Package leaflet: Information for the user

Angeliq 1 mg / 2 mg film-coated tablets

Oestradiol / Drospirenone

Read all of this leaflet carefully before you start taking 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, 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:
For the **leaflet** version of the Angeliq package insert the table of content contains only the major headings 1 to 6:

1. What Angeliq is and what it is used for

Angeliq is a Hormone Replacement Therapy (HRT). It contains two types of female hormone, an oestrogen and a progestogen. Angeliq is used in postmenopausal women with at least 1 year since their last natural period.

Angeliq 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"). Angeliq alleviates these symptoms after menopause. You will be prescribed Angeliq 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 Angeliq to prevent osteoporosis after menopause.

2. What you need to know before you take Angeliq

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 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 Angeliq 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 Angeliq.

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

Do not take Angeliq
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 Angeliq.
Do not take Angeliq

- 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 lining of the womb (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)
- If you have or have ever had **a blood clot in a vein** (deep venous 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 anti-thrombin deficiency)
- If you have or recently have had a disease caused by blood clots of 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 have **severe kidney disease or acute kidney failure**
- If you are **allergic (**hypersensitive) to oestrogens, progestogens or to any other ingredient in Angeliq (listed in section 6).

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

Warnings and precautions

Talk to your doctor or pharmacist before taking Angeliq. Tell your doctor if you have ever had any of the following problems, before you start treatment, as these may return or become worse during treatment with Angeliq. 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 taking Angeliq and see a doctor immediately

If you notice any of the following when taking HRT:
- any of the conditions mentioned in the 'DO NOT take Angeliq' 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 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 breathing

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

Note: Angeliq 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 lining of the womb (endometrial cancer). The progestogen in Angeliq 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 Angeliq. However, if the irregular bleeding:
- carries on for more than the first 6 months

- starts after you have been taking Angeliq for more than 6 months
- carries on after you have stopped taking Angeliq

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. This 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
In 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-progestagen 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 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**:**

- 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 another organ
- you have systemic lupus erythematosus (SLE)
- you have cancer

For signs of a blood clot, see "Stop taking Angeliq 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-progestogen HRT for over 5 years, there will be 9 to 12 cases in 1000 users (i.e. an extra 5 cases).

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 getting 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 memory loss in women who start using HRT after the age of 65. Speak to your doctor for advice.

- If you have a **kidney disorder** and have high **serum potassium** levels, particularly if you are taking other medications that increase serum potassium, your doctor may check the potassium levels in your blood during the first month of treatment.
- If you have **high blood pressure,** treatment with Angeliq may decrease it. Angeliq should not be used to treat high blood pressure.
- If you have a tendency to develop **patches of discolouration** (chloasma) on the face you should avoid exposure to the sun or ultraviolet light whilst using Angeliq.

Other medicines and Angeliq

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines may interfere with the effect of Angeliq. This might lead to irregular bleeding.
This applies to the following medicines:

- medicines for **epilepsy** (such as barbiturates, phenytoin, primidone, carbamazepine, oxcarbazepine, topiramate and felbamate)
- medicines for **tuberculosis** (such as rifamipicin and rifabutin)
- medicin**es for HIV and Hepatitis C virus infections** (so-called protease inhibitors and non-nucleoside reverse transcriptase inhibitors such as nevirapine, efavirenz, nelfinavir and ritonavir)
- the herbal remedy **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 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. Angeliq contains estradiol instead of ethinylestradiol. It is not known whether an increase in ALT liver enzyme can occur when using Angeliq with this HCV combination regimen. Your doctor will advise you.
- medicines for **treatment of fungal infections** (such as griseofulvin, itraconazole, ketoconazole, voriconazole, fluconazole)
- medicines for **treatment of bacterial infections** (such as clarithromycin, erythromycin)
- medicines for **treatment of certain heart diseases, high blood pressure** (such as verapamil, diltiazem)
- grapefruit juice

The following may cause small increases in serum potassium:

- medicines used for the treatment of:
  - **inflammation** or **pain** (e.g. aspirin, ibuprofen)
  - **certain types of heart disease** or **high blood pressure** (e.g. diuretics (water tablets), ACE inhibitors (e.g. enalapril), angiotensin II receptor antagonists (e.g. losartan). If you are having treatment for high blood pressure and take Angeliq there may be an additional decrease in blood pressure.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines including medicines obtained without a prescription, herbal medicines or other natural products**.**

Laboratory tests

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

Pregnancy and breast-feeding

Angeliq is for use in post-menopausal women.
If you become pregnant, stop taking Angeliq immediately and contact your doctor.

Driving and using machines

There is nothing to suggest that the use of Angeliq affects driving and use of machines.

Angeliq contains lactose
Angeliq contains lactose (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Angeliq

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. Your doctor will decide how long you should take Angeliq for.
Take one tablet a day, preferably at the same time. Swallow the tablet whole with a drink of water. You can take Angeliq with or without food. Start your next calendar pack of tablets the day after you finish your current pack.
Do not take a break between packs.

If you have been taking other HRT preparations: carry on until you have finished your current pack and have taken all the tablets for that month. Take your first Angeliq tablet the next day. Do not leave a break between your old tablets and the Angeliq tablets.

If this is your first HRT treatment: you can start your Angeliq tablets any day.

