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EPAR summary for the public

Duavive

conjugated oestrogens / bazedoxifene

This is a summary of the European public assessment report (EPAR) for Duavive. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Duavive.

For practical information about using Duavive, patients should read the package leaflet or contact their doctor or pharmacist.

What is Duavive and what is it used for?

Duavive is a medicine used for the treatment of symptoms (such as hot flushes) caused by low blood levels of the female hormone oestrogen in women who have been through the menopause. It is used in women who still have their uterus (womb) and who cannot be treated with progestogen-containing medicines (medicines derived from the hormone called progesterone).

Duavive contains two active substances: conjugated oestrogens and bazedoxifene.

How is Duavive used?

Duavive can only be obtained with a prescription. It is available as modified release tablets (containing 0.45 mg conjugated oestrogens and 20 mg bazedoxifene) which release bazedoxifene immediately and conjugated oestrogens over a longer period of time.

The recommended dose of Duavive is one tablet once a day. Treatment should be for the shortest duration possible as long as benefits outweigh risks.

How does Duavive work?

One of the active substances in Duavive, conjugated oestrogens, works as hormone replacement therapy. It replaces the oestrogen hormones that are no longer produced naturally in women who have been through the menopause, thereby alleviating symptoms such as hot flushes.

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However, oestrogens used alone can cause hyperplasia (growth) of the endometrium (lining of the womb) which could lead to endometrial cancer. Duavive therefore also contains the active substance bazedoxifene, which blocks the effects of oestrogens on the womb and so reduces the risk of endometrial cancer.

Both active substances have been available in the European Union (EU) for a number of years. Conjugated oestrogens have been available for many years as hormone replacement therapy and bazedoxifene has been authorised in 2009 for the treatment of osteoporosis (a disease that makes bones fragile) in women who have been through the menopause.

What benefits of Duavive have been shown in studies?

Duavive was compared with placebo (a dummy treatment) in two main studies in 996 women who have been through the menopause, investigating the effects on either hot flushes or vulvovaginal atrophy (dryness, irritation and soreness around the genital area). An additional study also looked at the effects of Duavive on osteoporosis.

In the study investigating the effects on hot flushes, treatment with Duavive (conjugated oestrogen 0.45 mg and bazedoxifene 20 mg) over 12 weeks reduced the average daily number of moderate and severe hot flushes by 7.6 compared with 4.9 for placebo. Treatment with Duavive also led to a greater average fall in the daily severity score of hot flushes than placebo treatment: 0.9 versus 0.3. Similar results were seen with a higher strength of conjugated oestrogen (0.625 mg) plus bazedoxifene 20 mg when compared with placebo.

The study looking at the effects of Duavive on vulvovaginal atrophy found an improvement in some of the signs of vaginal atrophy but not in the most bothersome symptoms when compared with placebo.

Because studies with the higher strength combination did not sufficiently show that this strength was more effective than the approved strength of Duavive, the company withdrew its application for the former. One of the studies also looked at the effects of Duavive on osteoporosis; however, as there was no benefit of Duavive over the individual components the company withdrew its application for Duavive in the treatment of osteoporosis.

What are the risks associated with Duavive?

The most common side effect with Duavive (which may affect more than 1 in 10 people) is abdominal pain (stomach ache).

Some women must not use Duavive including those who have had problems with venous thromboembolism (blood clots in the veins) such as deep-vein thrombosis (DVT), pulmonary embolism (a blood clot in the lungs) and retinal-vein thrombosis (a blood clot at the back of the eye), or are at an increased risk of such problems. It must not be used in women who have had a stroke or heart attack. It must also not be used in women who have, are likely to have or have had breast cancer or other cancers that are known to be oestrogen-dependent. Duavive is only for use in women who have been through the menopause, so it must not be used in women who could become pregnant.

For the full list of all side effects and restrictions with Duavive, see the package leaflet.

Why is Duavive approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Duavive's benefits are greater than its risks and recommended that it be approved for use in the EU. Duavive was shown to improve the symptoms caused by lack of oestrogen in postmenopausal women when compared with

placebo. Because the observed treatment effects were smaller than what is seen with alternative treatments (progestogen-containing treatments) the CHMP therefore concluded that Duavive should be reserved for women who cannot take these alternative medicines.

Regarding safety, the long-term risk of endometrial hyperplasia has not been fully investigated and the CHMP recommended further studies to be carried out. The CHMP also noted that long-term use of Duavive is associated with a risk of stroke and venous thromboembolism which is similar to the risk with conjugated oestrogens and bazedoxifene when used alone.

What measures are being taken to ensure the safe and effective use of Duavive?

A risk management plan has been developed to ensure that Duavive is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Duavive, including the appropriate precautions to be followed by healthcare professionals and patients.

Further information can be found in the summary of the risk management plan.

Other information about Duavive

The European Commission granted a marketing authorisation valid throughout the European Union for Duavive on 16 December 2014.

The full EPAR and risk management plan summary for Duavive can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Duavive, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 12-2014.