Information Bulletin for the doctor

Please review and sign this before participation

Dear colleague,

The Berlin Center for Epidemiology and Health Research (ZEG) and Family Planning NSW are performing an observational study on the risks of using oral contraceptives, especially the contraceptive Zoely® (NOMAC-E2).

A balanced risk/benefit analysis of new oral contraceptives requires not only data on effectiveness but also robust data on potential side effects. Rare side effects often only show up in the course of long-term observation in clinical practice, or are so rare that they can only be detected in large-scale comparative studies. We are therefore performing a large, controlled, prospective international cohort study on the use of NOMAC-E2 as compared to levonorgestrel-containing combined oral contraceptives in clinical practice. The title of the study is the following:

PRO-E2

Prospective controlled cohort study on the safety of a monophasic oral contraceptive containing nomegestrol acetate (2.5 mg) and 17ß-estradiol (1.5 mg)

In this study, 101,000 women will be observed in Europe, Australia and Latin America, starting in 2014 and ending in 2020.

Because women usually receive their prescriptions for hormonal contraceptives as well as subsequent associated care from doctors in private practice, we are contacting you to request your support in this important scientific study.

We want this study to exert no influence whatsoever on your prescriptions or on the decisions made by individual patients. The option of participating in this study should only be discussed after you and your patient have already decided which combined oral contraceptive should be used. For this study we are seeking doctors who prescribe combined oral contraceptives on a regular basis and are able to motivate women to participate in a study in which they would be followed up for two years.

Which patients can be included in this study?

All patients who receive a prescription for either Zoely® or a levonorgestrel-containing combined oral contraceptive and who have not taken a combined oral contraceptive **in the past two months**.

What will your role be?

Recruiting women for a three-year observational study, i.e., informing women about the study and, if they are interested, providing them with informational material that we have already prepared. **For every patient you prescribe Zoely®, you should enroll one woman with a prescription for a levonorgestrel-containing combined oral contraceptive.**

To participate in the study, patients need to read the Declaration on Data Protection and Absolute Confidentiality, sign a consent form and fill out a short baseline questionnaire (4 pages). We request that you fill in the first question identifying the prescribed combined oral contraceptive. Your staff will place these documents in a pre-addressed and pre-paid envelope and send them to Family Planning NSW, preferably in batches but not later than three months after each woman is enrolled in the study. That is the extent of your work in normal cases.

If patients should report serious and/or unexpected side effects over the course of the study, we will generally contact a doctor who can provide information on possible medical background factors. In rare cases, it might be necessary for us to ask you for further information.

For your assistance, you will receive an expense allowance of $70 per patient following submission of the respective consent form and completed baseline questionnaire.

What do we expect from your patients?

The women should voluntarily consent to participate in the study and to report their experiences with their hormonal contraceptives. At the beginning of the study, they will sign a consent form and fill out a brief questionnaire (approx. 5 minutes). They will then receive no more than 3 additional brief questionnaires (3 pages) by mail, spread over one to two years, which they are requested to complete and return in the accompanying pre-paid envelopes – there will be no costs for your patients. Survey completion may also be offered by phone or email for their convenience.

Ethical approval for the study will be acquired following the rules in the respective countries. In Germany, approval from the Ethics Commission overseeing the Principal Investigator has already been acquired. Approval has also been obtained from the Family Planning NSW Ethics Committee (approval no. R2015-03). In accordance with the International Committee of Medical Journal Editors (ICMJE) initiative requiring prior entry of clinical studies in a public registry as a condition for publication, the study was registered in the U.S. National Institutes of Health's protocol registration database (www.clinicaltrials.gov). Furthermore, this study is registered in the ENCePP network (European Network of Centres for Pharmacoepidemiology and Pharmacovigilance) and received the quality seal of ENCePP.

If you are willing to participate in the PRO-E2 Study as described above, we ask that you fill in the following information, provide your signature and return this letter* to Lorraine Edney Family Planning NSW 328-336 Liverpool Rd Ashfield 2131.

I understand that my participation in this study is voluntary, and that Family Planning NSW or I may discontinue my participation at any time without providing notice.

First & last name (please print) . . . . . .

Work address ……. . . . . .

Telephone . . . . Email . . . . . .

Signature . . . . Date ……..

* Please keep a copy for your records.

If you have any questions, please do not hesitate to contact:

- **Dr Mary Stewart**
  Family Planning NSW
  Tel. + 61 2 8752 4340; Email: marys@fpnsw.org.au

- **Dr. Suzanne Reed**
  Berlin Center for Epidemiology and Health Research (ZEG)
  Tel. +49 (0) 945 10163; Email: reed@zeg-berlin.de

We look forward to working with you.

Sincerely yours,

Dr Mary Stewart
Family Planning NSW

Dr. Suzanne Reed
Dr. Jürgen Dinger
Berlin Center for Epidemiology and Health Research