


Review Article

# Diagnostic and Therapeutic Approach to Abnormal Uterine Bleeding in Women Using Etonogestrel Subdermal Implants

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## Abstract

Etonogestrel subdermal implants are widely used long-acting reversible contraceptives that provide highly effective pregnancy prevention through sustained hormonal release. The implant consists of a small flexible rod placed subdermally in the upper arm, designed to release etonogestrel continuously for up to three years. Its contraceptive effect is primarily mediated by suppression of ovulation through inhibition of the luteinizing hormone surge. Additional mechanisms include thickening of cervical mucus, which impairs sperm penetration, and structural and functional changes in the endometrium that reduce the likelihood of implantation. Despite their high contraceptive efficacy and favorable safety profile, menstrual bleeding alterations represent the most common adverse effect associated with this contraceptive method. Abnormal uterine bleeding in implant users can manifest as irregular bleeding, intermenstrual spotting, prolonged bleeding episodes, frequent bleeding, or amenorrhea. These patterns are highly variable and may evolve over time, particularly during the first months after implant insertion. The pathophysiology of implant-associated bleeding is multifactorial and involves progestin-induced endometrial atrophy, suppression of endometrial proliferation, stromal decidualization, and alterations in the endometrial microvasculature. Fragile blood vessels, disrupted angiogenesis, inflammatory cytokine activity, and altered matrix metalloproteinase expression

contribute to an imbalance between endometrial breakdown and repair processes, which promotes breakthrough bleeding. Clinical evaluation requires a systematic approach that includes detailed medical history, physical examination, and complementary diagnostic testing to exclude other potential causes of abnormal uterine bleeding. Management strategies focus on patient counseling, expectant management, and pharmacological interventions such as nonsteroidal anti-inflammatory drugs, combined hormonal contraceptives, oral progestins, or tranexamic acid. When bleeding persists despite treatment, implant removal and consideration of alternative contraceptive methods may be necessary. Appropriate counseling and individualized management are essential to improve patient satisfaction and continuation of the contraceptive method.

## Key words

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Abnormal uterine bleeding, etonogestrel implant, long-acting reversible contraception, irregular bleeding, endometrial alterations, contraceptive continuation.

## Introduction

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Abnormal uterine bleeding is defined as bleeding originating from the uterine corpus that is abnormal in volume, regularity, and/or timing. This condition has been the focus of updated clinical guidelines aimed at improving diagnostic accuracy and therapeutic decision-making in clinical practice [1]. Within reproductive health care, abnormal uterine bleeding represents a highly relevant clinical issue because it frequently prompts medical consultation and requires careful evaluation to determine its underlying causes. Beyond its clinical definition, abnormal uterine bleeding also has important consequences for patients' well-being. It significantly affects women's quality of life, producing physical discomfort as well as psychological stress that may impair daily functioning and overall health status [2]. Consequently, the management of abnormal uterine bleeding has become a common challenge in gynecological practice, requiring clinicians to maintain a comprehensive understanding of its possible etiologies as well as the therapeutic strategies available for its management [3].

Within this context, long-acting reversible contraception has emerged as an important strategy for preventing unintended pregnancies while providing reliable and sustained contraceptive protection. Long-acting reversible

contraceptive methods, including subdermal implants, offer prolonged contraceptive efficacy with minimal need for user maintenance, which contributes to improved adherence and reduced rates of unintended pregnancy. Among these methods, etonogestrel-releasing implants have demonstrated particularly high contraceptive effectiveness, with a reported failure rate of only four pregnancies per one thousand women over a five-year period. As a result, the use of these implants has expanded globally and continues to gain acceptance as a highly effective contraceptive option [3]. Despite these advantages, the use of subdermal implants is not without challenges. One of the most frequently reported adverse effects associated with these devices is irregular uterine bleeding, which has been identified as a leading cause of method discontinuation among users [4].

Alterations in menstrual patterns are therefore a common occurrence among women using etonogestrel subdermal implants. In many cases, these changes manifest as irregular bleeding episodes, which represent the most frequently reported adverse effect associated with this contraceptive method [5]. Although these bleeding patterns are generally not associated with serious pathology, they can have a substantial impact on patient satisfaction and on the continuation of the contraceptive method. Irregular bleeding frequently generates concern among users and may lead to dissatisfaction,

ultimately contributing to lower continuation rates and premature discontinuation of the implant [4]. For this reason, effective management strategies are essential to address these symptoms and to support continued contraceptive use when appropriate. Structured diagnostic and therapeutic approaches have therefore been explored, including the use of progestins such as desogestrel to regulate bleeding patterns and provide endometrial protection in women experiencing implant-associated bleeding disturbances [6].

