Due to regulatory changes, the content of the following Patient Information Leaflet may vary from the one found in your medicine pack. Please compare the 'Leaflet prepared/revised date' towards the end of the leaflet to establish if there have been any changes.

If you have any doubts or queries about your medication, please contact your doctor or pharmacist.

Package Booklet: Information for the user

Progynova TS 50 micrograms/24 hours transdermal patch
Estradiol

Read all of this booklet carefully before you start using this medicine because it contains important information for you.

- Keep this booklet. 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, even if their signs of illness are the same as yours.
- 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.

What is in this booklet

1. WHAT PROGYNOVA TS 50 IS AND WHAT IT IS USED FOR

Progynova TS 50 is a Hormone Replacement Therapy (HRT). It contains the female hormone oestrogen. Progynova TS 50 is used in postmenopausal women with at least 12 months (1 year) since their last natural period.

Progynova TS 50 is used for:

Relief of symptoms occurring after menopause

During the menopause, the amount of oestrogen produced by a woman's body drops. This can cause symptoms such as hot face, neck and chest ("hot flushes"). Progynova TS 50 alleviates these symptoms after menopause. You will only be prescribed Progynova TS 50 if your symptoms seriously hinder your daily life.

Prevention of osteoporosis

After the menopause some women may develop fragile bones (osteoporosis). You should discuss all available options with your doctor.

If you are at an increased risk of fractures due to osteoporosis and other medicines are not suitable for you, you can use Progynova TS 50 to prevent osteoporosis after menopause.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE PROGYNOVA TS 50

Medical history and regular check-ups

- The use of HRT carries risks which need to be considered when deciding whether to start using it, or whether to carry on using it.
- The experience in treating women with a premature menopause (due to ovarian failure or surgery) is limited. If you have a premature menopause the risks of using HRT may be different. Please talk to your doctor.
- **Before you start** (or restart) Progynova TS 50, your doctor will ask you about your own and your family's medical history. Your doctor may decide to perform a physical examination. This may include an examination of your breasts and/or an internal examination, if necessary.
- **Once you have started** on Progynova TS 50, you should see your doctor for regular check-ups (at least once a year). At these check-ups, discuss with your doctor the benefits and risks of continuing with Progynova TS 50.
- Your doctor may prescribe the hormone progestogen in addition to Progynova TS 50 for about 12 days each month:
- if you still have your womb
  or
- if you have a history of endometriosis.

  ➢ **Go for regular breast screening, as directed by your doctor.**

Do not use Progynova TS 50

If any of the following applies to you. If you are not sure about any of the points below, **talk to your doctor** before using Progynova TS 50
Do not use Progynova TS 50

- If you have or have ever had **breast cancer**, or if you are suspected of having it

- If you have a **cancer which is sensitive to oestrogens** (such as cancer of the womb lining (endometrium)), or if you are suspected of having it
- If you have **any unexplained vaginal bleeding**
- If you have **excessive thickening of the womb lining** (endometrial hyperplasia) that has not been treated
- If you have or have ever had **a blood clot in a vein** (thrombosis) such as in the legs (deep vein thrombosis) or in the lungs (pulmonary embolism)
- If you have a **blood clotting disorder** (such as protein C, protein S or antithrombin deficiency)
- If you have or recently have had a disease caused by blood clots in the arteries such as a **heart attack, stroke or angina**
- If you have or have ever had **a liver disease** and your liver function tests have not yet returned to normal
- **If you have a rare blood problem called "porphyria"** which is passed down in families (inherited)
- If you are **allergic** to oestrogens or any of the other ingredients of this medicine (listed in section 6)

If any of the above conditions appear for the first time while using Progynova TS 50, stop using it at once and consult your doctor immediately.

Warnings and precautions

Talk to your doctor or pharmacist before using Progynova TS 50.

