Evamax™ 2

Estradiol Valerate BP Film Coated Tablet

DESCRIPTION

Evamax™ contains estradiol valerate a prodrug of the natural human 17ß-estradiol which is an ester of the endogenous female estrogen. Ovulation is not inhibited during the use of **Evamax™** and the endogenous production of hormones is hardly affected. During the climacteric, the reduction and finally loss of ovarian estradiol secretion can result in instability of thermoregulation, causing hot flushes associated with sleep disturbance and excessive sweating, and urogenital atrophy with symptoms of vaginal dryness, dyspareunia and urinary incontinence. **Evamax™** replaces the hormone estradiol that the body no longer makes and prevents or relieves symptoms such as hot flushes, sweats, sleep disturbances, depressive moods, irritability, dizziness, headaches as well as vaginal dryness and burning. Hormone replacement therapy (HRT) with an adequate estrogen dosage as in **Evamax™** reduces bone resorption and retards or halts postmenopausal bone loss. The addition of a progestogen to an estrogen replacement regimen like **Evamax™** for at least 10 days per cycle is recommended in women with an intact uterus. It reduces the risk of endometrial hyperplasia and the attendant risk of adenocarcinoma in these women. The addition of a progestogen to an estrogen replacement regimen has not been shown to interfere with the efficacy of estrogen for its approved indications.

MECHANISM OF ACTION

Estradiol enters target cells freely (e.g., female organs, breasts, hypothalamus, pituitary) and interacts with a target cell receptor. When the estrogen receptor has bound its ligand, it can enter the nucleus of the target cell, and regulate gene transcription which leads to formation of messenger RNA. The mRNA interacts with ribosomes to produce specific proteins that express the effect of estradiol upon the target cell. Estrogens increase the hepatic synthesis of sex hormone binding globulin (SHBG), thyroid-binding globulin (TBG), and other serum proteins and suppress follicle-stimulating hormone (FSH) from the anterior pituitary. Increases in the down-stream effects of ER binding reverses some of the symptoms of menopause, which are primarily caused by a loss of estrogenic activity.

INDICATIONS

- Hormone replacement therapy (HRT) for the treatment of signs and symptoms of estrogen deficiency due to the menopause (whether natural or surgically induced).
- Prevention of postmenopausal osteoporosis.

DOSAGE AND ADMINISTRATION

Continuous Regimen: One tablet at the same time each day.
Combination Regimen: In women with an intact uterus, the concomitant use of an appropriate progestogen is advised for 10 - 14 days every 4 weeks (sequentially combined HRT) or with each tablet of estrogen (continuous combined HRT). At the same time each day.

- If forgets to take at the usual time, may take it within the following 12 to 24 hours.
- If the treatment is discontinued for longer, irregular bleeding may occur.
- Hormonal contraception should be stopped when HRT is started and the patient should be advised to take non-hormonal contraceptive precautions, if required.
- Hysterectomized patients may start at any time.
- If the patient is still menstruating and has an intact uterus, a combination regimen of **Evamax™** and a progestogen should begin within the first 5 days of menstruation. Patients whose periods are very infrequent or with amenorrhea or who are postmenopausal may start at any time, provided pregnancy has been excluded.
- Women changing from other HRT should complete the current cycle of therapy before initiating **Evamax™** therapy.

CONTRAINDICATIONS

Hormone replacement therapy (HRT) should not be started in the presence of any of the conditions listed below. If any of these conditions appear during use of estradiol valerate, treatment should be stopped immediately.

- Pregnancy or lactation
- Undiagnosed vaginal bleeding
- Known or suspected cancer of the breast
- Known or suspected premalignant conditions or malignancies, if sex steroid-influenced
- Presence or history of liver tumours (benign or malignant)
- Severe hepatic disease
- Acute arterial thromboembolism (myocardial infarction, stroke) or a recent history of these conditions
- Active deep venous thrombosis, thromboembolic disorders, thrombophlebitis, or a documented history of these conditions
- A high risk of venous or arterial thrombosis
- Hereditary or acquired predisposition to venous thrombosis (e.g. antithrombin III deficiency)
- Severe hypertriglyceridamia
- Hypersensitivity to estradiol valerate

SIDE EFFECTS

Weight increase or decrease, headache, abdominal pain, nausea, rash, pruritus, uterine/ vaginal bleeding including spotting are the common side effects. Uncommon adverse events include hypersensitivity reaction, dizziness, palpitations, visual disturbances, edema, breast pain and tenderness etc.

PRECAUTIONS AND WARNINGS

Estradiol valerate cannot be used as a contraceptive. Therapy should be discontinued immediately in case a contraindication is discovered, as well as in the following situations:

- Migrainous or frequent and unusually severe headaches that occur for the first time or other symptoms that are possible prodroma of cerebrovascular occlusion.
- Recurrence of cholestatic jaundice or cholestatic pruritus which occurred first during pregnancy or previous use of sex steroids.
- Symptoms of a thrombotic event or suspicion thereof.

USE IN PREGNANCY AND LACTATION

The use of estradiol valerate is contraindicated during pregnancy. If pregnancy occurs during treatment with estradiol valerate, treatment must be discontinued immediately. The use of estradiol valerate is contraindicated during lactation.

DRUG INTERACTION

- Interactions can occur with drugs that induce microsomal enzymes which can result in increased clearance of sex hormones and which may lead to changes in the uterine bleeding profile and/or reduction of the therapeutic effect.
- Substances increasing the clearance of sex hormones (diminished efficacy by enzyme-induction), e.g.: Phenytoin, barbiturates, primidone, carbamazepine, rifampicin and possibly also oxcarbazepine, topiramate, felbamate, griseofulvin.
- Strong and moderate CYP3A4 inhibitors such as azole antifungals (e.g. fluconazole, itraconazole, ketoconazole, voriconazole), verapamil, macrolides (e.g. clarithromycin, erythromycin), diltiazem and grapefruit juice can increase plasma concentrations of the estrogen.
- Substances that undergo substantial conjugation (e.g. paracetamol) may increase the bioavailability of estradiol by competitive inhibition of the conjugation system during absorption.

OVERDOSE

Acute toxicity studies did not indicate a risk of acute adverse effects in case of inadvertent intake of a multiple of the daily therapeutic dose. Nausea, vomiting, withdrawal bleeding may occur in some women. Treatment should be symptomatic.

PHARMACEUTICAL PRECAUTION

Do not store above 30 °C temperature. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Evamax™ 2 Tablet: Box containing 2 blisters of 10 tablets each. Each film coated tablet contains estradiol valerate BP 2 mg.

SK+F
Manufactured by
ESKAYEF PHARMACEUTICALS LTD.
RUPGANJ, NARAYANGANJ, BANGLADESH
TM TRADEMARK
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