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NCBI Schindler: **Dienogest in long-term treatment of endometriosis**

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Abstract

Endometriosis is a chronic disease primarily affecting women of childbearing age, in which endometriotic lesions form outside the uterus, typically leading to painful symptoms, fatigue, and infertility. The symptoms of endometriosis may cause significant impairment in quality of life and represent a substantial economic burden to patients, families, and society. There is no cure for endometriosis; management consists of alleviating pain and other symptoms, reducing endometriotic lesions, and improving quality of life. Recurrence after surgical intervention is common, while the clinical evidence to support the efficacy and safety of many medications currently used in endometriosis is limited.

Dienogest is an oral progestin that has been investigated extensively in the treatment of endometriosis in two clinical programs performed in Europe and Japan, including dose-ranging, placebo-controlled, active comparator-controlled, and long-term (up to 65 weeks) studies. These studies demonstrated that dienogest 2 mg daily effectively alleviates the painful symptoms of endometriosis, reduces endometriotic lesions, and improves indices of quality of life. Dienogest showed a favorable safety and tolerability profile in these studies, with predictable adverse effects, high rates of patient compliance, and low withdrawal rates. This review article describes the clinical trial evidence that characterizes the efficacy and safety of dienogest in endometriosis, including two studies characterizing dienogest in long-term use. The relevance of these findings to the management of endometriosis in clinical practice is discussed.

Dienogest has been investigated as a long-term treatment of endometriosis in two large trials performed in Europe and Japan, which included assessments of efficacy, change in quality of life, safety, and tolerability.

Women who completed the 12-week placebo-controlled study in Europe[54] were offered the opportunity to enter an open-label extension study of dienogest for up to 53 additional weeks, providing an overall treatment period of up to 65 weeks.[62] Notably, of the 188 women completing the placebo-controlled study, a large proportion (n = 168, 89%)consented to enter the long-term extension study. The intensity of pain showed significant, sustained improvements during the long-term study, in addition to the improvements associated with dienogest

during the placebo-controlled phase. Mean visual analog scores decreased from 56.9 mm at baseline of the placebo-controlled study to 34.1 mm at baseline of the long-term study, to 11.5 mm at the end of the 53 additional weeks of treatment (Figure 2). During a 24-week treatment-free period following the long-term study, visual analog scores increased only moderately, suggesting that dienogest induces a beneficial effect that may persist after treatment cessation. Short Form 36 Health Survey scores during the treatment-free period indicated minimal changes in physical or mental indices of quality of life over six months after cessation of dienogest.

Dienogest is a progestin investigated for the treatment of endometriosis. Dienogest at a dose of 2 mg daily has been studied extensively in clinical trial programs performed in Europe and Japan, including two studies with treatment durations of up to 65 weeks. These studies demonstrated that dienogest has an efficacy, safety, and tolerability profile that is favorable for long-term use. The intensity of pain associated with endometriosis decreased progressively, adverse events (mostly mild or moderate in intensity) were predictable and associated with low discontinuation rates, and bleeding irregularities reduced in intensity and frequency over time. Following cessation of dienogest treatment, menses returned to normal.

The impact of endometriosis on a woman's quality of life is substantial and wide ranging. Quality of life assessments in the dienogest studies indicated that improvements in both physical and mental indices were attained within 12-week and 24-week treatment durations, and that these benefits were sustained in studies of up to one year.

Also of major significance to clinical practice, compliance with dienogest treatment was high and rates of discontinuation due to adverse events were low in these studies. Contributors to this favorable compliance may include the efficacy of dienogest for symptom control and the predictability of adverse effects, which can be communicated to patients before treatment initiation. Large proportions of the women who were questioned expressed a willingness to continue dienogest treatment.

Together, the dienogest study programs performed in Europe and Japan indicate that dienogest represents a promising new medication for the long-term management of endometriosis.

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