PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

ANGELIQ 1 mg/2 mg film-coated tablet

Estradiol (as estradiol hemihydrate)/Drospirenone

Contains sugar (lactose monohydrate)

Read all of this leaflet carefully before you start taking ANGELIQ
- 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.
- ANGELIQ 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 ANGELIQ is and what it is used for
2. What you need to know before you take ANGELIQ
3. How to take ANGELIQ
4. Possible side effects
5. How to store ANGELIQ
6. Contents of the pack and other information

1. What ANGELIQ is and what it is used for

ANGELIQ is for hormone replacement therapy.

ANGELIQ provides hormone replacement therapy for the treatment of climacteric complaints in postmenopausal women, such as hot flushes and sweating attacks, sleep disorders, depressed moods, nervousness and signs of involution of the bladder and genital organs. It is also used for treating complaints that are due to greatly decreased activity of the sexual organs (hypogonadism), following the removal of the ovaries or when the ovaries do not work (primary ovarian failure). ANGELIQ is suitable for women who still have a womb (intact uterus).

Some women are more likely than others to develop osteoporosis in later life depending on their medical history and lifestyle. If it is appropriate you may be prescribed ANGELIQ to prevent osteoporosis. Your doctor will be able to advise you further.

2. What you need to know before you take ANGELIQ

Your doctor will carry out gynaecological, breast, blood pressure and other examinations as appropriate. If you are known to have any liver disease, your doctor will arrange for your liver function to be checked periodically.

ANGELIQ is not an oral contraceptive. If you still have the ability to become pregnant, ANGELIQ is unlikely to alter it. On the other hand, if your doctor has already advised you that you need no longer use any contraceptive, you need not do so while taking ANGELIQ.

Do not take ANGELIQ

Do not take ANGELIQ if you have, or have ever had any of the conditions listed below. If any of these apply to you, tell your doctor who will be able to advise you further.

- if you are hypersensitive (allergic) to estradiol or drospirenone or any of the other ingredients of ANGELIQ (listed in section 6).
- if you have unspecified vaginal bleeding.
- if you have or if there is a suspicion of cancer of the breast.
- if you have a family history of breast cancer.
- if you have or if there is a suspicion of other malignancies influenced by sex hormones.
- if you have or have had liver tumours (benign or malignant).
- if you have or have had severe liver disease and your laboratory values for liver function have not returned to normal.
- if you have or have had severe kidney (renal) disease and your laboratory values for kidney function have not returned to normal.
- if you recently had a heart attack and/or stroke.
- if you have or have had a thrombosis (the formation of a blood clot) in the blood vessels of the legs (deep venous thrombosis) or the lungs (pulmonary embolism).
- if you have a high risk of venous or arterial thrombosis.
- if you have severely elevated blood levels of triglycerides (special type of blood lipids).
- if you are pregnant or breastfeeding.

If any of these conditions appear for the first time while using ANGELIQ, stop taking it at once and consult your doctor.

Warnings and precautions

Before you start to take ANGELIQ

Your doctor will discuss with you the benefits and risks of ANGELIQ. Your doctor will check, e.g. whether you have a higher risk of getting a thrombosis due to a combination of risk factors or perhaps one very strong risk factor. In the case of a combination of factors the risk may be higher than simply adding two individual risks. If the risk is too high, your doctor will not prescribe hormone replacement therapy for you.

Close medical supervision (including periodic blood tests to measure your hormone (prolactin) levels) is necessary if you suffer from a benign tumour (adenoma) of the anterior lobe of the pituitary gland (a small gland at the base of the brain).

If ANGELIQ is used in the presence of any of the conditions listed below you will need to be kept under close observation. Your doctor can explain this to you.

Therefore, tell your doctor before starting to use ANGELIQ if:

- You are known to have inherited genetic changes called "BRCAl and/or BRCA2 genes".
- You started your menstrual periods before the age of 12 years.
- You have a history of non-cancerous breast diseases such as atypical hyperplasia or lobular carcinoma in situ.
- You had any previous treatment using radiation therapy to the chest or breast.
- You have been treated or exposed while in your mother's womb to a medicine called diethylstilbestrol (DES).
- You have an increased risk of thrombosis (the formation of a blood clot) in your veins.

