Package leaflet: Information for the user

IMVAGGIS 0.03 mg pessary

Estriol

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, please 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 leaflet

1. What IMVAGGIS is and what it is used for

IMVAGGIS belongs to a group of medicines called vaginal Hormone Replacement Therapy (HRT).

It is used to relieve menopausal symptoms in the vagina such as dryness or irritation. In medical terms this is known as ‘vaginal atrophy’. It is caused by a drop in the levels of oestrogen in your body. This happens naturally after the menopause.

IMVAGGIS works by replacing the oestrogen which is normally produced in the ovaries of women. It is inserted into your vagina, so the hormone is released where it is needed. This may relieve discomfort in the vagina.

2. What you need to know before you use IMVAGGIS

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) 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 IMVAGGIS 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 IMVAGGIS.

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

Before starting treatment with IMVAGGIS vaginal infections should be treated with appropriate medicines.

Do not use IMVAGGIS

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 IMVAGGIS .

Do not use IMVAGGIS

- if you have or have had **breast cancer**, or if you are suspected to 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 problem called "porphyria" which is passed down in families (inherited);
- if you are allergic to estriol 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 IMVAGGIS, stop using it at once and consult your doctor immediately.

Warnings and precautions

Tell your doctor if you have ever had any of the following problems, before you start the treatment, as these may return or become worse during treatment with IMVAGGIS. 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 very high level of fat in your blood (triglycerides);
- fluid retention due to cardiac or kidney problems;
- hereditary and acquired angioedema.

Stop using IMVAGGIS and see a doctor immediately

If you notice any of the following when using HRT:

- any of the conditions mentioned in the "Do not use IMVAGGIS" section;
- yellowing of your skin or the whites of your eyes (jaundice). These may be signs of a 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: IMVAGGIS 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 tablets for a long time can increase the risk of developing cancer of the womb lining (the endometrium).

It is uncertain whether there is a similar risk when IMVAGGIS is used for repeated or long term (more than one year) treatments. However, IMVAGGIS has been shown to have very low absorption into the blood, therefore the addition of a progestagen is not necessary.

If you get bleeding or spotting, it is usually nothing to worry about, but you should make an appointment to see your doctor. It could be a sign that your endometrium has become thicker.

The following risks apply to hormone replacement therapy (HRT) medicines which circulate in the blood. However, IMVAGGIS is for local treatment in the vagina and the absorption into the blood is very low. It is less likely that the conditions mentioned below will get worse or come back during treatment with IMVAGGIS, but you should see your doctor if you are concerned.

Breast cancer
Evidence suggests that using Imvaggis does not increase the risk of breast cancer in women who had no breast cancer in the past. It is not known if Imvaggis can be safely used in women who had breast cancer in the past.

- **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.

Ovarian cancer
Ovarian cancer is rare - much rarer than breast cancer. The use of oestrogen-only 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).

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 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/m^2);
- 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 another organ;
- you have systemic lupus erythematosus (SLE);
- you have cancer.

For signs of a blood clot, see "Stop using IMVAGGIS and see a 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-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)
For women taking oestrogen-only therapy there is no increased risk of developing a heart disease.

Stroke
The risk of getting 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. 3 extra 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.

Other medicines and IMVAGGIS
Tell your doctor or pharmacist if you are taking/using, have recently taken/used or might take/use any other medicines.
IMVAGGIS is used for a local treatment in the vagina and is not likely to affect other medicines.
IMVAGGIS may affect other vaginally applied treatments but is not likely to affect other medicines.

If IMVAGGIS is used simultaneously with condoms made of latex it can decrease the tensile strength and thus impair the safety of condoms.

Pregnancy and breast-feeding

IMVAGGIS is for use in postmenopausal women only. If you become pregnant, stop taking IMVAGGIS and contact your doctor.
Driving and using machines
IMVAGGIS has no influence on the ability to drive and use machines.

