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FURTHER ADVICE ON SAFETY OF HORMONE REPLACEMENT THERAPY (HRT) : NO LONGER RECOMMENDED AS FIRST CHOICE FOR PREVENTION OF OSTEOPOROSIS

Following a European-wide review of the balance of risks and benefits of HRT in its licensed indications, the National Regulatory Authorities for Medicinal Products throughout Europe are advising prescribers that conventional oestrogen-only and oestrogen plus progestogen (combined) HRT should no longer be considered as first choice of therapy for prevention of osteoporosis.

The review, which was initiated in response to growing concern about the safety of HRT in long-term use, concluded that:

- For the treatment of menopausal symptoms, HRT is beneficial in the short-term. The minimum effective dose should be used for the shortest duration.
- The balance of risks and benefits of HRT when used in the long-term for preventing osteoporosis, suggest that it should not be the first choice of therapy.
- HRT is of no benefit in healthy women without symptoms.

Over the last 18 months, important new information on the safety of HRT has become available, most notably from the Women's Health Initiative (WHI) study and the UK Million Women Study. Findings from these and previous studies indicate that oestrogen-only HRT is associated with a duration-dependent increase in the risk of breast cancer, endometrial cancer and possibly ovarian cancer. For combined (oestrogen plus progestogen) HRT, the Million Women study has shown that there is an increase in risk of breast cancer is substantially higher than that for oestrogen-only products, although combined HRT is known to reduce and may avoid the risk of endometrial cancer that is associated with oestrogen-only HRT. Importantly, this study confirmed that, in all cases, this increase in breast cancer risk begins to decline when HRT is stopped and, by 5 years, returns to the same level as in women who have never taken HRT.

In addition, HRT is no longer thought to have a beneficial effect on cardiovascular disease and has been shown to increase the risk of heart attacks and venous thromboembolism (VTE or blood clots), especially in the first year, and to increase the risk of stroke.

The risk of most of these conditions increases with age therefore increasing the overall risks the longer HRT is taken. HRT has also been shown to have no beneficial effects on cognitive function or on the quality of life in women who do not have menopausal symptoms.

1. Concern throughout Europe about the long-term safety of HRT has culminated in the present review, which was carried out by a European Expert Group on HRT. The recommendations of the Group have been adopted by the European Committee for Proprietary Medicinal Products (CPMP) and endorsed by the Heads of Agencies..

Recommendations for prescribers are:

- For the treatment of menopausal (climacteric) symptoms that adversely affect quality of life the balance of risks and benefits of HRT is generally favourable. However, the lowest effective dose should be used for the shortest possible duration; each decision to start HRT should be made on an individual basis with a fully informed woman; and treatment should be re-evaluated at least annually in light of new knowledge and any changes in a woman's risk factors.
- For the prevention of osteoporosis in woman with an increased risk of fractures the benefit-risk balance of HRT, with different kinds of oestrogens and oestrogen-progestogen combinations is, on the basis of available evidence, not favourable. Hence, it is not favorable as first line treatment for this indication.
- The use of HRT for the prevention of osteoporosis in postmenopausal women at high risk for future fractures who are intolerant to other drugs approved for the prevention of osteoporosis, after careful assessment of the individual benefit-risk balance, remains a treatment option.

BACKGROUND

Throughout Europe, Hormone Replacement Therapy (HRT) products are indicated for the treatment of menopausal symptoms, and many are also licensed for the prevention of osteoporosis.

The European Expert Group on HRT has reported its findings to the Committee for Proprietary Medicinal Products (CPMP). A statement regarding this review is available via the website of the European Medicines Evaluation Agency (EMA, www.emea.eu.int).

BRIEF INFORMATION ON THE FOLLOW-UP MEASURES

The Heads of Agencies agreed on the necessity that the Members States' Competent Authorities should undertake a timely coordinated action on the matter. To this purpose an Action plan has been elaborated and agreed.

The implementation of the Action Plan will be undertaken in two phases. Firstly, a rapid implementation on the restriction of the indication in osteoporosis is considered necessary. Secondly, agreement of required changes to the core SPC and implementation of these changes in a co-ordinated manner will follow.