**Synopsis**

**TITLE OF TRIAL**
Impact of professional societies recommendations on practical use of hormone replacement therapy – project “WOMAN 2005”

**INVESTIGATORS**
Dr. Jitka Matlochová was appointed as a Principal Investigator.

**TRIAL SITES**
Total of 112 sites throughout the Czech Republic participated in the study.

**PUBLICATIONS**
None at the time of this report.

**TRIAL PERIOD**
The duration of the study was 15 months,
First Patient First Visit: 1 April 2005
Last Patient Last Visit: 30 June 2006

**OBJECTIVES**
**Primary Objectives:**
- Verify therapeutic effects of low-dose HRT on a relevant sample of female patients over adequately long time period. in conditions normal clinical practice
- Specification of correct usage of low-dose HRT in the given group of female patients.

**Secondary Objective:**
- to determine satisfaction of patients with low-dose HRT and continuation of the treatment

**METHODOLOGY**
This was an open, non-controlled, non-randomised, multi-centre study run in Czech Republic.

**NUMBER OF SUBJECTS PLANNED AND ANALYSED**
A total of 3000 subjects were planned to be included in the study. The total of 3760 subjects were analysed and started treatment with Activelle or Novofem or Estrofem.

**DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION**
The selection of the subjects was at the discretion of the individual physician. Particular attention was paid to the drug interactions that are listed within the product label. There were included patient where the treating physician set patient to Activelle or Novofem or Estrofem (low dose HRT therapy). The trial main portion population comprised post-menopausal women suffering with climacteric syndrome and younger female patients with hormonal deficiency.

**TEST PRODUCT, DOSE AND MODE OF ADMINISTRATION, BATCH NUMBER**
Activelle one tablet taken orally at the same time each day of treatment.
Estrofem 1mg one tablet taken orally at the same time each day of treatment.
Novofem one tablet taken orally at the same time each day of treatment.

**DURATION OF TREATMENT**
Duration of treatment was 12 weeks (3 lunar months)

**REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION, BATCH NUMBER**
Not Applicable
**CRITERIA FOR EVALUATION – EFFICACY/SIDE EFFECTS**
- Breast tenderness
- Oedema of lower extremities
- Headache
- Weight change
- Hot flushes
- Local skin irritation
- Bleeding
- Sweating
- Patient treatment satisfaction

**CRITERIA FOR EVALUATION – SAFETY**
- Adverse drug reaction (not included in side effects above) to the Activelle or Novofem or Estrofem.

**STATISTICAL METHODS**
The statistical analyses were based on the Intention-to-Treat analysis set (ITT). This means that all exposed subjects contributed with all data for each analysis. For efficacy and safety each subject acted as her own control and the descriptive statistics and graphics focused on describing potential changes versus time. The change in questionnaire endpoints after previous standard therapy versus low-dose HRT were analysed by fitting a binomial model to the number of women that changed the therapy and exact p-values were calculated.

**DEMOGRAPHY OF STUDY POPULATION**
The average age of patients at the time of their entry into the surveillance was 52.6 years, the youngest patient was 17 years old, the oldest patient was 77 years old. The largest share of patients included women in postmenopause (41.5%) in perimenopause (34.3%) and after hysterectomy (20.6%).
The average weight at the time of entry into the surveillance was 72.0 kg. The weight of patients ranged between 42.0 and 145.0 kg.

**EFFICACY RESULTS**
- The total of 1947 (51.8%) patients of all patients participating in the surveillance were previously treated by standard HRT. These women most commonly received previous therapy for 1 to 2 years (36.9%), or 3 to 5 years (32.6%) respectively. The total of 1666 (44.3%) patients were not previously by standard HRT.
- Klimonorm was the most commonly used drug, which was administered to 394 (20.04%) women, followed by Cyclo-Menorette which was administered to 242 (12.31%) women during previous standard HRT.
- The total of 1025 (52.6%) women treated with standard HRT had experience with side-effects during the treatment. The most common side effects included tension in breasts (603 patients), weight gain (524 patients) and headache (487 patients). The total of 52 patients, who were not treated with standard HRT, had a record of certain side-effect. These patients were not included in the statistics.
- The additional site effects during the standard HRT treatment were also analysed. The most common additional side effects included hot flushes (24.20%), spotting (10.83%), bleeding (8.92%) and sweating (7.01%).
- The largest number of patients (77.9%) was switched to low-dose therapy based on recommendations of attending gynaecologist. The total of 1766 (47.0%) patients were treated with Activelle®, 1157 (30.8%) women were treated with Novofem® and 820 (21.8%) were treated with Estrofem®. In 15 (0.4%) patients, type of therapy was not specified.
- From the total of 3687 patients, who came for the final visit, 746 (20.2%) of women experienced side effects. The most common complaints included tension in the breasts (371 patients) and headache (223 patients).
- The additional side effects during the low dose HRT treatment were analysed. The most common additional side effects included flushes (14.46%), weight gain (14.46%) and sweating (10.84%).
- The majority of patients (94.8%) were satisfied with low-dose HRT. Reasons of dissatisfaction most commonly included spotting (11.05%) and headache (9.94%).
- The average time period between initial and final visit was 94 days. The total of 73 patients did not attend the
final visit and 3478 (94.3%) patients continued with the treatment.

- The relationship between continuation of the treatment and type of the treatment were analysed. The lowest share of patients continuing with the treatment was noted in patients taking Novofem.

**SAFETY RESULTS**

- During the study there were recorded no serious or non-serious drug reactions to Activelle or Novofem or Estrofem.

**CONCLUSIONS**

- By switching the patient to low-dose HRT, clear decrease of incidence side effects was observed and if they occurred, they were classified as mild.
- High share of patients, who were satisfied with low-dose treatment, only confirms the recommendations of scientific societies, which suggest that low-dose HRT is suitable for 90% of patients.
- After the patients had been switched from standard therapy, breast tension decreased in nearly ¾ of patients.
- Headache was reported by 4 times lower number of patients on low-dose therapy compared to standard therapy.
- From the total number of patients on low-dose therapy, 79% did not report any side effects.

The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice.