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Editorial

Long-term dienogest treatment in endometriosis: Consensus from Taiwanese experts

A B S T R A C T

Dienogest has been proven effective as long-term therapeutic option for pelvic pain caused by endometriosis. However, in Taiwan, there is a lack of a well-tailored consensus on its long-term administration. To address this gap, Taiwanese experts in collaboration with the Taiwan Endometriosis Society (TES), convened to provide structured recommendations on dienogest treatment and monitoring strategies. Drawing from clinical evidence and collective expertise, the experts formulated individualized treatment strategies based on treatment objectives and the patient's demographics. The experts recommend long-term dienogest administration for endometriosis patients for appropriate symptom control while reducing the risk of disease recurrence. Specifically, they recommend regular ultrasound examinations and relevant blood tests to monitor disease progression and therapeutic response with additional breast screening for patients at high risk for breast cancer. These recommendations aim to provide physicians with comprehensive guidance on the long-term administration of dienogest for endometriosis, ensuring patient safety and optimizing treatment outcomes.

Endometriosis is a chronic gynecological condition characterized by the ectopic presence of endometrial tissue and affects approximately 1 in 10 women of reproductive age [1,2]. Patients with endometriosis experience chronic pelvic pain and infertility, accompanied by several systemic comorbidities such as thyroid disease, dyschesis, immunological dysfunction, and even ovarian cancers. Dienogest, a 4th generation synthetic progestin, has emerged as a promising therapeutic option due to its effectiveness in managing endometriosis symptoms [2–4]. However, in Taiwan, there is a lack of consensus on dienogest administration in treating endometriosis.

To address this issue, 13 Taiwanese experts convened and deliberated on the extended use of dienogest (>2 years) across diverse patient profiles. Before the meeting, a comprehensive survey was conducted to ascertain the current landscape of endometriosis treatment with dienogest. The survey results served as the foundation for discussions during the expert meeting, where specific polling questions were provided to establish consensus on addressing key challenges associated with the long-term use of dienogest and to formulate monitoring strategies during dienogest treatment. The Taiwan Endometriosis Society served as a reviewer during the entire process and approved the consensus recommendations.

Grounding on the pre-meeting survey results, the experts subsequently formulated individualized treatment plans for endometriosis according to age group and their corresponding treatment goals, and the type of endometriosis. Additionally, they provided guidance on monitoring strategies for both the general population and subgroups with specific concerns pertinent to dienogest treatment. These recommendations were specifically tailored for obstetrician-gynecologists or other healthcare providers managing endometriosis patients undergoing extended dienogest treatment.

The pre-meeting survey revealed that ovarian endometriosis (OMA) and adenomyosis, commonly referred to as endometriosis of the uterus, are among the most frequently encountered and treated types of endometriosis. Most experts prescribed dienogest for their patients with a treatment duration extending beyond two years. Notably, clinicians commonly observed that those with adenomyosis and individuals in their 30s–40s, often require longer treatment durations. Based on the experts' collective clinical experience, symptom management and mitigating recurrence emerged as the two most important considerations determining the patient's treatment continuity. Some experts suggested that ovarian function preservation could serve as a motivating factor for patients to continue dienogest treatment.

The experts recommend dienogest as the first-line treatment for symptomatic endometriosis patients unless surgery is required. In cases where patients require surgery, dienogest is recommended to be continued as maintenance hormone therapy post-surgery [4–6]. An observational study found that patients receiving hormonal therapy before and after surgery had significantly lower reoperation rates due to recurrence compared to those receiving hormonal therapy only after their first surgery [5]. Presently, the consensus among Taiwanese experts recommends a minimum of two years of dienogest administration to manage symptoms and

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Table 1
Proposed Management and Monitoring Plan of Patients with Endometriosis undergoing Long-Term Dienogest Therapy.

Age group (years)	Main goal of long-term treatment	Long-term monitoring plan
12–18	Pain management and preservation of normal BMD	Standard monitoring[a]
19–29	Primary goal: Pain management Secondary goal: Preservation of fertility	Standard monitoring[a]
30–40	Preservation of ovarian function in patients planning to conceive	Standard monitoring[a]
>40	Sustained treatment until menopause	Standard monitoring, plus breast cancer screening. For patients <45 years, breast ultrasound is recommended over mammograms

BMD, bone mineral density; E2, estradiol.
[a] Standard monitoring includes ultrasound examinations every 3–6 months; relevant blood test every 6–12 months; and testing for serum E2 levels as necessary to maintain serum E2 levels between 40 and 60 pg/mL.

mitigate recurrence effectively. A comprehensive medical history and appropriate patient counseling are essential, along with early lifestyle modifications and health education on risk factors and preventive measures.