Recent advances in research have also begun to explore the biological mechanisms underlying bleeding variability among implant users. Gene expression studies have identified specific molecular patterns that may be associated with unfavorable bleeding profiles. For example, lower expression of the chemokine CXCL1 has been linked to more problematic bleeding patterns, suggesting that molecular markers may eventually serve as potential predictors of bleeding responses in women using hormonal implants [5]. These findings highlight the growing interest in identifying biological predictors that could guide individualized contraceptive counseling and management strategies.

In addition to pharmacological approaches aimed at managing implant-related bleeding, alternative contraceptive options have also been considered for patients who experience persistent or unacceptable symptoms. Among these alternatives, the levonorgestrel-releasing intrauterine system has demonstrated effectiveness in the management of abnormal uterine bleeding and may represent a viable option for individuals who develop adverse bleeding effects with subdermal implants. The availability of different therapeutic and contraceptive strategies underscores the importance of individualized clinical assessment and shared decision-making in the management of abnormal uterine bleeding associated with hormonal contraceptive methods [7].

The objective of this article is to review the diagnostic and therapeutic approach to abnormal uterine bleeding in women using etonogestrel subdermal implants, analyzing its clinical context, underlying mechanisms, and management strategies in order to facilitate appropriate clinical evaluation, guide treatment decisions, and improve patient satisfaction and continuation of this contraceptive method.

## **Methodology**

This manuscript was developed as a structured narrative review aimed at providing an updated and clinically integrated analysis of abnormal uterine bleeding in women using etonogestrel subdermal implants, with particular emphasis on bleeding patterns, underlying mechanisms, diagnostic evaluation, and contemporary therapeutic strategies. The review was conducted in accordance with the SANRA (Scale for the Assessment of Narrative Review Articles) framework and followed a predefined methodological protocol established prior to literature screening. Given the variability of bleeding patterns, differences in clinical evaluation, and the heterogeneity of management approaches reported in the literature, a narrative interpretative synthesis was selected instead of quantitative pooling. This approach allowed the integration of pathophysiological, diagnostic, and therapeutic considerations into a coherent framework applicable to clinical practice. Particular attention was given to the mechanisms associated with implant-related bleeding, strategies to exclude other causes of abnormal uterine bleeding, and currently available medical treatments aimed at improving symptom control and continuation of the contraceptive method.

A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science to identify peer-reviewed articles published in English or Spanish between January 2020 and December 2026. The final search was performed in March 2026. This timeframe was selected to capture recent advances in the understanding of bleeding profiles associated with etonogestrel

implants, updated diagnostic recommendations for abnormal uterine bleeding, and emerging therapeutic interventions. Foundational studies were included when necessary to contextualize contraceptive pharmacology or the pathophysiological mechanisms involved. The search strategy combined MeSH and free-text terms using Boolean operators related to abnormal uterine bleeding, irregular bleeding, unscheduled bleeding, etonogestrel implant, subdermal contraceptive implant, long-acting reversible contraception, diagnosis, and treatment. Searches were conducted in titles, abstracts, and indexed subject headings to maximize sensitivity.

The initial search yielded 126 records. After removal of duplicates, 87 articles remained for title and abstract screening. Of these, 56 underwent full-text evaluation and 26 studies were included in the final synthesis. Study selection was performed independently by two authors, with disagreements resolved through discussion and consensus. Eligible studies included randomized controlled trials, observational cohorts, systematic reviews, meta-analyses, expert consensus statements, and contemporary international guidelines in gynecology and reproductive health. Studies involving reproductive-age women using etonogestrel subdermal implants were prioritized. Exclusion criteria included non-peer-reviewed publications, isolated case reports, editorials without outcome data, redundant datasets, and studies that did not address bleeding patterns, diagnostic evaluation, or therapeutic management in implant users.

Data extraction was performed using a standardized form. Extracted variables included study design, population characteristics, duration of implant use, reported bleeding patterns, diagnostic methods used to exclude alternative etiologies, therapeutic interventions, treatment response, continuation or discontinuation rates, and adverse events. The primary outcomes of interest were bleeding patterns, response to

medical management, and continuation of the contraceptive method. Methodological quality and internal validity were assessed narratively by considering study design, risk of bias, sample size, duration of follow-up, and consistency in outcome definitions. In cases of conflicting evidence, greater interpretative weight was assigned to higher-level evidence and guideline-supported recommendations.

