

New Zealand Datasheet

Name of Medicine

Ethinylloestradiol

Presentation

Tablet: 10mcg.

Uses

Indications

Postmenopausal symptoms due to oestrogen deficiency including prevention of postmenopausal osteoporosis. In women with an intact uterus the addition of a progestogen is essential.

Treatment of metastatic breast cancer in postmenopausal women.

Treatment of prostatic cancer.

Dosage and Administration

This will depend on the particular indication used, but treatment should be undertaken with as low a dose as possible and for as short a period as is necessary.

Menopausal symptoms: 0.01-0.05mg daily.

Osteoporosis: 0.02-0.05mg daily.

Prostatic and mammary carcinoma: 1-2mg daily.

Contraindications

Pregnancy.

Active or recent (e.g. within the last year) arterial thromboembolic disease (e.g. angina, myocardial infarction, stroke)

Known or suspected oestrogen-dependent tumours.

Endometrial hyperplasia, uterine fibromyomata, undiagnosed vaginal bleeding.

Active deep venous thrombosis, thromboembolic disorders, or a documented history of these conditions

Severe liver disease.

Porphyria.

Warnings and Precautions

Warnings

Oestrogens with or without progestogens should not be used for the long-term maintenance of general health, including the primary prevention of cardiovascular disease as the risks of long-term treatment with HRT in most circumstances, outweigh the benefits. The Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli and deep

vein thrombosis in postmenopausal women during five years of treatment with conjugated equine oestrogens (0.625 mg) combined with medroxyprogesterone acetate (2.5 mg) relative to the placebo (See table below).

The WHI study was designed to investigate the efficacy and safety of long-term HRT in preventing coronary heart disease in healthy postmenopausal with an intact uterus. A total of 8506 women received HRT and 8102 women received placebo for an average of 5.2 years.

Summary of the incidence of adverse events described in the WHI study

Adverse Event	Relative Risk of HRT vs placebo at 5.2 years (95% CI)	Change in number of adverse events per 10,000 women in one year
Breast cancer	1.26 (1.00-1.59)	8 extra
Heart disease	1.29 (1.02-1.63)	7 extra
Stroke	1.41 (1.07-1.85)	8 extra
Pulmonary embolism	2.13 (1.39-3.25)	8 extra
Myocardial infarction	1.32 (1.02-1.72)	*
Deep vein thrombosis	2.07 (1.49-2.87)	*
Colorectal cancer	0.63 (0.43-0.92)	6 fewer
Hip fracture	0.66 (0.45-0.98)	5 fewer

* Information not available

Other doses of conjugated oestrogens and medroxyprogesterone acetate and other combinations of oestrogens and progestogens were not studied in the Women's Health Initiative (WHI) and, in the absence of comparable data, these risks should be assumed to be similar. Because of these risks, oestrogens and progestogens should be prescribed at the lowest effective doses and for the shortest duration (generally not longer than 3-4 years), consistent with the treatment goals and risks for the individual woman.

All prospective and current users of HRT should be advised of the risks and benefits of oestrogens and progestogens and the need for treatment with HRT should be reviewed on a yearly basis.

Prolonged monotherapy with estrogens increases the risk of endometrial hyperplasia and carcinoma in postmenopausal women. Oestrogen or oestrogenic compounds must not be used alone as hormone replacement therapy in women who have not had a hysterectomy. Close clinical surveillance of all women taking oestrogens is important. Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. Studies have found that protection from this effect is achieved with 10 or more days of progestogen therapy per month.

An increased risk of ovarian cancer in menopausal women taking oestrogen only replacement therapy was observed in a large US study enrolling over 40,000 women on HRT. These women were followed up for a mean duration of 13.4 years (range 1 month to 19.8 years). The increased risk of ovarian cancer in those taking oestrogen replacement therapy was 80%, RR 1.8 (95% CI, 1.1-3.0) at 10 to 19 years. This risk increased with duration of use; RR for 20 or more years of use was 3.2 (95% CI, 1.7-5.7). This equates to approximately 3 and 8 additional cases per 10,000 women-years at these time points; (the incidence of ovarian cancer in non-users was 4.4 per 10,000 women years). This observation was most obvious in those women on long-term oestrogen replacement therapy who had a prior history of hysterectomy (defined as simple hysterectomy or hysterectomy with unilateral oophorectomy). In this subpopulation, the RR was 2.0 (95% CI, 0.96-4.3) for between 10 and 19 years of use and 3.4 (95% CI, 1.6-7.5) for 20 years or more.

Severe varicose veins - the benefits of oestrogen-containing preparations must be weighed against the possible risks.

Cardiac failure, latent or overt.

Epilepsy or migraine, or a history of these conditions.

Sickle cell haemoglobinopathy, since under certain circumstances e.g. infections or anoxia, oestrogen-containing preparations may induce thromboembolic processes in patients with this condition.

Untreated polycythaemia or pulmonary hypertension.

Precautions

Mild hypertension or a history of it, blood pressure should be monitored at regular intervals. If hypertension develops in patients receiving oestrogens, treatment should be stopped.

Risk of deep vein thrombosis is temporarily increased when undergoing major surgery or prolonged immobilisation, therefore treatment should be stopped before surgery.

If any signs of thrombosis develop in patients receiving oestrogen, discontinue treatment.

Glucose tolerance may be lowered and may, therefore, increase the need for insulin or other anti-diabetic drugs in diabetics.

Thyroid hormone binding globulin may be increased leading to increased circulating total thyroid hormone, therefore care must be taken in interpreting thyroid function tests. History of gall stones, cholestatic jaundice in pregnancy or jaundice due to oral contraceptives.

If liver function tests become abnormal during oestrogen therapy, discontinue treatment.

Use with cautions in women with impaired renal function.

Adverse Effects

Genito-urinary tract: Endometrial neoplasia, intermenstrual bleeding, increase in the size of uterine fibromyomata, endometrial proliferation or aggravation of endometriosis, excessive production of cervical mucus.

Breast: Tenderness, pain, enlargement, secretion.

Gastrointestinal tract: Nausea, vomiting, cholelithiasis, cholestatic jaundice.

Cardiovascular system: Hypertension, thrombosis, thrombophlebitis, thromboembolism.

Skin: Erythema nodosum, rash, chloasma.

Eyes: Corneal discomfort if contact lenses are used.

CNS: Headache, migraines, mood changes (elation or depression).

Metabolic: Sodium and water retention, reduced glucose tolerance, and change in bodyweight.

In Men: Feminisation, gynaecomastia, testicular atrophy, and impotence.

Pharmaceutical Precautions

Store below 25°C.

Medicine Classification

Prescription Medicine.

Package Quantities

10mcg, 100's.

Name and Address

New Zealand Medical and Scientific Ltd
PO Box 24-138
Royal Oak
Auckland
Ph (9) 259 4062
Fax (9) 259 4067

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