If you take more Angeliq than you should

Overdose may cause nausea and vomiting and irregular bleeding. No specific treatment is necessary but you should consult your doctor if you are concerned.

If you forget to take Angeliq

If you forget to take a tablet at your usual time and you are less than 24 hours late, take it as soon as possible. Take the next tablet at the usual time.
If you are more than 24 hours late, leave the forgotten tablet in the pack. Continue to take the rest of the tablets at the usual time every day. Do not take a double dose to make up for a forgotten tablet.
If you forget to take your tablet for several days you may experience irregular bleeding.

If you stop taking Angeliq

You may begin to feel the usual symptoms of menopause again, which may include hot flushes, trouble sleeping, nervousness, dizziness or vaginal dryness. You will also start to lose bone mass when you stop taking Angeliq. Consult your doctor or pharmacist if you want to stop taking Angeliq tablets. If you have any further questions on the use of this medicine, 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 Angeliq. You may need to stop taking Angeliq 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 taking Angeliq again.

4. Possible side effects

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

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 loss of memory if HRT is started over the age of 65

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

Like all medicines, Angeliq can cause side effects, although not everybody gets them
The following is a list of side effects that have been linked to the use of Angeliq.

Most frequent side effects (affecting more than 1 patient in every 10 patients):
- unexpected menstruation-like bleeding (see also section 2 "HRT and cancer")
- breast tenderness
- breast pains.

Unexpected menstruation-like bleeding occurs during the first few months of treatment with Angeliq. It is usually temporary and normally disappears with continued treatment. If it does not, contact your doctor.

Common side effects (affecting between 1 and 10 in every 100 patients):
- depression, mood changes, nervousness
- headache
- stomach ache, nausea, stomach enlargement
- lumpy breast (benign breast neoplasm), swollen breasts
- increase in size of uterine fibroids
- non-cancerous growth of cells at the neck of the womb (benign cervical growth)
- irregularities in your vaginal bleeding
- vaginal discharge
- loss of energy, localised fluid retention.

Uncommon side effects (affecting between 1 and 10 in every 1000 patients):
- weight increase or decrease, loss or increase of appetite for food, increase blood fats
- sleep problems, anxiety, decrease in sex drive
- burning or pricking sensation, decreased concentration, dizziness
- eye problems (e.g. red eyes), visual disturbance (e.g. blurred vision)
- palpitations
- blood clot, venous thrombosis (also see section 2 "Blood clots in a vein (thrombosis)"), high blood pressure, migraine, inflammation of the veins, varicose veins
- breathlessness
- stomach disorder, diarrhoea, constipation, vomiting, dry mouth, wind, altered sense of taste
- altered liver enzymes (will show up in blood tests)
- skin problems, acne, hair loss, itchy skin, excessive hair
- backache, joint pain, pain in limbs, muscle cramps
- urinary tract disorders and infections
- breast cancer, thickening of the lining of the womb, benign unusual growth in the uterus, thrush, vaginal dryness and itchiness of the vagina

- lumpy breast (fibrocystic breast), disorders of the ovaries, cervix and uterus, pelvic pain
- generalised fluid retention, chest pain, feeling generally unwell, increase in sweating.

Rare side effects (affecting between 1 and 10 in every 10,000 patients):
- anaemia
- giddiness
- ringing in the ears
- gall stones
- muscle pain
- inflammation of the fallopian tubes
- milky discharge from the nipples
- chills.

The following side effects have occurred in clinical trials of women with high blood pressure:
- high potassium levels (hyperkalaemia) sometimes causing muscle cramps, diarrhoea, nausea, dizziness or headache
- heart failure, enlargement of the heart, heart flutter, effects on heart rhythm
- increase in blood aldosterone.

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

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.

Ireland
HPRA Pharmacovigilance
Website: www.hpra.ie

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

5. How to store Angeliq

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

Do not use this medicine after the expiry date which is printed on the carton box and blister after "EXP". The expiry date refers to the last day of that month.

Angeliq does not require any special storage conditions.

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 to protect the environment.

6. Contents of the pack and other information

What Angeliq contains

The **active substances** are oestradiol (as oestradiol hemihydrate) and drospirenone; each tablet contains 1 mg oestradiol and 2 mg drospirenone.
The **other ingredients** are lactose monohydrate, maize starch, pregelatinized maize starch, povidone and magnesium stearate (E470b). The ingredients of the tablet coating are hypromellose (E464), macrogol 6000, talc (E553b), titanium dioxide (E171) and ferric oxide (E172).

What Angeliq looks like and contents of the pack

Angeliq tablets are red round convex coated tablets. One side is marked with the letters DL in a regular hexagon.

They are supplied in a blister pack containing 28 tablets with the days of the week printed on the blister. Boxes containing one or three blisters packs are available.

Marketing Authorisation Holder
Bayer Limited, 1st Floor, The Grange Offices, The Grange, Brewery Road, Stillorgan, Co. Dublin, A94 H2K7, Ireland

Manufacturer
Bayer AG
Müllerstrasse 170 – 178
D-13353 Berlin

This medicinal product is authorised in the Member States of the EEA under the following names:

Angeliq – Belgium, Croatia, Czech Republic, Estonia, Germany, Finland, France, Ireland, Italy, Lithuania, Latvia, Luxembourg, Malta, Netherlands, Poland, Portugal, Slovenia, Spain,

Angemin – Sweden

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