When to take special care with Progynova TS 50

Tell your doctor if you have ever had any of the following problems, before you start treatment, as these may return or become worse with Progynova TS 50. If so, you should see your doctor more often for check-ups:

- fibroids inside your womb
- growth of womb lining outside your womb (endometriosis) or a history of excessive growth of the womb lining (endometrial hyperplasia)
- increased risk of developing blood clots (see 'Blood clots in a vein (thrombosis)')
- increased risk of getting an oestrogen-sensitive cancer (such as having a mother, sister or grandmother who has had breast cancer)
- high blood pressure
- a liver disorder, such as benign liver tumour
- diabetes
- gallstones
- migraine or severe headaches
- a disease of the immune system that affects many organs of the body (systemic lupus erythematosus, SLE)
- epilepsy
- asthma
- a disease affecting the eardrum and hearing (otosclerosis)
- a very high level of fat in your blood (triglycerides)
- fluid retention due to cardiac or kidney problems
- hereditary and acquired angioedema

Stop using Progynova TS 50 and see your doctor immediately

If you notice any of the following when using HRT:

- any of the conditions mentioned in the 'Do not use Progynova TS 50' section
- yellowing of the skin or the whites of your eyes (jaundice). These may be signs of liver disease
- swollen face, tongue and/or throat and/or difficulty swallowing or hives, together with difficulty breathing which are suggestive of an angioedema
- a large rise in your blood pressure (symptoms may be headache, tiredness, dizziness)
- migraine-like headaches which happen for the first time
- if you become pregnant
- if you notice signs of a blood clot, such as:
  - painful swelling and redness of the legs
  - sudden chest pain
  - difficulty in breathing

For more information, see 'Blood clots in a vein (thrombosis)'

Note: Progynova TS 50 is not a contraceptive. If it is less than 12 months since your last menstrual period or you are under 50 years old, you may still need to use additional contraception to prevent pregnancy. Speak to your doctor for advice.

HRT and cancer

Excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer)

Using oestrogen-only HRT will increase the risk of excessive thickening of the lining of the womb (endometrial hyperplasia) and cancer of the lining of the womb (endometrial cancer).

Using a progestogen in addition to the oestrogen for at least 12 days of each 28 day cycle protects you from this extra risk. So your doctor will prescribe a progestogen separately if you still have your womb. If you have had your womb removed (a hysterectomy), discuss with your doctor whether you can safely take this product without a progestogen.

In women who still have a womb and who are not taking HRT, on average, 5 in 1000 will be diagnosed with endometrial cancer between the ages of 50 and 65.

For women aged 50 to 65 who still have a womb and who take oestrogen-only HRT, between 10 and 60 women in 1000 will be diagnosed with endometrial cancer (i.e. between 5 and 55 extra cases), depending on the dose and for how long it is taken.

Unexpected bleeding

You will have a bleed once a month (so-called withdrawal bleed) while using Progynova TS 50. But, if you have unexpected bleeding or drops of blood (spotting) besides your monthly bleeds, which:

- carries on for more than the first 6 months
- starts after you have been using Progynova TS 50 more than 6 months
- carries on after you have stopped using Progynova TS 50

see your doctor as soon as possible.

Breast cancer

Evidence shows that taking combined oestrogen-progestogen or oestrogen-only hormone replacement therapy (HRT) increases the risk of breast cancer. The extra risk depends on how long you use HRT. The additional risk becomes clear within 3 years of use. After stopping HRT

the extra risk will decrease with time, but the risk may persist for 10 years or more if you have used HRT for more than 5 years.

Compare

Women aged 50 to 54 who are not taking HRT, on average, 13 to 17 in 1000 will be diagnosed with breast cancer over a 5-year period.

For women aged 50 who start taking oestrogen-only HRT for 5 years, there will be 16-17 cases in 1000 users (i.e. an extra 0 to 3 cases).

For women aged 50 who start taking oestrogen-progestogen HRT for 5 years, there will be 21 cases in 1000 users (i.e. an extra 4 to 8 cases).

Women aged 50 to 59 who are not taking HRT, on average, 27 in 1000 will be diagnosed with breast cancer over a 10-year period.

For women aged 50 who start taking oestrogen-only HRT for 10 years, there will be 34 cases in 1000 users (i.e. an extra 7 cases)

For women aged 50 who start taking oestrogen-progestogen HRT for 10 years, there will be 48 cases in 1000 users (i.e. an extra 21 cases).