Reference lists of included studies were manually screened to identify additional relevant publications. Because of its narrative design, this review may be subject to selection bias and does not provide pooled quantitative estimates. Artificial intelligence-based tools were used solely to assist in literature organization and structural coherence, while study selection, critical appraisal, synthesis, and final interpretation were conducted independently by the authors to preserve methodological rigor.

### **Etonogestrel subdermal implants: pharmacological foundations**

The etonogestrel implant is a small, flexible rod composed of ethylene vinyl acetate that measures approximately four centimeters in length and two millimeters in diameter. It is designed for subdermal placement in the upper arm and represents a discreet and long-acting contraceptive option that provides effective pregnancy prevention without requiring daily user adherence. The device is approved for up to three years of use and functions through the continuous release of etonogestrel into the bloodstream. This sustained hormonal release maintains stable circulating levels of the progestin and ensures consistent contraceptive efficacy throughout the approved duration of use [3].

The contraceptive effectiveness of the implant is primarily mediated through the inhibition of ovulation. Etonogestrel suppresses the mid-cycle surge of luteinizing hormone that is necessary for ovulation to occur, thereby preventing the release of an oocyte and effectively blocking the

possibility of fertilization. In addition to suppressing ovulation, the implant exerts several complementary mechanisms that further enhance contraceptive protection. One of these mechanisms involves the thickening of cervical mucus, which creates a physical barrier that limits sperm penetration into the uterine cavity. At the same time, etonogestrel induces structural and functional alterations within the endometrium, which reduce the likelihood of successful implantation should fertilization occur [8].

Following insertion of the implant, etonogestrel is systemically absorbed into the bloodstream and maintains effective plasma concentrations over time. The device releases the hormone gradually, allowing for sustained contraceptive action during the entire period of approved use [3]. However, the pharmacokinetic response to etonogestrel may vary among individuals, reflecting differences in metabolism, hormonal sensitivity, and endometrial response. This interindividual variability can influence both contraceptive effectiveness and the occurrence of adverse effects, including abnormal uterine bleeding [4, 5].

Although the etonogestrel implant is widely recognized for its high contraceptive efficacy, its use is not free from clinical challenges. One of the most significant adverse effects associated with this contraceptive method is abnormal uterine bleeding, which may lead some patients to request early removal of the device. Recent studies have suggested that molecular mechanisms may contribute to this variability in bleeding patterns. Alterations in gene expression have been associated with unfavorable bleeding outcomes, including lower expression of CXCL1 and higher expression of BCL6 and BMP6, findings that highlight potential biological factors involved in implant-related bleeding disturbances [5].

### **Definition and bleeding patterns associated with the implant**

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Abnormal uterine bleeding is defined as uterine bleeding that deviates from normal menstrual cycles in terms of frequency, duration, and volume. This clinical entity encompasses several alterations in menstrual patterns, including heavy menstrual bleeding, which is typically defined as blood loss exceeding 80 milliliters per menstrual cycle [9]. The characterization of abnormal uterine bleeding relies on established parameters that define normal menstruation. Under physiological conditions, menstrual cycles usually occur every 21 to 35 days, last between 4 and 7 days, and involve an average blood loss of approximately 30 to 40 milliliters per cycle. Abnormal uterine bleeding is therefore diagnosed when these parameters are exceeded or when menstrual bleeding becomes irregular in timing or volume. In contrast to normal menstrual bleeding, which is generally predictable and consistent, abnormal uterine bleeding tends to be unpredictable and may significantly affect a woman's quality of life and daily functioning [1, 10].

Among women using etonogestrel subdermal implants, alterations in menstrual bleeding patterns are frequently reported. One of the most common manifestations is irregular bleeding, characterized by unpredictable bleeding episodes that may cause concern and discomfort among users [5]. In addition to irregular bleeding, intermenstrual spotting is commonly observed and often contributes to the perception of persistent or abnormal bleeding between menstrual periods. Some users may also experience prolonged bleeding episodes, in which bleeding persists for an extended duration, a pattern that may ultimately contribute to dissatisfaction with the contraceptive method and lead to discontinuation of the implant [11]. Increased frequency of bleeding episodes has also been reported, representing another pattern of menstrual disturbance among implant users [5]. Conversely, a proportion of women develop amenorrhea during implant use. In adolescent populations, for example, studies have reported that approximately 29 percent of users were

amenorrheic twelve months after implant placement [12].

