

Tibolone (Livial) and risk of VTE and other risks

Final SmPC and PL wording agreed by PhVWP in November 2011

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SUMMARY OF PRODUCT CHARACTERISTICS

The texts of the 3rd revision of the Core SPC for HRT products, as published on the CMDh website, should be included in the SmPC. Where a statement in the Core SPC for HRT products applies equally to HRT and tibolone this should be made clear by replacing 'HRT' with 'HRT or tibolone' in the tibolone SmPC.

In addition to the texts of the 3rd revision of the Core SPC for HRT products, the following wordings have to be added:

SmPC Section 4.4:

Under subheading 'Ovarian cancer'

In the Million Women Study it was shown that the relative risk for ovarian cancer with use of tibolone was similar to the risk associated with use of other types of HRT

Under subheading 'Venous thromboembolism'

In an epidemiological study using a UK database, the risk of VTE in association with tibolone was lower than the risk associated with conventional HRT, but only a small proportion of women were current users of tibolone and a small increase in risk compared with non-use cannot be excluded.

Under subheading 'Coronary artery disease (CAD)'

In an epidemiological study using the GPRD no evidence was found of protection against myocardial infarction in postmenopausal women who received tibolone.

SmPC section 4.8:

Under 'Breast cancer risk'

In Table 2: Million women study – estimated additional risk of breast cancer after 5 years' use

| Age range (years) | Additional cases per 1000 never-users of HRT over a 5 year period*2 | Risk ratio & 95%CI# | Additional cases per 1000 HRT users over 5 years (95%CI) |
|--------------------------------------|---|---------------------|--|
| Estrogen only HRT | | | |
| 50-65 | 9-12 | 1.2 | 1-2 (0-3) |
| Combined estrogen-progestagen | | | |
| 50-65 | 9-12 | 1.7 | 6 (5-7) |

| Tibolone | | | |
|--|------|-----|---------|
| 50-65 | 9-12 | 1.3 | 3 (0-6) |
| #Overall risk ratio. The risk ratio is not constant but will increase with increasing duration of use. | | | |

Under ‘Ovarian cancer’

Long term use of estrogen-only and combined estrogen-progestagen HRT has been associated with a slightly increased risk of ovarian cancer. In the Million Women Study 5 years of HRT resulted in 1 extra case per 2500 users. This study showed that the relative risk for ovarian cancer with tibolone was similar to the risk with other types of HRT.

Under ‘Risk of coronary artery disease’

The risk of coronary artery disease is slightly increased in users of combined oestrogen-progestagen HRT over the age of 60 (see section 4.4). There is no evidence to suggest that the risk of myocardial infarction with tibolone is different to the risk with other HRT.

PACKAGE LEAFLET

The texts of the 3rd revision of the Core PL for HRT products, as published on the CMD(h) website, should be included in the PIL. Where a statement in the Core PL for HRT products applies equally to HRT and tibolone this should be made clear by replacing ‘HRT’ with ‘HRT or tibolone’ in the tibolone PIL.

In addition to the texts of the 3rd revision of the Core PL for HRT products, the following wordings have to be added:

PL Section 2:

Under subheading ‘Breast cancer’, ‘Compare’ section

Women taking Livial have a lower risk than women using combined HRT and a comparable risk with estrogen-only HRT.

Under subheading ‘Ovarian cancer’, ‘Compare’ section

With use of Livial, the increased risk of ovarian cancer is similar to other types of HRT

Under subheading ‘Blood clots in a vein (thrombosis)’, ‘Compare’ section

With use of Livial, the increased risk of getting a blood clot in a vein is lower than with other types of HRT.

Under subheading ‘Heart disease (heart attack)’

There is no evidence that HRT will prevent a heart attack.

Under subheading ‘Stroke’

Compare

Looking at women in their 50s who are not taking Livial - on average, over a 5-year period, 3 in 1000 would be expected to have a stroke. For women in their 50s who are taking Livial, the figure would be 7 in 1000 (i.e. an extra 4 cases).

Looking at women in their 60s who are not taking Livial - on average, over a 5-year period, 11 in 1000 would be expected to have a stroke. For women in their 60s who are taking Livial, the figure would be 24 in 1000 (i.e. an extra 13 cases).