# Do Not Use!

## Oral Contraceptives Containing Desogestrel with Ethinyl Estradiol (DESOGEN, ORTHO-CEPT)

In the new edition of *Worst Pills, Best Pills* we listed the combination oral contraceptives containing desogestrel with ethinyl estradiol (DESOGEN, ORTHO-CEPT) among the 160 drugs that you should not use because there are safer and equally effective alternatives available.

The most popular oral contraceptives are combinations of the hormones estrogen and progestin. Combination oral contraceptives are classified as either "second" or "third" generation pills based on their progestin component. In this country, DESOGEN and ORTHO-CEPT are the only available third-generation pills. Both contain 0.15 milligrams of the progestin desogestrel and 0.03 milligrams of the estrogen ethinyl estradiol. Second-generation contraceptives, in contrast, contain the progestins norgestrel, levonorgestrel or norethindrone.

DESOGEN and ORTHO-CEPT accounted for more than 7.6 million prescriptions filled in 1998 in the U.S.

A firestorm of controversy erupted in late 1995 and early 1996 when several observational studies were published showing that the risk of deep venous thrombosis (blood clots) is two times higher with third-generation oral contraceptives than with second-generation birth control pills.

A worldwide study conducted by the World Health Organization (WHO) published in late 1995 in the British medical journal *The Lancet* found that the third-generation pills containing desogestrel or gestodene (this progestin is not available in the U.S.) were associated with an increased risk of clotting. Shortly thereafter four more observational studies published in rapid succession again in *The Lancet* and the *British Medical Journal*, confirmed that the risk of life-threatening blood clots with the third-generation pills was two times greater than with the older second-generation contraceptives.

In October 1995, the United Kingdom's equivalent of our Food and Drug Administration (FDA), the Committee on Safety of Medicines (CSM), warned the British public that third-generation pills could double the risk of blood clots compared to older second-generation oral contraceptives. British doctors were told that the third-generation products should not be routinely prescribed and that women should be offered the choice to switch to the older, safer second-generation pills. The CSM decided that the increased risk—estimated at 30 cases of blood clots for every 100,000 users of third-generation pills a year, compared with 15 cases for every 100,000 women on second-generation pills a year—was sufficient to warrant an urgent alert to women and prescribers.

Proponents of the third-generation pills, mainly their manufacturers, maintained that any increase in the

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risks of blood clots may be offset by a reduced risk of heart attack. The key phrase in the last sentence is "may be." The third-generation pill proponents have not been able to produce any convincing evidence that the newer pills protect women against heart attack.

While the British authorities took the responsible step in 1995 to fully inform women about the risk of blood clots with the third-generation pills, the FDA took no similar action in alerting the public. The action of the British authorities allowed "the user to be the chooser" by providing women with the information to make an informed decision about which contraceptive to use.

The professional product labeling, or package insert, and the patient labeling for ORTHO-CEPT now warns of the doubling in risk of blood clots, but few doctors or pharmacists read the product labeling and not every woman may receive the FDA-approved patient labeling. This is the statement contained in the ORTHO-CEPT professional labeling:

*Data from case-control and cohort studies report that oral contraceptives containing desogestrel (ORTHO-CEPT contains desogestrel) are associated with a two-fold increase in the risks of venous thromboembolic disease [blood clots] as compared to other low-dose (containing less than 50 micrograms of estrogen) pills containing other progestins. According to these studies, this two-fold risk increases the yearly occurrence of venous thromboembolic disease by about 10-15 cases per 100,000 women.*

The ORTHO-CEPT package insert also makes reference to the unsubstantiated theory that third-generation birth control pills protect women from heart attack. This is the statement, again directly from the ORTHO-CEPT package insert:

*Desogestrel has minimum androgenic activity, and there is some evidence that the risk of myocardial infarction (heart attack) associated with oral contraceptives is lower when the progestogen has minimal androgenic activity.*

Organon, the producer of DESOGEN, makes similar statements about the risks of blood clots and heart attacks in the DESOGEN package insert.

To settle questions about the oral contraceptives, the World Health Organization (WHO) convened an international meeting of experts in Switzerland in November 1997 with the overall objective of reviewing the current scientific data on the use of oral contraceptives and the risk of heart attack, stroke, and blood clots. Regarding blood clots and heart attack the scientific group concluded that:

- Current users of combined oral contraceptives have a low absolute risk of venous thromboembolism (blood clots) which is nonetheless 3- to 6-fold higher than in non-users. The risk is probably highest in the first year of use and declines thereafter, but persists until discontinuation.
- Combined oral contraceptive preparations containing desogestrel and gestodene probably carry a small risk of venous thromboembolism beyond that attributable to combined oral contraceptives containing levonorgestrel. There are insufficient data to draw conclusions with regard to combined oral contraceptives containing levonorgestrel. There are insufficient data to draw conclusions with regard to combined oral contraceptives containing norgestimate.
- The available data do not allow a conclusion that the risk of myocardial infarction (heart attack) in users of low-dose combined oral contraceptives is related to progestogen type. The suggestion that gestodene- or desogestrel-containing low-dose combined oral contraceptives may carry a lower risk of myocardial infarction compared with low-dose formulations containing levonorgestrel remains to be substantiated.

The symptoms of blood clots are given in the box accompanying this article.

Recently, in February 1999, New Zealand's Centre for Adverse Reactions Monitoring reported it had received seven reports of death related to blood clots in women taking third-generation oral contraceptives. There was also one case of a blood clot in the lungs and cardiac arrest leading to severe brain damage in a woman taking third-generation pills. One of the deaths occurred in the absence of any known risk factors for blood clots. Only one woman may have had a known contraindication—a previous blood clot in the lung that may have been undiagnosed.

Some of the risk factors for blood clots are a previous clot, a close family member who has had a blood clot, bad varicose veins, being overweight, cancer, recent surgery and being immobilized. Women who have had a previous blood clot

*continued on page 39*

The symptoms of a blood clot in the leg are swelling, tenderness and pain, but a blood clot may occur without symptoms.

Breathlessness occurs with a blood clot in the lungs. These symptoms can also occur for other reasons.

If you are taking an oral contraceptive pill and you develop any of these symptoms you should see a doctor immediately. You should be particularly alert to these symptoms if you have a risk factor for blood clots.

ORAL CONTRACEPTIVES, from page 37

should not take a combination oral contraceptive product. You should tell your doctor if any of these risk factors apply to you. Your risk of having a blood clot can be increased temporarily, for example, by a long flight, being immobilized by injury or illness, or by having surgery.

## What You Can Do

The risk of blood clots with combined oral contraceptives is small, but it is a real risk, and this risk is greater with the third-generation pills than with the second-generation oral contraceptives. There is no acceptable scientific evidence that a woman taking third-generation pills reduces her risk of heart attack over that of a woman using the second-generation products, and second- and third-generation pills are equally effective in preventing pregnancy. In summary, there is no reason why women should be using third-generation oral contraceptives when equally effective and safer oral contraceptives are available.