The evolution of bleeding patterns among implant users may change over time. During the initial months following implant insertion, menstrual bleeding patterns are often highly variable. Some individuals experience unfavorable bleeding profiles during this early period, which may be associated with underlying molecular mechanisms such as changes in gene expression. With continued use, some women may experience a stabilization of their menstrual patterns; however, this stabilization does not occur uniformly in all users [5]. Overall, there is considerable interindividual variability in the way bleeding patterns develop during implant use. This variability may be influenced by several factors, including obesity and prior contraceptive exposure, both of which have been associated with differences in bleeding outcomes among implant users [12]).

### **Epidemiology and associated factors**

Irregular bleeding represents one of the most frequently reported adverse effects among users of etonogestrel subdermal implants. Abnormal menstrual patterns are consistently described in clinical studies as the most common side effect associated with this contraceptive method and constitute an important factor contributing to discontinuation in some patients. Although the implant provides highly effective and long-acting contraception, its influence on menstrual bleeding patterns varies considerably across individuals. Clinical studies have demonstrated substantial variability in bleeding outcomes, with some women experiencing amenorrhea while others report frequent or prolonged bleeding episodes during implant use [4, 12]. In addition, bleeding patterns may evolve over time. Some users initially present with unfavorable bleeding profiles during the early months following insertion, whereas in other cases these patterns may stabilize or persist throughout the duration of implant use [5].

These bleeding alterations have important implications for contraceptive continuation. Irregular bleeding is widely recognized as a major reason for early implant removal, with abnormal uterine bleeding consistently reported as the most common side effect leading to discontinuation of the device [13]. Patient satisfaction with the implant is closely related to the expectations established prior to insertion. When women are adequately informed about the possibility of irregular bleeding and other menstrual changes, they are more likely to tolerate these alterations and continue using the method [14]. Consequently, effective counseling prior to implant placement plays a critical role in preparing patients for potential bleeding changes. Adequate pre-insertion counseling has been shown to improve acceptance of bleeding variability, enhance continuation rates, and increase overall satisfaction with the contraceptive method [11].

Several factors may predispose individuals to bleeding patterns during implant use. Age and reproductive characteristics appear to influence bleeding outcomes, with younger women sometimes demonstrating different bleeding profiles and discontinuation patterns compared with adult populations. For example, adolescents have been reported to exhibit different rates of implant discontinuation compared with older women [13]. Previous menstrual history also appears to play a role in determining bleeding patterns after implant insertion. Women who experienced amenorrhea or irregular cycles prior to implant placement may be more likely to develop similar menstrual alterations following initiation of the method. In addition, body mass index has been associated with variations in bleeding patterns. Evidence suggests that obesity may increase the likelihood of amenorrhea among implant users, indicating that metabolic factors may influence hormonal responses and endometrial behavior [12]. Beyond these clinical characteristics, individual variability in endometrial response to progestins also contributes to differences in bleeding outcomes.

Recent research has identified specific patterns of gene expression that may be associated with unfavorable bleeding profiles, suggesting that biological mechanisms at the molecular level may partially explain the heterogeneity observed among implant users [5].

### **Pathophysiology of etonogestrel-associated uterine bleeding**

Etonogestrel induces several endometrial alterations that contribute to the development of abnormal uterine bleeding in implant users. One of the principal effects involves the induction of endometrial atrophy, a condition characterized by thinning of the endometrial lining. This atrophic endometrium lacks the structural stability typically required for coordinated menstrual shedding, which may result in irregular or unpredictable bleeding episodes [1]. In addition to promoting endometrial thinning, progestins such as etonogestrel suppress endometrial proliferation by inhibiting the proliferative effects of estrogen. As a result, the endometrial lining becomes less robust and more susceptible to irregular bleeding patterns [5]. Progestin exposure also produces structural changes within the endometrial stroma. These alterations include decidualization of stromal cells and modifications in their secretory profile, processes that influence local endometrial physiology and may further contribute to alterations in bleeding patterns [15].

Beyond these structural changes, etonogestrel also affects the endometrial microvasculature. One of the mechanisms involved is the alteration of angiogenesis, which leads to the development of immature and fragile blood vessels within the endometrium. These vascular changes have been identified as an important factor in the pathogenesis of abnormal uterine bleeding associated with progestin-containing contraceptives. The fragility of the microvascular network increases the susceptibility of these vessels to rupture, thereby raising the likelihood of microhemorrhages within the endometrial tissue. The coexistence of fragile vessels and

disrupted angiogenic processes ultimately promotes the occurrence of microhemorrhages, which represent a direct mechanism underlying breakthrough bleeding among users of etonogestrel implants [15, 16].