- **Regularly check your breasts. See your doctor if you notice any changes such as:**
- dimpling of the skin
- changes in the nipple
- any lumps you can see or feel

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

Ovarian cancer

Ovarian cancer is rare - much rarer than breast cancer. The use of oestrogen-only or combined oestrogen-progestogen HRT has been associated with a slightly increased risk of ovarian cancer.

The risk of ovarian cancer varies with age. For example, in women aged 50 to 54 who are not taking HRT, about 2 women in 2000 will be diagnosed with ovarian cancer over a 5-year period. For women who have been taking HRT for 5 years, there will be about 3 cases per 2000 users (i.e. about 1 extra case).

Effects of HRT on heart and circulation

Blood clots in a vein (thrombosis)

The risk of **blood clots in the veins** is about 1.3 to 3-times higher in HRT users than in non-users, especially during the first year of using it.

Blood clots can be serious and if one travels to the lungs, it can cause chest pain, breathlessness, fainting or even death.

You are more likely to get a blood clot in your veins as you get older and if any of the following applies to you. Inform your doctor if any of these situations applies to you:

- you are unable to walk for a long time because of major surgery, injury or illness (see also section 3 'If you need to have surgery')
- you are seriously overweight (BMI >30 kg/m²)
- you have any blood clotting problem that needs long term treatment with a medicine used to prevent blood clots
- if any of your close relatives has ever had a blood clot in the leg, lung or any other organ
- you have systemic lupus erythematosus (SLE)
- you have cancer

For signs of a blood clot, see "Stop using Progynova TS 50 and see your doctor immediately"

Compare

Looking at women in their 50s who are not taking HRT, on average, over a 5-year period, 4 to 7 in 1000 would be expected to get a blood clot in a vein.

For women in their 50s who have been taking oestrogen-progestogen HRT for over 5 years, there will be 9 to 12 cases in 1000 users (i.e. an extra 5 cases).

For women in their 50s who have had their womb removed and have been taking oestrogen-only HRT for over 5 years, there will be 5 to 8 cases in 1000 users (i.e. 1 extra case).

Heart disease (heart attack)

There is no evidence that HRT will prevent a heart attack.

Women over the age of 60 years who use oestrogen-progestogen HRT are slightly more likely to develop heart disease than those not taking any HRT.

For women who have had their womb removed and are taking oestrogen-only therapy there is no increased risk of developing heart disease.

Stroke

The risk of having a stroke is about 1.5-times higher in HRT users than in non-users. The number of extra cases of stroke due to use of HRT will increase with age.

Compare

Looking at women in their 50s who are not taking HRT, on average, 8 in 1000 would be expected to have a stroke over a 5-year period. For women in their 50s who are taking HRT, there will be 11 cases in 1000 users over 5 years (i.e. an extra 3 cases).

Other conditions

- HRT will not prevent memory loss. There is some evidence of a higher risk of memory loss in women who start using HRT after the age of 65. Speak to your doctor for advice.
- If you have a tendency to develop **blotchy brown patches** (chloasma) on the face you should avoid exposure to the sun or ultraviolet light whilst using Progynova TS 50.
- Women with **hereditary angioedema** who take Progynova TS 50 may experience a return or a worsening of their symptoms.
- Your doctor will monitor you carefully if you have heart or kidney problems.

Other medicines and Progynova TS 50

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines including medicines obtained without a prescription, herbal medicinces or other natural products.

Some medicines may interfere with the effect of Progynova TS 50. This might lead to irregular bleeding. This applies to the following medicines.

