IMPORTANT SAFETY INFORMATION

Important safety concerns on the use of Diane-35

December 19, 2002

The Marketed Health Products and Therapeutic Products Directorates wish to draw your attention to an article published in the October 2002 issue of CURRENT PROBLEMS in Pharmacovigilance (Medicines Control Agency, United Kingdom) regarding **important safety concerns on the use of cyproterone acetate** (marketed as Diane-35 in Canada, and as Dianette in the United Kingdom). The October 2002 issue is available at:
http://www.mca.gov.uk/ourwork/monitorsafequalmed/currentproblems/cpprevious.htm#2002

Cyproterone acetate (Dianette): Risk of venous thromboembolism

It should only be used to treat severe acne and hirsutism

Dianette is indicated for women with severe acne which has not responded to oral antibiotics, or for moderately severe hirsutism. It contains cyproterone acetate (2mg), an anti-androgenic progestogen, and ethinylestradiol (35µg) and it is administered for 21 days of each menstrual cycle. It therefore has a similar composition to that of a combined oral contraceptive (COC) and provides effective contraception.

However, Dianette is **not** authorised for the sole purpose of oral contraception and should be discontinued 3 to 4 menstrual cycles after the woman's androgen-related condition has completely resolved. The use of a COC carries an increased risk for venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, compared with no use.

Epidemiological studies have shown that the incidence of VTE in users of oral contraceptives with low oestrogen content (<50µg ethinylestradiol) is up to about 40 cases per 100,000 women-years. This compares with 5-10 cases per 100,000 women-years for non-users of COCs and 60 cases per 100,000 pregnancies.

There is some epidemiological evidence that the incidence of VTE in users of Dianette is higher than in users of low- dose oestrogen COCs[1-4]. A recent case-control study using the UK General Practice Research Database (GPRD) found a four-fold increase in the risk of VTE in 24,401 women taking oral contraceptives that contain cyproterone acetate/ethinylestradiol compared with 75,000 women taking

second generation oral contraceptives that contain levonorgestrel/ethinylestradiol[1].

In the UK, Dianette usage has increased in recent years. Women with androgen-related conditions may have an inherently increased cardiovascular risk. Product information is being updated to reflect these new findings.

Prescribers are reminded that:

- Dianette is not indicated for use solely as an oral contraceptive.
- Dianette is a treatment for women with severe acne that has not responded to oral antibiotics, or for moderately severe hirsutism.
- Dianette should be withdrawn 3 to 4 cycles after the treated condition has completely resolved.
- The incidence of VTE in Dianette users is higher than that in women who use low-dose oestrogen COCs.
- Dianette is contraindicated in women with a personal or close family history of confirmed, idiopathic VTE and in those with a known current venous thrombotic or embolic disorders.
- Women who have severe acne or hirsutism may have an inherently increased cardiovascular risk.

References:

1. Vasilakis-Scaramozza C and Jick H. Lancet 2001;358: 1427-29.
2. WHO Study. Lancet 1995; 346: 1582-88.
3. Pini M et al. Rec Prog Med 1996; 87(7/8): 331-7.
4. Parkin L et al. Lancet 2000; 355: 2133-4.

Any suspected adverse drug reactions can also be reported to:

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0201C2
OTTAWA, Ontario, K1A 1B9
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 ADR Reporting Form and the ADR Guidelines can be found on the TPD web site or in *The Canadian Compendium of Pharmaceuticals and Specialties*.