Inflammatory mediators and processes involved in tissue remodeling also play a role in the development of abnormal uterine bleeding in this context. Progestins can enhance the local production of inflammatory cytokines within the endometrium, including interleukin 8, thereby contributing to a proinflammatory microenvironment that may exacerbate bleeding tendencies [15]. At the same time, the activity of matrix metalloproteinases is modulated by progestin exposure. These enzymes participate in extracellular matrix degradation and tissue remodeling, and their altered activity may disrupt the balance between endometrial breakdown and repair processes. When these regulatory mechanisms become dysregulated, the normal processes responsible for endometrial repair may be impaired, resulting in a persistent imbalance between tissue injury and regeneration. This disruption can ultimately contribute to ongoing or recurrent bleeding disturbances in women using etonogestrel implants [17].

### **Clinical evaluation and diagnostic assessment**

The clinical evaluation of abnormal uterine bleeding in women using etonogestrel implants begins with a detailed and targeted medical history. Careful assessment of the onset, duration, and pattern of bleeding is essential, as these characteristics can provide important clues regarding the underlying cause of the bleeding. Abnormal bleeding patterns may reflect hormonal disturbances or the presence of structural abnormalities within the uterus, making this initial assessment a key component of the diagnostic process [1, 18]. In addition, determining the timing of bleeding in relation to implant insertion is particularly relevant. Bleeding that occurs shortly after insertion may represent an expected early side effect of the

contraceptive method, whereas persistent or late-onset bleeding may suggest other contributing factors that warrant further evaluation [5]. A comprehensive gynecological and obstetric history is also necessary, including information on previous menstrual patterns, pregnancies, and prior gynecological conditions, as these factors may help identify potential causes of abnormal uterine bleeding [1]. Furthermore, reviewing the use of concomitant medications is important because certain drugs may interact with hormonal contraceptives and influence bleeding patterns in implant users [3].

Following the clinical history, a thorough physical examination should be performed. General clinical evaluation may help identify systemic conditions that can contribute to abnormal uterine bleeding, including endocrine disorders such as thyroid dysfunction [18]. Particular attention should also be given to the assessment of signs of anemia, since prolonged or heavy bleeding may lead to iron deficiency and associated clinical manifestations. A gynecological examination, including pelvic evaluation, is necessary to detect structural abnormalities that may contribute to bleeding, such as uterine fibroids or endometrial polyps [19, 20]. In women using subdermal implants, verification of correct implant placement is also recommended in order to exclude mechanical issues related to device positioning that could potentially influence bleeding patterns [3].

Complementary diagnostic evaluation may be required to further clarify the cause of abnormal bleeding. Pregnancy testing is an essential initial step in order to exclude pregnancy-related causes of bleeding, including ectopic pregnancy [21]. A complete blood count should also be performed to evaluate the degree of blood loss and identify the presence of anemia [19]. Imaging studies play an important role in the diagnostic workup as well. Transvaginal pelvic ultrasound is commonly used to evaluate the uterus and adnexa and can identify structural abnormalities such as fibroids or adenomyosis. In situations

where ultrasound findings are inconclusive, additional imaging modalities such as magnetic resonance imaging may be considered to provide further assessment of uterine structural pathology [18, 20].

The diagnostic evaluation must also consider a broad differential diagnosis. Pregnancy, whether intrauterine or ectopic, must always be excluded when evaluating abnormal uterine bleeding [21]. Structural uterine abnormalities, including endometrial polyps and uterine fibroids, represent common causes of abnormal bleeding and can generally be detected through imaging studies [19]. Gynecological infections should also be considered, as inflammatory processes may either cause bleeding directly or exacerbate existing bleeding patterns. In addition, endocrine disorders such as thyroid dysfunction can influence menstrual regulation and should be evaluated when clinically indicated [18].