The experts advise a structured approach based on age group and treatment goals. For adolescents (aged12-18), the treatment goal is symptom control, with consideration on the benefit-risk ratio of dienogest 2 mg, particularly regarding risk of bone loss in this population. Given the importance of bone accretion during adolescence, whenever dienogest is prescribed, it should be paired with appropriate exercise and calcium supplementation [7]. For women in their 20s, the primary treatment objective is symptom management, particularly pain control and fertility preservation. On the other hand, for those aged between 30 and 40 years, fertility and reproductive plans should be carefully considered and discussed with the patients. Dienogest may be offered to preserve ovarian function in those not immediately seeking to conceive. Women over 40 years are typically motivated to receive treatment until menopause, warranting a more individualized assessment and monitoring. The strategy includes a comprehensive medical history before drug initiation, followed by regular monitoring. The treatment and the monitoring plan for long-term dienogest therapy are shown in Table 1.

Dienogest is recommended as the first-line medical therapy for all types of endometriosis, including OMA, adenomyosis, and deep infiltrating endometriosis (DIE) [2,4]. Despite its well-substantiated efficacy, the risk of bleeding remains a challenge [8], particularly in patients with adenomyosis. Based on the experts' clinical experience, bleeding usually occurs within the first three months of treatment. For persistent bleeding, hysteroscopy is advised to assess endometrial pathologies. If irregular shedding is observed, combining treatment with Mirena® (levonorgestrel-intrauterine device [IUD]) or a gonadotropin-releasing hormone (GnRH) agonist is advised [9]. Estrogen may be incorporated into the treatment if endometrial atrophy is present. For patients with DIE, medical therapy with dienogest may be initially considered, with surgery being an alternative if medical therapy is inadequate. Overall, a personalized approach, considering the type and severity of endometriosis, and individual patient factors and preferences, is essential for optimizing treatment outcomes.

According to published guidelines, follow-up and psychological support are crucial in women with confirmed endometriosis, especially those with OMA and DIE [10]. The Taiwanese experts recommend a monitoring regimen focused on monitoring disease progression and assessing drug response across all types of endometriosis and patient populations. The recommended monitoring plan includes ultrasound examinations every 3–6 months and relevant blood tests every 6–12 months. Serum estradiol (E2) levels may also be monitored to ensure the patient's reference range remains between 40 and 60 pg/mL. The recommended monitoring strategy and tests for endometriosis patients undergoing long-term dienogest treatment are detailed in Table 1.

The experts highlight that patient perception about the safety of long-term dienogest treatment may pose a significant challenge to extending its use beyond two years. On the contrary, a recent study from the National Taiwan University Hospital [11] found no increased risk of breast cancer with long-term dienogest therapy. Nevertheless, for patients in their 40s or those concerned about breast cancer risk, regular breast cancer screening is recommended following Taiwan's breast cancer prevention guidelines [12]. Additional breast examinations are advised for patients with palpable breast tumors, breast discomfort, or a family history of the disease [11]. Whenever concerns about venous thromboembolism (VTE) risk arise, blood coagulation studies may be conducted every six months during treatment initiation, followed by annual monitoring once the patient's condition stabilizes [13]. Notwithstanding, international guidelines underscored that progestogen-only pills, including dienogest, do not increase the risk of VTE [14]. A study also revealed that coagulation parameters remain within the normal range for patients undergoing dienogest therapy for up to 60 months [8].

Additionally, the experts recommend drug holidays [15] based on the patient's treatment response and desire to continue the therapy. If adequate pain control is not achieved after nine months, a three-month course of GnRH agonist therapy is advised [1], followed by the resumption of dienogest upon symptom improvement. This strategy may improve patient adherence and treatment outcomes. Furthermore, cyclic administration of dienogest is also suggested to manage bleeding during treatment [16].

In summary, the experts propose strategies for the long-term use of dienogest in women with endometriosis and address the associated challenges. They also recommend comprehensive and individualized monitoring tailored to address patients' concerns across different age groups and endometriosis subtypes. This consensus will be updated as new data emerges.

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Conflicts of interest

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