



London, 4 September 2001  
CPMP/PhVWP/2758/01

**SPC Wording for  
medicinal products used in hormone replacement therapy  
with regard to increased risk of venous thromboembolism  
as agreed by the PhVWP in September 2001**

#### 4.3 Contraindications

- ...
- Current or previous idiopathic venous thromboembolism (deep venous thrombosis, pulmonary embolism)
- ...

#### 4.4 Special warnings and precautions for use

...

##### Conditions which need supervision:

- If any of the following conditions are present, have occurred previously, and/or have been aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised. It should be taken into account that these conditions may recur or be aggravated during treatment with <product name>, in particular:
  - ...
  - A history of, or risk factors for, thromboembolic disorders (see below)
  - ...

...

##### Reasons for immediate withdrawal of therapy:

- Venous or arterial thromboembolic disorders
- ...

...

##### Venous thromboembolism

- HRT is associated with a higher relative risk of developing venous thromboembolism (VTE), i.e. deep vein thrombosis or pulmonary embolism. There is a two- to three-fold higher risk for users compared with non-users, which for healthy women amounts to at least 1 to 2 additional cases of VTE in 10,000 patient-years of treatment with HRT. The occurrence of such an event is more likely in the first year of HRT than later.
- Generally recognised risk factors for VTE include a personal history or family history, severe obesity (BMI > 30 kg/m<sup>2</sup>) and systemic lupus erythematosus (SLE). There is no consensus about the possible role of varicose veins in VTE.
- Patients with a history of VTE or known thrombophilic states have an increased risk of VTE. HRT may add further to this risk. Personal or strong family history of thromboembolism, or personal recurrent spontaneous abortion, should be investigated in order to exclude a thrombophilic predisposition. Until a thorough evaluation of thrombophilic factors has been made or anticoagulant treatment initiated, use of HRT in such patients should be viewed as contraindicated. Those women already on anticoagulant treatment require careful consideration of the benefit-risk of use of HRT.

- The risk of VTE may be temporarily increased with prolonged immobilisation, major trauma or major surgery. As in all postoperative patients, scrupulous attention should be given to prophylactic measures to prevent VTE following surgery. Where prolonged immobilisation is liable to follow elective surgery, particularly abdominal or orthopaedic surgery to the lower limbs, consideration should be given to temporarily stopping HRT 4 to 6 weeks earlier, if possible. Treatment should not be restarted until the woman is completely mobilised.
- If VTE develops after initiating therapy, the drug should be discontinued. Patients should be told to contact their doctors immediately when they are aware of a potential thromboembolic symptom (e.g., painful swelling of a leg, sudden pain in the chest, dyspnea).

...

#### **4.8. Undesirable effects**

...

- Venous thromboembolism, i.e. deep leg or pelvic venous thrombosis and pulmonary embolism, is more frequent among hormone replacement therapy users than among non-users. For further information, see section 4.3 Contraindications and 4.4 Special warnings and precautions for use.

....