### **Therapeutic management of abnormal uterine bleeding**

Counseling and expectant management represent essential components in the clinical management of abnormal uterine bleeding among women using etonogestrel implants. Patients should be appropriately educated about the potential changes in bleeding patterns associated with this contraceptive method. These changes may include irregular bleeding episodes or the development of amenorrhea, both of which are commonly observed during implant use. Providing clear information regarding these expected patterns allows patients to better understand the physiological effects of the implant, which can help manage expectations and reduce anxiety related to unexpected bleeding episodes. In addition to explaining possible bleeding patterns, clinicians should also discuss the natural course of these alterations over time. Some women experience irregular bleeding during the first months after implant insertion, but these disturbances may decrease or stabilize as the body adapts to the hormonal effects of the device. Regular clinical follow-up

is therefore recommended, particularly during the early phase of implant use, to monitor bleeding patterns and address any concerns or complications that may arise during this period [5].

When bleeding symptoms are persistent or clinically significant, pharmacological treatment may be considered. Nonsteroidal anti-inflammatory drugs represent one of the therapeutic options for the short-term management of bleeding episodes. These medications reduce bleeding by inhibiting prostaglandin synthesis, a mechanism involved in endometrial shedding and menstrual blood loss [22]. Another potential strategy involves the temporary use of combined hormonal contraceptives. These agents can promote stabilization of the endometrial lining and contribute to the regulation of bleeding patterns, particularly in women who experience pronounced bleeding irregularities during implant use. Additional therapeutic options include the administration of oral progestins, which can modulate the endometrial response to hormonal stimulation and may help reduce both the frequency and volume of bleeding episodes in implant users. Tranexamic acid may also be considered in selected cases of heavy bleeding. This antifibrinolytic agent reduces menstrual blood loss by inhibiting fibrin degradation and stabilizing clot formation within the endometrium [19, 22, 23].

### **Management of persistent or refractory bleeding**

Evaluation of the therapeutic response is an essential step in the management of abnormal uterine bleeding among women using etonogestrel implants. Continuous clinical monitoring of bleeding patterns allows clinicians to assess both the severity and frequency of bleeding episodes over time. This monitoring is important for determining whether the current therapeutic strategy is effective or whether adjustments to treatment are required [1, 10]. In addition to documenting the bleeding pattern

itself, assessment of symptom improvement should incorporate both subjective patient-reported outcomes and objective clinical findings. Improvements in bleeding regularity, reductions in bleeding volume, and resolution of associated complications such as anemia should be carefully evaluated and recorded as part of the clinical follow-up. When bleeding persists despite appropriate medical management, it may be necessary to reconsider the initial diagnostic evaluation. In such situations, further investigation may be warranted to exclude other potential etiologies of abnormal uterine bleeding, including structural abnormalities such as uterine fibroids or systemic conditions such as coagulation disorders [10, 19].

In cases where bleeding remains persistent or severe despite therapeutic interventions, removal of the implant may be considered. Clinical indications for implant removal include refractory bleeding that does not respond to medical treatment, as well as situations in which the patient prefers discontinuation or develops contraindications to continued use of the device [20, 24]. Decisions regarding implant removal should ideally be made through a process of shared decision-making between the clinician and the patient. This process involves discussing the potential benefits and limitations of continuing or discontinuing the implant, as well as reviewing alternative management strategies while considering the patient's preferences, reproductive goals, and lifestyle factors [19, 24]. When implant removal is ultimately performed, alternative contraceptive options should be discussed to ensure continued reproductive planning when desired. One possible alternative is the levonorgestrel-releasing intrauterine system, which has demonstrated effectiveness in the management of heavy menstrual bleeding and may represent a suitable contraceptive option for some women following implant removal [25, 26].

### **Conclusions**

Etonogestrel subdermal implants represent a highly effective long-acting contraceptive method whose pharmacological action is primarily mediated through ovulation suppression, cervical mucus thickening, and endometrial alterations that reduce the likelihood of implantation. Despite their high contraceptive efficacy and sustained hormonal release, their use is frequently associated with alterations in menstrual bleeding patterns, reflecting complex interactions between progestin-induced endometrial changes, microvascular alterations, inflammatory mediators, and individual biological variability.

Abnormal uterine bleeding in implant users is a multifactorial condition that requires a structured clinical approach involving careful history taking, physical examination, appropriate diagnostic evaluation, and individualized therapeutic management. Early patient counseling, targeted pharmacological interventions, and continuous clinical monitoring are essential strategies to improve symptom control, enhance patient satisfaction, and reduce premature discontinuation of the contraceptive method.

