

SCHEDULING STATUS

S4

BIJUVA, 1 mg/100 mg, soft gel capsules
estradiol hemihydrate / progesterone
Sugar free.

Read all of this leaflet carefully before you start taking BIJUVA.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- BIJUVA has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What BIJUVA is and what it is used for.
2. What you need to know before you take BIJUVA.
3. How to take BIJUVA.
4. Possible side effects.
5. How to store BIJUVA.
6. Contents of the pack and other information.

1. What BIJUVA is and what it is used for

BIJUVA is a hormone replacement therapy (HRT). It contains two types of female hormones, an oestrogen and a progestogen. BIJUVA is used in postmenopausal women with at least 12 months (1 year) since their last natural period.

Relief of symptoms occurring after menopause

During the menopause, the amount of oestrogen produced by a woman's body decreases. This can cause symptoms such as feeling hot in the face, neck and chest ("hot flushes"). BIJUVA alleviates these symptoms after menopause.

You will only be prescribed BIJUVA if your symptoms seriously hinder your daily life.

2. What you need to know before you take BIJUVA

Medical history and regular check-ups

The use of HRT carries risks which need to be considered when deciding whether to start taking it, or whether to carry on taking 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) HRT, your doctor will ask 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 BIJUVA, 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 to take BIJUVA.

Go for regular breast screening, as recommended by your doctor.

Do not take BIJUVA:

If any of the following applies to you. If you are not sure about any of the points below, talk to your doctor before taking BIJUVA.

- if you are hypersensitive (allergic) to estradiol hemihydrate, progesterone or any of the other ingredients of BIJUVA (see **What BIJUVA contains**).
- if you have or have ever had **breast cancer**, or if you are suspected of having it
- if you have **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 is not being treated
- if you have or have ever had a **blood clot in a vein** (thrombosis), such as in the legs (deep venous thrombosis) or 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 returned to normal
- if you have a rare blood disorder called **porphyria** which is passed down in families (inherited).

If any of the above conditions appear for the first time while taking BIJUVA, stop taking it at once and consult your doctor immediately.

Warnings and precautions

Tell your doctor if you have or ever had any of the following problems, before you start the treatment, as these may return or become worse during treatment with BIJUVA. 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 a 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 high level of fat in your blood (triglycerides)
- fluid retention due to heart or kidney problems.

Stop taking BIJUVA and see a doctor immediately

If you notice any of the following when taking BIJUVA:

- any of the conditions mentioned in the 'Do not take BIJUVA' section
- yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a liver disease
- 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)** below.
- a very high level of fat in your blood (triglycerides)
- fluid retention due to cardiac or kidney problems.

Note: BIJUVA 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)

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

The progestogen in BIJUVA protects you from this extra risk.

Irregular bleeding

You may have irregular bleeding or drops of blood (spotting) during the first 3 – 6 months of taking BIJUVA. However, if the irregular bleeding:

- carries on for more than the first 6 months
- starts after you have been taking BIJUVA for more than 6 months
- carries on after you have stopped taking BIJUVA

see your doctor as soon as possible.

Unexpected bleeding

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

- carries on for more than the first 6 months
- starts after you have been taking BIJUVA for more than 6 months
- carries on after you have stopped taking BIJUVA

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.

- 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 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 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.

Effect 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 taking 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:

- if 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)
- if you are seriously overweight (BMI > 30 kg/m²)
- if 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
- if you have systemic lupus erythematosus (SLE)
- if you have cancer.

For signs of a blood clot, see “**Stop taking BIJUVA and see a doctor immediately**”.

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.

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.

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.

Children

BIJUVA should not be used in children.

Other medicines and BIJUVA

Always tell your health care provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

BIJUVA can affect the way some other medicines work. Some medicines may interfere with the effect of BIJUVA. This might lead to irregular bleeding. This applies to the following medicines:

- medicines for epilepsy (such as phenobarbitone, phenytoin and carbamazepine)
- medicines for tuberculosis (such as rifampicin, rifabutin)
- medicines for HIV infection (such as nevirapine, efavirenz, ritonavir and nelfinavir)

- herbal remedies containing St John's Wort (*Hypericum perforatum*)
- ketoconazole, griseofulvin (used for fungal infections)
- ciclosporin (used to suppress the immune system)
- lamotrigine (used to control seizures).

Laboratory tests

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

Pregnancy, breastfeeding and fertility

BIJUVA is for use in postmenopausal women only. If you become pregnant, stop taking BIJUVA and contact your doctor.

Driving and using machines

BIJUVA can cause side effects, such as dizziness, vertigo, visual impairment or fatigue. Do not drive a vehicle, operate machinery, or do anything else that requires your attention until you know how BIJUVA affects you.

BIJUVA contains the colourant Allura Red

Allura Red may cause allergic reactions.

