oestrogen-progestogen combined hormone replacement therapy for several years increases the risk of breast cancer. The risk increases with the duration of hormone replacement therapy use and returns to normal within about 5 years after stopping hormone replacement therapy. Women using combined hormone replacement therapy have a slightly greater risk of developing breast cancer than women using oestrogen-only hormone replacement therapy.

It is not known whether SYNAPAUSE VAGINAL CREAM is associated with the same higher risk of breast cancer as other hormone replacement therapy. 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.

Ovarian cancer (Cancer of the ovaries)

Ovarian cancer (cancer of the ovaries) is very rare, but it is a serious condition. It can be difficult to diagnose, because there are often no obvious signs of the disease. Ovarian cancer is much rarer than breast cancer.

Long-term (at least 5 to 10 years) use of oestrogen-only hormone replacement therapy, 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)

SYNAPAUSE VAGINAL CREAM is not recommended for women who have heart disease, or have had heart disease recently. If you have ever had heart disease, talk to your doctor to see if you may use SYNAPAUSE VAGINAL CREAM.

Women taking oestrogen-progestogen hormone replacement therapy, are slightly more likely to get heart disease during the first year of taking the medication than those not taking any hormone replacement therapy. For other types of hormone replacement therapy, the risk is likely to be similar, although this is not yet certain.

If you have symptoms that might indicate that you have a heart disease (such as pain in your chest that spreads to your arm or neck), see a doctor as soon as possible. Do not take any more hormone replacement therapy until your doctor says you can.

Stroke

Combined oestrogen-progestogen and oestrogen-only hormone replacement therapy 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

Hormone replacement therapy 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 have had one or more miscarriages
- if you use oestrogens 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
- 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

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

Pregnancy and breastfeeding

If you are pregnant or breastfeeding while using SYNAPAUSE VAGINAL CREAM, please consult your doctor, pharmacist or other healthcare professional for advice.

If you are pregnant or think you may be pregnant, you should not use SYNAPAUSE VAGINAL CREAM.

You should not breastfeed your infant if you are using SYNAPAUSE VAGINAL CREAM.

Driving and using machinery

As far as is known, SYNAPAUSE VAGINAL CREAM has no influence on alertness or concentration.

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).

Taking other medicines with SYNAPAUSE VAGINAL CREAM

Always tell your healthcare professional if you are taking any other medicine (This includes complementary or traditional medicines).

Especially tell your doctor if you take or are to receive:

- Corticosteroid hormones
- Oral anticoagulants (medicines to stop blood clots)
- Succinylcholine (medicine used for muscle relaxation during anaesthesia)
- Theophyllines (medicines for asthma)
- Medicines for epilepsy or sleeplessness
- Medicines for fungal or bacterial or viral infections.

4. HOW TO USE SYNAPAUSE VAGINAL CREAM

SYNAPAUSE VAGINAL CREAM should be used as directed by your health care professional. You should read the instructions on the label of your medicine. If you are not sure how to use SYNAPAUSE VAGINAL CREAM, ask your doctor or pharmacist.

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

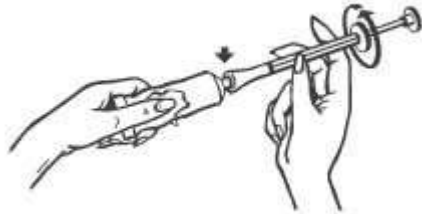
Use the applicator to apply the cream in the vagina.

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

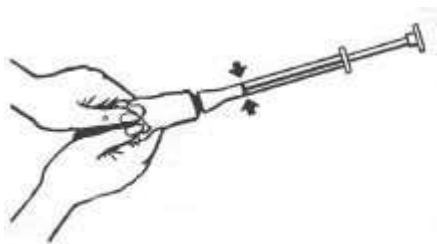
One application (applicator filled to the ring mark) contains 0,5 g of SYNAPAUSE VAGINAL CREAM, which has 0,5 mg estriol in it.

Instructions:

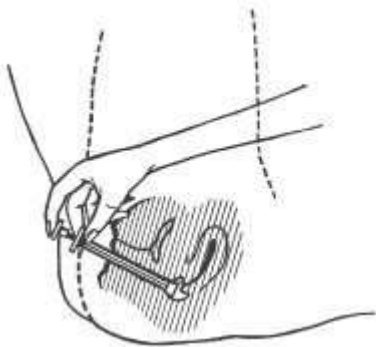
1. Remove cap from the tube, invert it, and use the sharp point to open the tube.
2. Screw the end of the applicator onto the tube. Make sure the plunger is fully inserted into the barrel.



3. Squeeze tube 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 replace cap on tube.
5. To apply the cream, lie down, insert the end of the applicator deep into the vagina and slowly push plunger all the way in until the applicator is empty.



After use, pull plunger out of barrel and wash both in warm, soapy water.

Do not use detergents. Rinse well afterwards.

DO NOT PUT THE APPLICATOR IN HOT OR BOILING WATER.

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 use more SYNAPAUSE VAGINAL CREAM than you should

If you have swallowed some cream, you should consult a doctor. Symptoms that may arise are nausea and vomiting; in females vaginal bleeding may occur after a few days.

If you forget to use SYNAPAUSE VAGINAL CREAM

If you forget to administer a dose, administer it as soon as you remember, unless you notice the missed dose at the day of your next dose. If you notice the missed dose at the day of your next dose, do not administer the missed dose, and just carry on with the next dose as normal. Never administer two doses on the same day.

POSSIBLE SIDE EFFECTS

SYNAPAUSE VAGINAL CREAM can have side effects.

In general

SYNAPAUSE VAGINAL CREAM may cause side effects such as:

- Local irritation or itching or excessive cervical mucous production
- Swelling and increased tenderness (sometimes painful) of the breasts.

Consult your doctor at once if unexpected vaginal bleeding occurs, if side effects are troublesome, or if you notice any other unusual or unexpected symptoms during treatment with SYNAPAUSE VAGINAL CREAM.

Other side effects which may occur with SYNAPAUSE VAGINAL CREAM

- Benign and malignant hormone-dependent tumours such as endometrial cancer
- Heart attack and stroke
- Gall bladder disease
- Skin- or subcutaneous 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)
- Venous thromboembolism i.e. deep leg or pelvic vein blood clots which may pass to your lungs (see BEFOFE YOU APPLY SYNAPAUSE VAGINAL CREAM - Blood clots).

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

Not all side effects reported for SYNAPAUSE VAGINAL CREAM are included in this leaflet.

If your general state of health worsens or if you experience any untoward effects while using SYNAPAUSE VAGINAL CREAM, please consult your doctor, pharmacist or other healthcare professional for advice.

STORAGE AND DISPOSING OF SYNAPAUSE VAGINAL CREAM

Keep your tube of SYNAPAUSE VAGINAL CREAM in the original box in a safe place out of the reach of children. Store in a cool place at or below 25 °C. Do not freeze.

PRESENTATION OF SYNAPAUSE VAGINAL CREAM

SYNAPAUSE VAGINAL CREAM is filled in collapsible aluminium tubes containing 15 g of cream. The tubes are provided with a polyethylene screw cap. The applicator consists of a polystyrene barrel and a polyethylene plunger. Each tube is packed, together with an applicator in a carton.



IDENTIFICATION OF SYNAPAUSE VAGINAL CREAM

A white to almost white, smooth, homogenous, cream mass.

REGISTRATION NUMBER

V/18.6/201

**NAME, BUSINESS ADDRESS AND TELEPHONE NUMBER OF THE HOLDER OF THE
CERTIFICATE OF REGISTRATION**

PHARMACARE LIMITED

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