- Medicines for **epilepsy** (such as barbiturates, phenytoin, primodone, carbamazepine and possibly oxcarbazepine, topiramate and felbamate)
- Medicines for **tuberculosis** (such as rifampicin, rifabutin)
- Medicines for **HIV and Hepatitis C Virus infections** (so-called protease inhibitors and non-nucleoside reverse transcriptase inhibitors such as nevirapine, efavirenz, ritonavir and nelfinavir)
- Herbal remedies containing **St. John's wort** (*Hypericum perforatum*)
- Medicines for Hepatitis C virus (HCV) (such as combination regimen ombitasvir/paritaprevir/ritonavir with or without dasabuvir as well as regimen glecaprevir/pibrentasvir) may cause increases in liver function blood test results (increase in ALT liver enzyme) in women using CHCs (combined hormonal contraceptives) containing ethinylestradiol. Progynova TS 50 contains estradiol instead of ethinylestradiol. It is not known whether an increase in ALT liver enzyme can occur when using Progynova TS 50 with this HCV combination regimen. Your doctor will advise you.
- Medicines for **treatment of fungal infections** (such as griseofulvin, fluconazole, itraconazole, ketoconazole and voriconazole)
- Medicines for **treatment of bacterial infections** (such as clarithromycin and erythromycin)
- Medicines for **treatment of certain heart diseases, high blood pressure** (such as verapamil and diltiazem)
- **Grapefruit juice.**

Laboratory tests

If you need a blood test, tell your doctor or the laboratory staff that you are using Progynova TS 50, because this medicine can affect the results of some tests.

Pregnancy, breast-feeding and fertility

Progynova TS 50 is for use in post-menopausal women only.

If you become pregnant, stop using Progynova TS 50 and contact your doctor.

Driving and using machines

No effects on ability to drive and use machines have been observed in users of Progynova TS 50.

3. HOW TO USE PROGYNOVA TS 50

Always apply Progynova TS 50 exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. Your doctor will tell you how long you should apply Progynova TS 50 for and whether you should have a gap week (no patch for 7 days).

Do not start using Progynova TS 50 until at least twelve months after your last natural period.

Applying the patch

Remove the protective liner from the patch. Place the patch, sticky side down, on a clean, dry area of the skin of your lower abdomen or buttocks. Do not apply Progynova TS 50 patches to the breasts. Apply the patch to a different site every time. Never apply the patch to the same place twice in a row. Do not choose an area that is oily, damaged or irritated. Avoid the waistline since tight clothing may rub the patch off. Apply the patch immediately after opening the pouch and removing the protective liner. Press the patch firmly in place with the palm of the hand for about 10 seconds, making sure there is good contact, especially around the edges. Change the patch once a week. If the patch is applied correctly, you can bath or shower as usual. However, the patch might come off in very hot bath water or in the sauna.

If you have been taking other HRT preparations: carry on until you have finished your current pack and have taken all the treatment for that month. Start with the first Progynova TS 50 patch the next day. Do not leave a break between your old tablets and Progynova TS 50.

If you have been using HRT treatment with a gap week: start Progynova TS 50 immediately after the gap days.

If this is your first HRT treatment: you can start using Progynova TS 50 any day.

Continuous use: Apply 1 patch per week. Remove this patch after 7 days and apply a fresh patch to a different site on your body.

Cyclical use (includes a gap week): Apply 1 patch per week for 3 weeks. Take a 7-day break and then start again with the next patch.

You will have a bleed once a month (so-called withdrawal bleed) while using Progynova TS 50.

If you apply more Progynova TS 50 than you should

Only apply one patch at a time. If you apply more by mistake you may feel sick, throw up or have some menstruation-like bleeding. If this happens remove the patches. No specific treatment is necessary but you should consult your doctor or pharmacist if you are concerned.

If a patch falls off or if you forget to apply Progynova TS 50

If a patch falls off before 7 days are up, it may be reapplied. If necessary, you can apply a new patch for the rest of the 7 days. If you forget to replace the patch for several days you might have breakthrough bleeding and spotting.

If you stop using Progynova TS 50

You may begin to feel the usual symptoms of the menopause again, which may include hot flushes, trouble sleeping, nervousness, dizziness or vaginal dryness. Consult your doctor or pharmacist if you are considering stopping your Progynova TS 50 treatment.

If you need to have surgery

If you are going to have surgery, tell the surgeon that you are using Progynova TS 50. You may need to stop using Progynova TS 50 about 4 to 6 weeks before the operation to reduce the risk of a blood clot (see section 2, 'Blood clots in a vein'). Ask your doctor when you can start using Progynova TS 50 again.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following diseases have been reported more often in women using HRT compared to women not using HRT:

- breast cancer
- abnormal growth or cancer of the lining of the womb (endometrial hyperplasia or cancer)
- ovarian cancer
- blood clots in the veins of the legs or lungs (venous thromboembolism)
- heart disease
- stroke
- probable loss of memory if HRT is started over the age of 65

For more information about these side effects see Section 2.

