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**SPC Wording for
Medicinal Products used in Hormone Replacement Therapy
with regard to Increased Risk of Breast Cancer
as agreed by the PhVWP in July 2001**

SPC Wording for oestrogen-only, progestin-only and oestrogen-progestin combination products:

Section 4.3 on Contraindications

Known or suspected breast cancer or history of breast cancer.

Section 4.4 on Special warnings and precautions for use

Before initiating or re-instituting Hormone Replacement Therapy (HRT), a complete personal and family medical history should be taken. Physical (including pelvic and breast) examinations should be guided by this and by the contraindications and warnings for use. During treatment, periodic check-ups are recommended of a frequency and nature adapted to the individual woman. Women should be encouraged to report any changes in their breasts to their doctor or nurse. Investigations including mammography and cervical cytology should be carried out in accordance with currently accepted screening practices, modified according to the clinical needs of the individual. A careful appraisal of the risks and benefits should be undertaken over time in women treated with HRT.

Epidemiological studies have reported an increased risk of breast cancer in women taking oestrogens or oestrogen-progestin combinations for HRT (see Section 4.8). This excess risk increases with duration of intake of HRT and seems to return to baseline in the course of about five years after stopping treatment. Women using oestrogen-progestin combined HRT had a similar or possibly higher risk as compared with women who used oestrogens alone. Therefore, combinations of a progestin and oestrogen in HRT are not recommended for women who had their uterus removed unless endometriosis was previously diagnosed.

This increased risk was found mostly for women with a lean or normal body build, rather than for obese women. Breast cancers diagnosed in current or recent users of HRT were less likely to have spread outside the breast than those found in non-users. Women whose breast cancers developed after HRT tended to have less aggressive tumour characteristics and possibly better survival as compared with women with breast cancer who had not received HRT.

The reported associations between long-term HRT exposure and an increased risk of breast cancer may be due to an earlier diagnosis, an actual effect of HRT or a combination of both.

Section 4.8 on Undesirable effects

In table under “Uncommon side effects”:

Breast cancer * (See below)

As a separate bullet point after the table on side effects:

The risk of breast cancer increases with the number of years of HRT intake. According to data from epidemiological studies - 51 epidemiological studies performed during the 1970ies to the early 1990ies and reported in a re-analysis, and from more recent studies - the best estimate of the relative risk is in the range of 1.5 to 2.5 for women who had current or recent use of HRT that had lasted for 10-15 years or longer.

In women not using HRT, in total about 45 women in every 1000 women are expected to have a breast cancer diagnosed over the period from ages 50 to 70 years. It is estimated on the basis of the relative risk estimates that among those with current or recent use of HRT for 10-15 years, the total number of *additional* cases during the corresponding period will be in the range of 5 to 20 per 1000 treated women.

Additional SPC Wording for oestrogen-only products:

Section 4.2 on Posology and method of administration

In hysterectomized women who did not have endometriosis diagnosed, it is not recommended to add a progestin.