The Efficacy of Dienogest for the Treatment of Endometriosis and Its Pharmaco-Economic Assessment in the Caucasian Region

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Introduction :

- Endometriosis remains a highly prevalent and long-lasting condition in women of reproductive age
- The exact prevalence of endometriosis is unknown but estimates range from 2 to 10% within the general female population, but up to 50% in infertile women[2].
- Prevalence of endometriosis might vary with ethnicity and it is one of the most common problem for the **Caucasian region**.
- Dienogest is an oral progestin that is approved in many countries for the treatment of endometriosis in women of reproductive age[6].
- DNG provides a focused therapeutic effect on endometrial tissue, with no relevant androgenic, mineralocorticoid or glucocorticoid activity[6].

Objective :

According to the official data, based on the birth rate in the Caucasian region and its low social-economic status, we decided to study :

- The **therapeutic efficacy** and **safety** of **Dienogest**
- To assess its **pharmaco-economic effect** in our region.

Methods :

- Open, single-center, randomized trial
- Patients are administered DNG orally at a daily dose 2 mg (n=34) or 4 mg (n=38) for a maximum period of 6 months
- A total of 72 patients (30±6years of age) with histologically confirmed endometriosis at stages I, II or III according to the rAFS score - were randomized to receive study medication[3]
- Participants had good general health
- Tablets of Dienogest were taken orally, regardless of food intake, at the same time every day

- There were no notable differences between the treatment groups in mean age to menarche, parity, mean number of abortions, infertility or menstrual history or prior use of medication
- Women were required to use a nonhormonal barrier contraceptive method throughout the study
- Patients were randomised to one of two treatment groups via random selection
- 34 patients were included in the 2mg group and 38-in the 4mg. group
- Each patient received 24 weeks of treatment after a screening visit and a baseline observation period covering one menstrual cycle
- Endometriosis symptoms were recorded at baseline and after 4,16 and 24 weeks of treatment[1]
- The effect of DNG on endometriotic lesions was assessed by transvaginal ultrasound (GE Voluson Expert)
- The final assessment of the effect was done via endoscopy (Karl Storz endoscope) after the end of the treatment
- Adverse events were documented throughout the study.

Results :

- After 24weeks of treatment, the rates for **dysmenorrhea** were reduced from 73% to 14% in the 2mg group and 12% in the 4mg group (P<0,001). Figure1-A
- Pre-menstrual pain** was reported by 4% of patients out of 51% in both treatment groups (P<0,001) (Figure 1-B), whereas
- The degree of **dyspareunia** was reduced from 63% to 9% in the 2mg group and 7% in the 4mg group (P<0,001) according to VAS. Figure1-C

Figure 1. Endometriosis symptoms at baseline and after 24 week of treatment in the 2mg. group and in the 4 mg. group

The most common **adverse events** were:

- Mood swings** -12% in the 2mg group and 14,2% in the 4mg group (P<0,001);
- Headache** -7,1% in the 2mg group and 9,7% in the 4mg group (P<0,001);
- Acne** - 7% in the 2mg group and 9,4% in the 4mg group (P<0,001);
- Nausea** - 5% in the 2mg. group and 7,2% in the 4mg group (P<0,001). (Figure 2.)

Figure 2. Adverse events to receive Dienogest in both treatment groups

Conclusions :

In Caucasian women the 2mg/day dose of DNG has almost the **same effect** as the 4mg dose[4-6]. Moreover, its more safe and comfortable for patients with less severe adverse affects and thus has a clear economic advantage (DNG 2mg. N28 costs-58,2 € according to the Georgian National Bank's official exchange rate). Correct treatment based on the principle - balanced clinical and economic results is observed in case of treatment with Dienogest 2mg. which is profitable for patients, clinics and also insurance companies.

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