This risk increases with increasing age and may also be higher if:
- you or anyone in your immediate family has ever had a thrombosis in the blood vessels of the legs or lungs;
- you are overweight;
- you have varicose veins;
- you are already using ANGELIQ, tell your doctor well in advance of any expected hospitalisation or surgery. This is because the risk of having deep venous thrombosis may be temporarily increased as a result of an operation, serious injuries or immobilisation;
- you suffer from a mild to moderate kidney disease and are taking medicine for this (potassium sparing medicines). In this case tell your doctor what kind of medicine you are taking and they will be able to advice you further;
- you have fibroids of the womb;
- you have, or have ever had, endometriosis (the presence of tissue of the lining of the womb in places in the body where it is not normally found);
- you have liver or gall-bladder disease;
- you have had jaundice during pregnancy or previous use of sex hormones;
- you suffer from diabetes;
- you have elevated levels of triglycerides (a special type of blood lipids);
- you have high blood pressure;
- you have or have had chloasma (yellow brown patches on the skin); if so, avoid too much exposure to the sun or ultraviolet radiation;
- you suffer from epilepsy;
- you have lumpy or painful breasts (benign breast disease);
- you suffer from asthma;
- you suffer from migraine;
- you have the inherited disease called porphyria;
- you suffer from inherited deafness (otosclerosis);
- you have systemic lupus erythematosus (SLE; a chronic inflammatory disease);
- you have or have had chorea minor (illness with unusual movements);
- you suffer from hereditary angioedema (episodes of swelling in body parts such as hands, feet, face, airway passages that are caused by a defect in the gene that controls a blood protein called C1-inhibitor). The hormone estradiol in ANGELIQ may induce or exacerbate symptoms of hereditary angioedema;
- you are 65 years or older when hormone replacement therapy is initiated. The reason is that there is limited evidence from clinical studies that hormonal treatment may increase the risk of significant loss of intellectual abilities such as memory capacity (dementia).

Hormone replacement therapy and cancer

Endometrial cancer
The risk of cancer of the lining of the womb (endometrial cancer) increases when estrogens are used alone for prolonged periods.

Breast cancer
Breast cancer has been diagnosed slightly more often in women who use menopausal hormone therapy (MHT) than in women of the same age who do not use MHT. This slight increase in the numbers of breast cancer diagnoses gradually disappears during the course of the 10 years after stopping use MHT. When you are using ANGELIQ, you must perform monthly breast self-examinations. Your doctor will advise you on when to report for breast examinations and any appropriate investigations.

ANGELIQ may change how the image taken in mammography looks (increases the density of mammographic images). This may complicate the mammographic detection of breast cancer in some cases. Therefore, your doctor may choose to use other breast cancer screening techniques as well.

Ovarian cancer
Ovarian cancer is rare - much rarer than breast cancer. The use of estrogen-only or combined estrogen 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 2 000 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 2 000 users (i.e. about 1 extra case).

Liver tumour
During or after the use of hormones such as those that are contained in ANGELIQ, benign liver tumours have rarely occurred, and malignant liver tumours even more rarely. In isolated cases, bleeding from such tumours into the abdominal cavity has endangered life. Although such events are extremely improbable, you should inform your doctor about any unusual feelings in your upper abdomen that do not disappear within a short time.

ANGELIQ and depression

Some women using hormone-containing medicines including ANGELIQ have reported depression or depressed mood. Depression can be serious and may sometimes lead to suicidal thoughts. If you experience mood changes and depressive symptoms contact your doctor for further medical advice as soon as possible.

Reasons for stopping ANGELIQ immediately

You should stop treatment at once and consult your doctor if you have any of the following conditions:
- your very first attack of migraine (typically a throbbing headache and nausea preceded by visual disturbances);
- worsening of pre-existing migraine, any unusually frequent or unusually severe headaches;
- sudden disturbances of vision or hearing;
- inflamed veins (phlebitis).

If you get a blood clot while you are taking ANGELIQ or if you suspect this has happened, you should stop taking it immediately and contact your doctor. Warning signs to look out for are:
- coughing blood;
- unusual pains or swelling of your arms or legs;
- sudden shortness of breath;
- fainting.

ANGELIQ must also be stopped at once if you become pregnant or if you develop jaundice.

If bleeding occurs after a prolonged interval of amenorrhoea, talk to your doctor, as this may need to be investigated.

Additional information on special populations

Children and adolescents
ANGELIQ is not indicated for use in children and adolescents.

Elderly patients
There are no data suggesting a need for dosage adjustment in elderly patients. Tell your doctor if you are 65 years or older (see section 'Warnings and precautions').

Patients with liver impairment
In women with mild or moderate liver impairment, ANGELIQ is well tolerated. Do not take ANGELIQ if you have had liver tumours. Do not take ANGELIQ if you have severe liver disease (see section 'Do not take ANGELIQ').

Patients with kidney impairment
ANGELIQ is contraindicated in women with severe kidney disease (see section 'Do not take ANGELIQ').

Other medicines and ANGELIQ

Always tell your health care provider if you are taking any other medicines. This includes complementary or traditional medicines. Also tell any other doctor or dentist who prescribes another medicine (or the dispensing pharmacist) that you use ANGELIQ.

Some medicines
- can have an influence on the blood levels of ANGELIQ,
- can stop ANGELIQ from working properly,
- can cause unexpected bleeding.

