

****Embargoed until 3 pm Wednesday 3rd December 2003****

This message can be cascaded immediately to those on the distribution list but the contents of this letter are embargoed until 3pm Wednesday 3rd December. It is important that those on the distribution list have copies in advance so that they can familiarise themselves with the content before an announcement is made. This information will not be placed on the internet until 3pm today.

PUBLIC HEALTH LINK

To: Directors of Public Health of PCTs to forward to:

- All GENERAL PRACTITIONERS - please ensure this message is seen by all practice nurses and non-principals working in your practice and retain a copy in your 'locum information pack'.
- Deputising services
- Project manager/Nurse lead in Walk in Centres
- Lead nurses in PCTs to forward to PCT employed nurses
- Leads at nurse-led PMS Pilots
- Well women clinics within the PCT
- Family planning clinics within the PCT
- PCT Pharmaceutical Advisers to forward to community pharmacists
- PCT Prescribing Advisers

To: Medical Directors of NHS Trusts to forward to:

- Consultant Oncologists
- Consultant Obstetricians and Gynaecologists
- Hospital Physicians with an interest in HRT
- Well women clinics within NHS Trust
- Family planning clinics within NHS Trust
- Breast screening services within NHS Trust
- Nurse Executive Directors of NHS Trusts to forward to Heads of Midwifery
- Trust Chief Pharmacists to forward to Medicines Information Pharmacists

Cc:

- Regional Directors of Public Health
- Directors of Public Health of Strategic Health Authorities to forward to SHA pharmaceutical advisers and SHA lead nurses
- UK CMOs
- Chairmen of Professional Executive Committee

From: Professor Gordon Duff, Chairman – Committee on Safety of Medicines

Date: 3rd December 2003

Reference: CEM/CMO/2003/19, Gateway ref: 2421

Category: ****URGENT MESSAGE****

****PLEASE ACTIVATE THE CASCADE ****

FURTHER ADVICE ON SAFETY OF HRT : RISK:BENEFIT UNFAVOURABLE FOR FIRST-LINE USE IN PREVENTION OF OSTEOPOROSIS

Dear Colleague

I last wrote to you in August 2003 at the time of publication of the Million Women Study, with the immediate implications for advice to women about hormone replacement therapy (HRT). This letter provides further advice and is based on the outcome of a more detailed review of recent studies with regard to long-term risks and benefits of HRT. This review has been adopted by the European Committee for Proprietary Medicinal Products (CPMP) and endorsed by the Regulatory Authorities throughout Europe, including the UK's

Committee on Safety of Medicines (CSM) Expert Working Group on HRT. The conclusions of the review are:

- **The risk:benefit of HRT is favourable for treatment of menopausal symptoms. The minimum effective dose should be used for the shortest duration.**
- **The risk:benefit of HRT is unfavourable for the prevention of osteoporosis as first-line use.**
- **In healthy women without symptoms, the risk:benefit of HRT is generally unfavourable.**

Product information will be changed to reflect this new advice.

Background

A review of the balance of risks and benefits of HRT in its licensed indications was initiated in response to growing concern about its safety following the recent publication of several important studies, most notably the Women's Health Initiative (WHI)[Ref 1] and the UK Million Women Study [Ref 2]. These and previous studies provide good evidence that use of HRT increases the risk of breast cancer, endometrial cancer and ovarian cancer in a duration-dependent manner. There is no evidence for a beneficial effect of HRT on cardiovascular disease – in fact HRT has been shown to increase the risk of myocardial infarction and VTE, especially in the first year of use, and to increase the risk of ischaemic stroke. The risk of most of these conditions increases with age, therefore increasing the overall risks the longer HRT is taken. HRT also has no beneficial effect on cognitive function and may increase the risk of dementia in the elderly. HRT has also been shown to have no beneficial effect on the quality of life of women who do not have menopausal symptoms.

The benefits of HRT include the effective relief of menopausal symptoms and the prevention of osteoporosis and fractures in the long-term. HRT has also been shown to reduce the risk of colorectal cancer.

Despite its effectiveness in preventing osteoporosis, the review concluded that for long-term use, the balance of risks and benefits is such that HRT should no longer be considered as a first-line therapy for preventing osteoporosis.

Which products does this affect?

The conclusions of the review apply to **all** conventional oestrogen-only and combined (oestrogen plus progestogen) HRT products that are authorised for the prevention of osteoporosis.

Advice for prescribers

Short-term treatment of menopausal symptoms

The outcome of this review does not have any implications for women who are using HRT for the short-term treatment of menopausal symptoms, as the benefits are still considered to outweigh the risks for the majority of women. The lowest effective dose should be used for the shortest duration; each decision to start HRT should be made on an *individual* basis with a fully informed woman; and treatment should be reviewed at least annually in light of new knowledge and any changes in a woman's risk factors.