The following is a list of side effects that have been linked to the use of Progynova TS 50:

Most frequent side effects*:*

- breakthrough bleeding at unexpected times (see also section 2 'HRT and cancer')
- breast tenderness
- breast pain

These side effects occur during the first few months of treatment with Progynova TS 50. They are usually temporary and normally disappear with continued treatment. If they do not, contact your doctor.

Common side effects (may affect up to 1 in 10 people):

- depression, dizziness, nervousness, lack of energy, increased sweating, hot flushes
- headache
- wind, nausea
- itching or rash at the site of application
- fluid retention, weight gain
- irregularities in your menstrual period, changes in vaginal discharge
- generalized pain

Uncommon side effects (may affect up to 1 in 100 people):

- increase in blood cholesterol
- anxiety, inability to sleep, apathy, mood swings, poor concentration, extreme feelings of euphoria, tremor, agitation, altered sex drive
- pins and needles
- migraine
- visual disturbance, dry eye
- palpitations
- superficial inflammation of the veins (phlebitis), high blood pressure
- breathlessness, runny or blocked nose
- increased appetite, constipation, indigestion, diarrhoea, rectal disorder
- unusual bleeding or bruising under the skin (purpura)
- acne, hair loss, dry skin, nail problems, small skin swellings, excessive hair growth
- joint pain, muscle cramps
- increased and frequent urge to pass urine, urinary incontinence, bladder infections (cystitis), discoloured urine, blood in the urine
- benign growths in the lining of the womb, thickening of the lining of the womb, problems with the womb, swollen breasts, tender breasts

- tiredness, irregular blood tests, high temperature, lack of energy, feeling generally unwell

Additional side effects reported by healthcare professionals:

- reduced oxygen flow to the brain or to a section of the brain (see Section 2 'Stroke')
- abdominal pain, bloating, yellowing of the skin or eyes (jaundice)
- exacerbation of hereditary angioedema **(swelling of face, tongue and/or throat and/or difficulty swallowing, hives, breathing difficulties)**
- contact dermatitis
- fibroids

The following side effects have been reported with other HRTs:

- gall bladder disease
- a variety of skin disorders:
  - discoloration of the skin especially of the face and neck known as "Pregnancy patches" (chloasma)
  - painful reddish skin nodules (erythema nodosum)
  - rash with target-shaped reddening or sores (erythema multiforme)

If you get any side effects, talk to your doctor or pharmacist. This includes any side effects not listed in this leaflet.

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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

5. HOW TO STORE PROGYNOVA TS 50

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

Do not use this medicine after the expiry date which is stated on the label after "EXP". The expiry date refers to the last day of that month.

Store your patches in the original packaging to protect from moisture. Store below 30°C.

After use the patch still contains the active ingredient, which may have harmful effects on the environment. Therefore, the used patch should be discarded carefully. Fold any used or unused patches in half, sticky side together, and dispose of them in household rubbish. Do not throw away any medicines via wastewater or household waste . Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Progynova TS 50 contains

Progynova TS 50 is a hormone patch. The **active substance** is estradiol hemihydrate.

Each 12.5 cm^2 patch contains 3.8 mg estradiol (from 3.9 mg estradiol hemihydrate), releasing 50 micrograms of estradiol per 24 hours.

The **other ingredients** are isooctyl acrylate, acrylamide, vinyl acetate copolymer, ethyl oleate, isopropyl myristate and glycerol monolaurate on a polyester release liner protected by a backing film.

What Progynova TS 50 looks like and contents of the pack

Progynova TS 50 patches are oval translucent patches. They are supplied in packs of 4 or 12 patches each.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Bayer plc
400 South Oak Way
Reading, RG2 6AD

Manufacturer

Bayer Weimar GmbH and Co. KG, 99427 Weimar, Germany.

This leaflet was last revised in May 2022