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Pfizer Canada Inc.

Health Canada Endorsed Important Safety Information on DEPO-PROVERA* (medroxyprogesterone acetate injectable suspension, USP)

June 30, 2005

Dear Health Care Professional,

Subject: Important Safety Update: Potential effect of DEPO-PROVERA* (medroxyprogesterone acetate injectable suspension, USP) on Bone Mineral Density (BMD) changes in adults and adolescents

Pfizer Canada Inc. in consultation with Health Canada, would like to inform you of important updated safety information and upcoming changes to the Product Monograph for DEPO-PROVERA (medroxyprogesterone acetate injectable suspension, USP), indicated for conception control (prevention of pregnancy), treatment of endometriosis, adjunctive and/or palliative treatment of recurrent and/or metastatic endometrial or renal cell carcinoma (hypernephroid carcinomas) and adjunctive or palliative treatment of hormonally-dependent, recurrent, inoperable or metastatic carcinoma of the breast in post-menopausal women.

As a result of new clinical studies, one with premenopausal adult women (age 25-35 years) and one with adolescent women (age 12-18 years) using DEPO-PROVERA 150 mg IM for contraception, we now have data regarding the use of DEPO-PROVERA and its associated effect on bone mineral density (BMD). The data indicate that women who use DEPO-PROVERA may lose significant BMD. The data also indicate that bone loss is greater with increasing duration of use and may not be completely reversible.
The DEPO-PROVERA Product Monograph has been revised to include the following new information in addition to a summary of the available data:

Boxed WARNINGS

- The use of DEPO-PROVERA has been associated with loss of bone mineral density (BMD) which may not be completely reversible. Loss of bone mineral density is greater with increasing duration of use.
- It is unknown if use of DEPO-PROVERA during adolescence or early adulthood, a critical period of bone accretion, will reduce peak bone mass and increase the risk for osteoporotic fracture in later life.
- DEPO-PROVERA should be used as a birth control method or endometriosis treatment **only** if other treatments have been considered to be unsuitable or unacceptable, and should be used for the shortest period of time possible. The risks and benefits of treatment should be carefully re-evaluated on a regular basis in all users of the drug

INDICATIONS and CLINICAL USE

- Although there are no studies addressing whether calcium and vitamin D may lessen BMD loss in women using DEPO-PROVERA, all patients should have adequate calcium and vitamin D intake. Cessation of smoking and regular weight bearing exercise should be discussed with all patients.

CONTRAINDICATIONS

- DEPO-PROVERA should not be used before menarche.

WARNINGS

Loss of Bone Mineral Density

Contraception/Endometriosis

- Use of DEPO-PROVERA should be considered a risk factor for osteoporosis. The use of DEPO-PROVERA should be considered in light of a patient's possible other risk factors for osteoporosis (including metabolic bone disease, chronic alcohol and/or tobacco use, anorexia nervosa, strong family history of osteoporosis or chronic use of drugs that can reduce bone mass such as anticonvulsants or corticosteroids).

- BMD should be monitored in women using DEPO-PROVERA for longer than 2 years, or earlier as clinically appropriate. In adolescent females, interpretation of BMD results should take into account patient age and skeletal maturity. If a clinically significant decrease in BMD is detected, treatment with DEPO-PROVERA should be reconsidered.

Oncology

- There are no studies on the effects of the high doses of parenteral medroxyprogesterone acetate (e.g. for oncology use). If a patient is using DEPO-PROVERA as part of adjunctive or palliative treatment of endometrial, renal cell or breast carcinoma, evaluation of BMD is recommended as deemed clinically appropriate.

Post-marketing experience

- In post-marketing experience, there have been cases of osteoporosis including osteoporotic fractures reported in patients taking DEPO-PROVERA. Patient age ranged from 16 years to 48 years.

INFORMATION FOR THE CONSUMER
Will be updated to reflect the above new information.

We trust this information is useful in providing guidance on the appropriate use of DEPO-PROVERA.

Pfizer Canada Inc. is committed to providing you with the most current product safety information on its products and routinely assesses safety information and updates Product Monographs accordingly.

Reporting rates determined on the basis of spontaneously reported post-marketing adverse events are generally presumed to underestimate the risks associated with drug treatments.

The identification, characterization, and management of marketed health product-related adverse reactions are dependent on the active participation of health care professionals in adverse drug reaction reporting programmes. Any occurrences of osteopenia, osteoporosis, fracture or other serious and/or unexpected adverse reactions in patients receiving DEPO-PROVERA (medroxyprogesterone acetate injectable suspension, USP) should be reported to Pfizer Canada Inc. and/or Health Canada at the following addresses:

Pfizer Canada Inc.
Safety and Medical Information
P.O. Box 800
Pointe-Claire, Quebec
H9R 4V2
1-800-463-6001

Any suspected adverse incident can also be reported to:
Canadian Adverse Drug Reaction Monitoring Programme (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
OTTAWA, Ontario, K1A 0K9
Tel: (613) 957-0337 or Fax: (613) 957-0335
Toll free for consumers and health professionals: Tel: 866 234-2345, Fax: 866 678-6789
cadrmp@hc-sc.gc.ca

The AR Reporting Form (http://www.hc.sc.gc.ca/hpfb-dgpsa/tpd-dpt/adverse_e.html) and the AR Guidelines (http://www.hc.sc.gc.ca/hpfb-dgpsa/tpd-dps/adr_guideline_e.html) can be found on the Therapeutic Product Directorate website or in *the Canadian Compendium of Pharmaceutical and Specialties*.

Sincerely,

Bernard Prigent, M.D., M.B.A.
Vice President & Medical Director
Pfizer Canada Inc.