Prevention of osteoporosis

HRT should not be considered first-line therapy for the long-term prevention of osteoporosis in women who are over 50 years of age and at an increased risk of fractures. HRT remains an option for those who are intolerant of other osteoporosis prevention therapies, for whom these are contraindicated, or for whom there is evidence

of a lack of response to other therapies. In such cases the individual risk:benefit balance should be carefully assessed.

This new advice does not necessitate any urgent changes but women currently receiving HRT as long-term prophylaxis should have their treatment reviewed at the next appointment.

Women with premature menopause

HRT may be used in younger women who have experienced a premature menopause (due to ovarian failure, surgery or other causes) for treating their menopausal symptoms and for preventing osteoporosis until the age of 50 years. After this age, therapy for preventing osteoporosis should be reviewed and HRT considered a second-line choice.

Sources of Further Information

An information sheet for women is attached and more detailed information about the safety of HRT is available on the MHRA website (<http://www.mhra.gov.uk>).

For telephone enquiries, please call the Medicines and Healthcare products Regulatory Agency 020 7273 0000 (and 020 7084 2000 from 8th December).

Information is also available on the website of the European Medicines Evaluation Agency (<http://www.emea.eu.int>) and the Heads of European Medicines Regulatory Agencies website (<http://heads.medagencies.org>).

Further information on the role of HRT in clinical practice is available on the website of the Royal College of Physicians (http://www.rcpe.ac.uk/esd/consensus/hrt_03.html)

Professor Gordon Duff
Chairman
Committee on Safety of Medicines

References:

1. Risks and benefits of estrogen plus progestin in healthy postmenopausal women. JAMA 2002; 288:321-333. <http://www.jama.com>
2. Breast cancer and hormone replacement therapy in the Million Women Study. Lancet 2003;362:419. <http://www.thelancet.com>

INFORMATION SHEET FOR WOMEN

USE OF HORMONE REPLACEMENT THERAPY (HRT) IN THE PREVENTION OF OSTEOPOROSIS: IMPORTANT NEW INFORMATION

You may have seen in the news that European experts, including the UK, have recommended that HRT should no longer be used as a first choice for the prevention of osteoporosis. This recommendation follows a European-wide review of all the risks and benefits of HRT and affects all EU countries, including the UK. If, after reading the information below, you are concerned, you should make a **routine** appointment to see your doctor. There is no need for any urgent changes to treatment.

Use of HRT

In the UK, 'conventional' HRT products (containing either oestrogen alone or in combination with a progestogen) are licensed for helping relieve unpleasant symptoms of the menopause, including hot flushes, vaginal dryness and night sweats. Some of these products are also licensed for longer-term use for preventing osteoporosis, which can cause bone fractures.

Further Review of the Risks and Benefits of HRT

Recent publications (such as the Women's Health Initiative (WHI) and the UK Million Women Study) have highlighted a number of safety concerns regarding long-term use of HRT. As a result, a group of experts on HRT from a number of European countries, including the UK, has now reassessed all the risks and benefits of HRT and provided new recommendations about its use. The conclusions of the review are that:

- For short-term treatment of menopausal symptoms the balance of risks and benefits is favourable - HRT therefore remains a suitable treatment option. The minimum effective dose should be used for the shortest duration.
- For long-term use for preventing osteoporosis the balance of risks and benefits is unfavourable. HRT should only be used for preventing osteoporosis by those who are unable to take other osteoporosis prevention treatments or for whom other treatments have been unsuccessful.
- In healthy women without symptoms, the balance of risks and benefits is generally unfavourable and HRT is not recommended.

Key message

- There is no need to contact your doctor urgently.
- There is no need to change your treatment if you are taking HRT in the short-term for the relief of menopausal symptoms, but you should discuss your treatment with your doctor (at least annually) to make sure that it is still right for you.
- If you are aged 50 or more, taking HRT for the prevention of osteoporosis (and are not suffering from menopausal symptoms) you should make a routine appointment with your doctor to discuss whether an alternative might be more suitable.
- There is no need to change your HRT therapy if you have experienced an early menopause, and are not yet 50 years old. Your therapy should be reviewed regularly and your doctor might advise a change in therapy when you are about 50 years of age.
- If in doubt, make a routine appointment to see your doctor.

Further information

Further information and advice may be found on the Medicines and Healthcare products Regulatory Agency's website (www.mhra.gov.uk). Here you can find more details about the other risks and benefits of HRT treatment, which may help to answer some of the questions you may have about these new findings.

NHS Direct may also be able to answer your questions (Tel 0845 4647).

Information is also available on the website of the European Medicines Evaluation Agency (<http://www.emea.eu.int>) and the Heads of European Medicines Regulatory Agencies website (<http://heads.medagencies.org>).