These include:
- medicines used for the treatment of:
  - epilepsy (e.g. phenytoin, barbiturates, primidone, carbamazepine, oxcarbazepine, topiramate, felbamate)
  - tuberculosis (e.g. rifampicin)
  - HIV and Hepatitis C Virus infections (so-called protease inhibitors and non-nucleoside reverse transcriptase inhibitors)

  - fungal infections (griseofulvin, itraconazole, ketoconazole, voriconazole, fluconazole)
  - bacterial infections (macrolides, e.g. clarithromycin, erythromycin)
  - certain heart diseases, high blood pressure (calcium channel blockers, e.g. verapamil, diltiazem)
- the herbal remedy St. John's wort
- grapefruit juice

If you have elevated blood pressure ANGELIQ has the potential to lower your blood pressure. In case you use any antihypertensive medicine, please inform your doctor, who will advise you.

ANGELIQ with alcohol

Excess intake of alcohol during use of ANGELIQ has an influence on the treatment. Your doctor will advise you.

Laboratory tests

The use of ANGELIQ may affect the results of certain laboratory tests. Always tell your doctor or the laboratory staff that you are using ANGELIQ.

Pregnancy and breastfeeding

ANGELIQ must not be taken by pregnant women or women who are breastfeeding.
However, observations have shown that sex hormones (such as the active substances in ANGELIQ) do not appear to increase the risk of birth defects in children born to women who had used such hormones prior to pregnancy or inadvertently during early pregnancy.
Small amounts of sex hormones may be excreted in human milk.

Driving and using machines

No effects on the ability to drive or use machines have been observed is users of ANGELIQ.

ANGELIQ contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take ANGELIQ

Do not share medicines prescribed for you with any other person.

Always take ANGELIQ exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

How and when should ANGELIQ be taken?

Each blister pack is for 28 days of treatment. You have to take one tablet daily.

If you are using hormone replacement therapy for the first time or if you change from a continuous combination hormone replacement therapy (each of the tablets contains the same ingredients), you may begin ANGELIQ tablet taking at any time.

If you are changing from a sequential combined hormone replacement therapy (tablets differ in their ingredients which is made visible with different colours), you should complete the current cycle of therapy before starting to take ANGELIQ.

It does not matter at what time of the day you take your tablet, but once you have selected a particular time, you should keep to it every day. The tablet should be swallowed whole with some liquid irrespective of food intake.

How long should ANGELIQ be taken or used?

When you have finished one pack, start the next pack on the following day. Never leave a break between packs. Tablet taking should be continuous. Your doctor will advise you with respect to the duration of treatment.

If you take more ANGELIQ than you should

There have been no reports of ill effects from overdose. Overdosage may cause nausea and vomiting and irregular bleeding. No specific treatment is necessary, but you should consult your doctor if you are concerned.
In the event of overdose, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take ANGELIQ

If you are less than 24 hours late, take your tablet as soon as possible. Take the next one at your normal time.

But if you are more than 24 hours late, leave the forgotten tablet in the blister pack. Continue to take the remaining tablets at the usual time every day.

If you stop taking ANGELIQ

If you do not take ANGELIQ for several days, irregular bleeding may occur.

If your bleeding pattern seems different

ANGELIQ has been made to provide you with hormone replacement therapy without cyclical bleeding. You may, however, get some bleeding during the first few months of treatment. It could occur at any time but it is unlikely to be heavy. Bleeding episodes should eventually get less and finally stop.

If significant bleeding continues or if at any time bleeding or spotting becomes unacceptable for you, ask your doctor whether you should discontinue treatment or change to a sequential therapy.

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

4. Possible side effects

ANGELIQ can have side effects.

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

The most commonly reported side effects with ANGELIQ are breast pain, vaginal bleeding (female genital tract bleeding) and abdominal pains.

During the first few months of treatment you may experience some vaginal bleeding at unexpected times (breakthrough bleeding and spotting). These are usually temporary and normally disappear with continued treatment. If they do not, contact your doctor.

Serious side effects are blood clots as well as breast cancer.

The following side effects of ANGELIQ are based on reports from clinical trials.

Frequent side effects
- breast pain, including breast discomfort
- vaginal bleeding (female genital tract bleeding)
- emotional lability
- headache
- abdominal pain
- cervical polyp

Less frequent side effects
- venous and arterial thromboembolic events (includes peripheral deep venous occlusion, thrombosis and embolism/pulmonary vascular occlusion, thrombosis, embolism and infarction/myocardial infarction/cerebral infarction and stroke not specified as haemorrhagic)
- breast cancer

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 "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of ANGELIQ.

5. How to store ANGELIQ

Store all medicines out of sight and reach of children.
Store at or below 30 °C.
Store in the original package.

Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What ANGELIQ contains

The active substances are estradiol 1 mg (as estradiol hemihydrate) and drospirenone 2 mg.

The other ingredients are hypromellose, lactose monohydrate, macrogol 6000, magnesium stearate, maize starch, maize starch pregelatinised, polyvidone, talc, titanium dioxide, ferric oxide red.

What ANGELIQ looks like and contents of the pack

ANGELIQ is a medium red, round tablet with convex faces, one side marked with letters “DL” in a regular hexagon.
ANGELIQ is presented as a calendar pack (blister strip) containing 28 or 84 tablets.

Holder of Certificate of Registration

Bayer (Pty) Ltd
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