3. How to take BIJUVA

Always take BIJUVA exactly as described in this leaflet or as your doctor or pharmacist have told you. Check with your doctor or pharmacist if you are not sure.

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

Take one capsule every day in the evening with food. Swallow the capsule with water.

The capsule should be taken every day without any break in the treatment.

If you take more BIJUVA than you should

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

Take this leaflet and the rest of the remaining BIJUVA with you so the doctor will know what you have taken.

The following effects may happen feeling drowsy, dizzy, sleepy or tired.

If you forget to take BIJUVA

If you forget a dose, take it as soon as you remember it. However, if more than 12 hours have lapsed, skip the missed dose.

Do not take a double dose to make up for a forgotten dose.

The likelihood of breakthrough bleeding or spotting may be increased.

If you stop taking BIJUVA

Do not stop taking BIJUVA without first talking to your doctor. If you have any further questions on the use of this product, ask your doctor or pharmacist.

If you need to have surgery

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

4. Possible side effects

BIJUVA can have side effects.

Not all side effects reported for BIJUVA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking BIJUVA, please consult your health care provider for advice.

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

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

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

The following diseases are 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 memory loss if HRT is started over the age of 65.

For more information about these side effects, see section 2.

Tell your doctor if you notice any of the following:

Side effects occurring frequently:

- tender breasts
- headache, dizziness
- back pain
- abdominal pain, feeling bloated
- breast pain, pain in the pelvic region
- weight gain
- acne
- hair loss
- feeling sick (nausea)
- severe contractions of the uterus, bleeding from the vagina or discharge from the vagina (white or yellowish discharge from the vagina)
- fatigue (feeling tired and weak)

Side effects occurring less frequently:

- pain in extremity (e.g. back pain, arms, legs, wrists, ankles)
- low iron content in blood
- high blood pressure
- excessive fluid in legs
- increased levels of cholesterol

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- excessive eating from increase hunger or appetite (hyperphagia)
- muscle pain
- difficulty sleeping or abnormal dreams, difficulty to concentrate
- tumours in uterus or fallopian tube
- memory loss, severe headaches
- tingling or prickling sensation in the hands, arms, legs or feet
- loss of smell
- mood swings, feeling irritable or agitated
- vomiting (being sick)
- dry mouth
- constipation
- diarrhoea
- weight loss
- chills
- acute pancreatitis
- feeling depressed or anxious
- more interest in sex than usual
- hot flushes
- irritation or burning sensation of vagina
- vaginal infections such as thrush
- vaginal discharge or vaginal bleeding
- blood clots
- dry and itchy skin
- rash or small, widened blood vessels on the skin (telangiectasia)
- vertigo (feeling off balance or a spinning feeling)
- excessive hair growth
- impairment of your vision
- abdominal discomfort or tenderness
- flatulence
- gastroenteritis (stomach flu)
- indigestion
- oral discomfort
- taste disturbances
- skin abscesses (boils)
- ear infection
- abnormal liver tests
- breast disorders, benign growths in the breasts, nipple pain
- muscle weakness
- benign growths in the uterus smooth muscle
- cysts close to the fallopian tube
- abnormal biopsy
- dark coloured urine

The following side effects have been reported with other HRTs:

- gall bladder disease
- various skin disorders including discoloration of the skin especially of the face or neck known as “pregnancy patches” (chloasma), painful reddish skin nodules (erythema nodosum), rash with target-shaped reddening or sores (erythema multiforme).

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 or pharmacist. 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. By reporting side effects, you can help provide more information on the safety of BIJUVA.

5. How to store BIJUVA

- Store at or below 25 °C.
- Keep the blister in the outer carton to protect from light.
- Store all medicines out of reach of children.
- Do not use after the expiry date printed on the carton.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What BIJUVA contains

Each soft capsule contains 1 mg estradiol (as estradiol hemihydrate) and 100 mg progesterone.

The other ingredients are:

Capsule content contains: medium chain mono/diglycerides, lauroyl macroglycerides 32

Capsule shell contains: gelatine (200 Bloom), hydrolysed gelatine, glycerin (E422), Allura Red (E129) (colourant), titanium dioxide (E171) (colourant)

Printing ink (Opacode® White WB) contains: propylene glycol (E1520), titanium dioxide (E171) (colourant), polyvinyl acetate phthalate, polyethylene glycol (E1521) and ammonium hydroxide (E527).

What BIJUVA looks like and contents of the pack

Oval, opaque, light pink on one side and dark pink on the other side imprinted '1C1' with white ink.

Clear PVC/PE/PCTFE/aluminium blister strips in an outer carton.

Pack sizes: 28 or 84 soft gelatine capsules.

Not all pack sizes may be marketed.

Holder of certificate of registration

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