## References

1. Gynecologic Endocrinology Subgroup, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association. Guideline on diagnosis and treatment of abnormal uterine bleeding: 2022 revisions. *Zhonghua Fu Chan Ke Za Zhi* [Internet]. 2022;57(7):481–90. Available from: <http://dx.doi.org/10.3760/cma.j.cn11214-1-20220421-00258>
2. Yu L, Janga B, McAlister R, Jeffe DB, Sonn T. Disparities in treatment decisions for abnormal uterine bleeding. *Journal of Women S Health* [Internet]. 2021 Feb 12;30(10):1519–25. Available from: <https://doi.org/10.1089/jwh.2020.8800>
3. Bahamondes L, Bahamondes MV, Juliato CRT. Subdermal contraceptive implants. *Best Practice & Research Clinical Obstetrics & Gynaecology* [Internet]. 2025 Mar 23;100:102604. Available from: <https://doi.org/10.1016/j.bpobgyn.2025.102604>
4. Moray K, Chaurasia H, Sachin O, Joshi B. A systematic review on clinical effectiveness, side-effect profile and meta-analysis on continuation rate of etonogestrel contraceptive implant. *Reproductive Health* [Internet]. 2021 Jan 6;18(1):4. Available from: <https://doi.org/10.1186/s12978-020-01054-y>
5. Torelli FR, Rodrigues-Peres RM, Monteiro I, Lopes-Cendes I, Bahamondes L, Juliato CRT. Gene expression associated with unfavorable vaginal bleeding in women using the etonogestrel subdermal contraceptive implant: a prospective study. *Scientific Reports* [Internet]. 2024 May 14;14(1):11062. Available from: <https://doi.org/10.1038/s41598-024-61751-7>
6. Soontrapa N, Rattanachaiyanont M, Warnnissorn M, Wongwananuruk T, Indhavivadhana S, Tanmahasamut P, et al. The effectiveness of desogestrel for endometrial protection in women with abnormal uterine bleeding-ovulatory dysfunction: a non-inferiority randomized controlled trial. *Scientific Reports* [Internet]. 2022 Jan 31;12(1):1662. Available from: <https://doi.org/10.1038/s41598-022-05578-0>
7. Bianchi P, Guo SW, Habiba M, Benagiano G. Utility of the Levonorgestrel-Releasing Intrauterine System in the treatment of Abnormal uterine bleeding and dysmenorrhea: A Narrative review. *Journal of Clinical Medicine* [Internet]. 2022 Oct

- 1;11(19):5836. Available from: <https://doi.org/10.3390/jcm11195836>
8. Gawron LM, Kaiser JE, Gero A, Sanders JN, Johnstone EB, Turok DK. Pharmacodynamic evaluation of the etonogestrel contraceptive implant initiated midcycle with and without ulipristal acetate: An exploratory study. *Contraception* [Internet]. 2024 Jan 20;132:110370. Available from: <https://doi.org/10.1016/j.contraception.2024.110370>
  9. James AH, James PD. What do we know about why women bleed and what do we not know? *Journal of Thrombosis and Haemostasis* [Internet]. 2023 Sep 12;22(2):315–22. Available from: <https://doi.org/10.1016/j.jth.2023.08.034>
  10. Jain V, Chodankar RR, Maybin JA, Critchley HOD. Uterine bleeding: how understanding endometrial physiology underpins menstrual health. *Nature Reviews Endocrinology* [Internet]. 2022 Feb 8;18(5):290–308. Available from: <https://doi.org/10.1038/s41574-021-00629-4>
  11. Sinthuchai N, Tapanwong N, Apirakviriya C, Pohthipornthawat N, Santibenchakul S, Jaisamrarn U. Effect of a single dose of a combination injectable contraceptive for treatment of bothersome uterine bleeding in contraceptive implant(s) users: A randomized double-blind placebo-controlled trial. *Contraception* [Internet]. 2023 Dec 14;131:110354. Available from: <https://doi.org/10.1016/j.contraception.2023.110354>
  12. Tsevat D, Mercier R, Bernheimer C, Lin S, Schwartz B. Amenorrhea in adolescents using the etonogestrel contraceptive implant. *Contraception* [Internet]. 2024 Feb 22;133:110413. Available from: <https://doi.org/10.1016/j.contraception.2024.110413>
  13. Chandi C, Uaamnuichai S, Phutrakool P, Wongwikrom W, Puapornpong P, Kaewthawon N, et al. Risk of early etonogestrel and levonorgestrel implant discontinuation in adolescents and adults. *BMC Public Health* [Internet]. 2024 Nov 18;24(1):3204. Available from: <http://dx.doi.org/10.1186/s12889-024-20681-9>
  14. Archer DF, Mansour D, Foidart JM. Bleeding Patterns of Oral Contraceptives with a Cyclic Dosing Regimen: An Overview. *Journal of Clinical Medicine* [Internet]. 2022 Aug 8;11(15):4634. Available from: <https://doi.org/10.3390/jcm11154634>
  15. Arlier S, Kayisli UA, Semerci N, Ozmen A, Larsen K, Schatz F, et al. Enhanced ZBTB16 levels by Progestin-Only contraceptives induces decidualization and inflammation. *International Journal of Molecular Sciences* [Internet]. 2023 Jun 23;24(13):10532. Available from: <https://doi.org/10.3390/ijms241310532>
  16. Middelkoop M, Don E, Hehenkamp W, Polman N, Griffioen AW, Huirne J a F. Angiogenesis in abnormal uterine bleeding: a narrative review. *Human Reproduction Update* [Internet]. 2023 Feb 28;29(4):457–85. Available from: <https://doi.org/10.1093/humupd/dmad004>
  17. Irigoyen M, Castagnola L, Gori S, Grasso E, Gnocchi D, Cattaneo A, et al. P-486 Alterations in endometrial programming lead to recurrent in vitro fertilization failures. *Human Reproduction* [Internet]. 2023 Jun 1;38(Supplement\_1). Available from: <http://dx.doi.org/10.1093/humrep/dead093.829>
  18. Greben S, Lee RK. Patient-Friendly summary of the ACR appropriateness Criteria: Abnormal uterine bleeding. *Journal of the American College of*