IMVAGGIS contains butylhydroxytoluene
Butylhydroxytoluene may cause local skin reactions (e. g. contact dermatitis), or irritation to the eyes and mucous membranes.

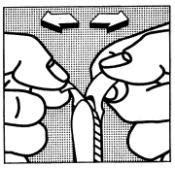
3. How to use IMVAGGIS

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

The recommended dose is:
During the first 3 weeks of treatment one pessary (corresponding to 0.03 mg estriol) is administered daily. Thereafter a maintenance dose of 1 pessary twice a week is recommended.

Your doctor will aim to prescribe the lowest dose to treat your symptom for as short as necessary. Speak to your doctor if you think this dose is too strong or not strong enough.

Method of administration
The pessary should be introduced deeply into the vagina, preferably in the evening before going to bed.



In order to administer a pessary, please tear the foil on top apart until it will be possible to remove the pessary easily.

If you use more IMVAGGIS than you should
If too many pessaries are applied to at any time, there is no need to worry. However, you should consult a doctor for advice. You might feel sick or be sick and some women may have some vaginal bleeding after a few days.

If you forget to use IMVAGGIS
- During daily use within the first 3 weeks of treatment:

If you do not realize the missed administration before the next day, you should skip the missed dose. In that case you should continue with the usual dosing schedule.

- During twice-weekly use:

If you have forgotten to administer IMVAGGIS at a scheduled date, please make up for the missed dose as soon as possible.

If you stop using IMVAGGIS
Even if your symptoms improve considerably, you should continue treatment to the end. However, if you want to interrupt or terminate treatment prematurely, please consult your doctor.

If you need to have surgery
If you are going to have surgery, tell the surgeon that you are using IMVAGGIS. You may need to stop using IMVAGGIS 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 using IMVAGGIS 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 are reported more often in women using HRT medicines which circulate in the blood compared to women not using HRT. These risks apply less to vaginally administered treatments such as IMVAGGIS:
- ovarian cancer;
- blood clots in the veins of the legs or lungs (venous thromboembolism);
- stroke;

– probable memory loss if HRT is started over the age of 65.

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

Local irritation may occur particularly at the beginning of treatment.

Common (may affect up to 1 of 10 users)
– vulvovaginal burning, itching and pain,
– discomfort when urinating (dysuria).

Uncommon (may affect up to 1 of 100 users)
– vaginal discharge,
– anorectal discomfort.

The following side effects have been reported with other HRTs:
– gall bladder disease;
– various skin disorders:
  - discolouration 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).

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

5. How to store IMVAGGIS

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 carton and the foil after “EXP” The expiry date refers to the last day of that month.

Do not store above 25 °C.

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 IMVAGGIS contains

The active substance is estriol.
1 pessary contains 0.03 mg estriol.

The other ingredients are: butylhydroxytoluene, glycerolmono/bis [(Z-R)-12-hydroxyoctadec-9-enoate], hard fat, macrogol cetostearyl ether.

What IMVAGGIS looks like and contents of the pack

IMVAGGIS are white pessaries.
IMVAGGIS is available in packages containing 10, 15, 20, 24 and 30 pessaries.

Not all packs sizes may be marketed.

Marketing Authorisation Holder
Laboratoires Besins International, 3, rue du Bourg L'Abbé, 75003 Paris, France.

Manufacturer
DR. KADE Pharmazeutische Fabrik GmbH, Rigistraße 2, Berlin, 12277, Germany

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Germany:	OeKolp Ovula 0,03 mg
Denmark, Finland, Norway, Sweden:	Estrokad
Hungary:	Estrokad hüvelykúp
Belgium, Luxembourg:	Oekolp 0,03 mg ovule/ovules/Vaginalzäpfchen
Italy:	Atrocom 0,03 mg ovuli
UK (Northern Ireland), Ireland:	IMVAGGIS 0.03 mg pessary
Netherlands:	Estriol DR. KADE 0,03 mg ovules
Austria:	Estrokad 0,03 mg Vaginalzäpfchen

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