- Radiology [Internet]. 2022 Aug 20;19(11):e51. Available from: <https://doi.org/10.1016/j.jacr.2022.05.034>
19. Vannuccini S, Petraglia F, Carmona F, Calaf J, Chapron C. The modern management of uterine fibroids-related abnormal uterine bleeding. *Fertility and Sterility* [Internet]. 2024 May 8;122(1):20–30. Available from: <https://doi.org/10.1016/j.fertnstert.2024.04.041>
20. Santulli P, Vannuccini S, Bourdon M, Chapron C, Petraglia F. Adenomyosis: the missed disease. *Reproductive BioMedicine Online* [Internet]. 2025 Apr 1;50(4):104837. Available from: <https://doi.org/10.1016/j.rbmo.2025.104837>
21. Trostian B, McCloughen A, Shaban RZ, Curtis K. What assessment, intervention and diagnostics should women with early pregnancy bleeding receive in the emergency department and when? A scoping review and synthesis of evidence. *Australasian Emergency Care* [Internet]. 2024 Oct 15;28(1):1–11. Available from: <https://doi.org/10.1016/j.auec.2024.09.006>
22. Rodriguez MB, Dias S, Jordan V, Lethaby A, Lensen SF, Wise MR, et al. Interventions for heavy menstrual bleeding; overview of Cochrane reviews and network meta-analysis. *Cochrane Database of Systematic Reviews* [Internet]. 2022 May 31;2023(2):CD013180. Available from: <https://doi.org/10.1002/14651858.cd013180.pub2>
23. Kuthiala S, Grabell J, Relke N, Hopman WM, Silva M, Jamieson MA, et al. Management of heavy menstrual bleeding in women with bleeding disorders in a tertiary care center. *Research and Practice in Thrombosis and Haemostasis* [Internet]. 2023 Mar 1;7(3):100119. Available from: <https://doi.org/10.1016/j.rpth.2023.100119>
24. Azenkot T, Schwarz EB. Special considerations for women of reproductive age on anticoagulation. *Journal of General Internal Medicine* [Internet]. 2022 May 31;37(11):2803–10. Available from: <https://doi.org/10.1007/s11606-022-07528-y>
25. Chen S, Liu J, Peng S, Zheng Y. LNG-IUS vs. medical treatments for women with heavy menstrual bleeding: A systematic review and meta-analysis. *Frontiers in Medicine* [Internet]. 2022 Aug 25;9:948709. Available from: <https://doi.org/10.3389/fmed.2022.948709>
26. Oderkerk TJ, Van De Kar MMA, Van Der Zanden CHM, Geomini PMAJ, Herman MC, Bongers MY. The combined use of endometrial ablation or resection and levonorgestrel-releasing intrauterine system in women with heavy menstrual bleeding: A systematic review. *Acta Obstetrica Et Gynecologica Scandinavica* [Internet]. 2021 Jun 24;100(10):1779–87. Available from: <https://doi.org/10.1111/aogs.14219>